THE EFFECT OF EXERCISE-INDUCED FATIGUE AND ECCENTRIC MUSCLE DAMAGE ON KINAESTHESIA

by

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Abstract

The senses of position and movement are known collectively as kinaesthesia. Muscle spindles are length sensitive receptors, considered pivotal to these senses. Mechanical muscle vibration artificially stimulates muscle spindles and this can lead to illusory limb postures and movements, thereby disrupting kinaesthesia. Exercise induced fatigue also impairs kinaesthesia and this impairment persists if the exercise involves lengthening contractions that create eccentric muscle damage. It is not entirely clear why these lasting impairments occur. Using a targeted movement sequence with the unseen arm (a task that relies heavily on muscle spindles), this study utilized a novel paradigm to investigate task performance both before and after an eccentric based exercise protocol. By investigating the influence of vibration applied to the involved musculature, the results provide insight into how exercise acutely disrupts kinaesthesia. It was found that mechanical muscle vibration created a robust effect on task accuracy at all points during the study, causing participants to undershoot the targets (as previously described in the literature). The effects of exercise also caused a consistent error in task performance, but did not appear to influence the effect of vibration. This suggests that the nervous system continues to rely heavily on muscle spindles, even when they reside in a muscle exposed to damaging eccentric contractions.

Lay Summary

The ability to sense where our limbs are in space and how they are moving is vitally important for normal interaction with the world around us. The main goal of this thesis was to broaden our knowledge of the negative effects that exercise and fatigue can have on our sense of limb position and movement. The findings from this thesis could be useful when designing strategies to reduce the incidence of injuries in sport and recreation and when applying fall prevention programs in the elderly population.

Preface

Dr. J. Timothy Inglis and myself conceptualized the study in this thesis, with later contributions and development from Dr. Romeo Chua and Dr. Mark Carpenter. The study was approved by the University of British Columbia's Research Ethics Board [certificate #H16-00874]. Dr. Romeo Chua and Dr. Ryan Peters designed the software used during data collection and analysis. I completed all data collection with assistance from Damian Manzone and Gregg Eschelmuller. Damian Manzone also created the main figure used to depict the experimental setup and assisted me in analysing the data with Dr. Romeo Chua.

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List of Abbreviations

CNS:	Central Nervous System
DOMS:	Delayed Onset Muscle Soreness
GTO:	Golgi Tendon Organ
MVC:	Maximal Voluntary Contraction
SD:	Standard Deviation
SEM:	Standard Error of the Mean
TTDPM:	Threshold To Detection of Passive Movement

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Dedication

To my Mother and Father, for your enduring love and support, late night calls and timely supportive messages.

Chapter 1: Introduction

Human movement enables us to interact with the world and our fellow human beings. For most individuals, it is an unheralded right of life. But a simple task such as reaching for a glass of water involves the integration of multiple systems, including a large reliance on sensory feedback. The visual system identifies the object and how far away it is, while muscle and joint receptors help control the trajectory of the limb towards the object and skin receptors confirm contact with the glass and regulate the grip as the senses of heaviness and effort contribute to how to lift the glass. This is to name but a few of the processes involved. This simple task requires motion at multiple joints, as do more complex tasks or *movement sequences*, such as throwing a Frisbee. These movement sequences rely heavily on our *proprioceptive* or *kinaesthetic* awareness.

The **overall objective** of this thesis was to further our understanding of the short-term negative effects that exercise-induced fatigue and eccentric muscle damage can have on kinaesthesia and provide some insight into the possible source of the disturbance. Aside from implications in sport and leisure, there are potential ramifications in fall prevention initiatives for the elderly, where the goal is often to improve kinaesthetic awareness via balance and strength training (Gschwind, Kressig, Lacroix, Muehlbauer, Pfenninger & Granacher, 2013; Rogers, Page & Takeshima, 2013). Exercises implemented in a strength-training program could be detrimental to kinaesthesia if the exercise is unaccustomed or excessive. Therefore, if exercise is indeed medicine (Tipton, 2014), the prescription, dosage and application of the exercise must be considered carefully.

In this first Chapter, I present background information and a review of the relevant literature to lay the foundation for this thesis. I introduce definitions for proprioception and kinaesthesia, and cover some of the various mechanisms that contribute to the latter, including some historical context and a review of our present understanding. I then cover the muscle spindle in greater detail, for it is of primary interest to this thesis, owing to its response to mechanical muscle vibration and involvement in this study. Following this, I introduce a movement sequence task that has previously been used to assess the senses of limb position and movement, before covering the effects that exercise has on these senses. The end of this chapter summarizes the objectives and hypotheses of this study. Chapter 2 provides detailed coverage of the experimental setup and procedures. Finally, Chapter 3 presents the results of the study and a discussion of the findings.

> *"…we are consciously aware of the position of our hands, but we do not perceive the information from individual joints and muscles, we simply perceive the position of the hand. This emphasises that proprioceptive information is combined into a synthesised representation of the body, and we perceive that representation which is updated continuously by sensory information…"* – Walsh, Taylor & Gandevia, 2014, p.128.

1.1 Proprioception and Kinaesthesia

The term *proprioception* refers to conscious sensations generated by the body's own actions and includes the sense of movement and limb position, specifically known as *kinaesthesia* (Proske & Gandevia, 2012). These terms are often wrongly used interchangeably. *Kinaesthesia* can be further divided into two distinct senses, one of movement and one of position. Specifically, it is "the ability to detect, without visual input, the spatial position and/or movement of limbs in relation to the rest of the body" (Fortier & Basset, 2012, p.796). Due to the focus of the present study and the distinction the term affords, *kinaesthesia* will be used throughout this thesis.

1.1.1 Position Sense and Movement Sense are Separate Entities

The concept of a position and movement sense dates back as far as 1833 (Bell, 1833) and possibly further (Walsh et al., 2014). The senses of position and movement are now accepted as separate entities (Allen & Proske 2006; Proske, Schaible & Schmidt, 1988; Proske & Gandevia, 2012), having originally been considered a single sense (Bastian, 1880). Walsh et al. (2014, p.133) provided a clear definition of the two when stating, "joint position sense is concerned with signaling the static position of the limbs, whereas movement sense is more concerned with signaling velocity." Whilst it is difficult to study the two individually due to movement sense being dependent on the degree of positional change (Gandevia, 1996), previous work has attempted to dissociate them. It had also been assumed that altering the velocity of a movement would influence movement sense without effecting position sense (Clark, Burgess, Chapin &

Lipscomb, 1985; Clark, Burgess & Chapin, 1986). On the contrary, it was later shown that changes in a joint's position could be perceived following very slow rotations of the joint without any overt sense of movement (Hobbs & Gandevia, 1985). In a task involving repetitive hand movements in the absence of vision, the direction and distance of the movements remain accurate, whilst the position of the hand drifts. This led to the conclusion that position and movement information are controlled by separate neural mechanisms (Brown, Rosenbaum & Sainburg, 2003). Finally, though muscle afferents contribute to conscious sensation of both position and movement (Goodwin, McCloskey & Matthews, 1972), later in this paper I explore thixotropy (a property of muscle tissue) and exercise-induced fatigue, both of which affect movement and position sense in different ways, again reinforcing the notion of two separate senses (Proske & Gandevia, 2012).

In a recent review, Proske (2015) put forward a further distinction, the notion that there exist two kinds of position sense; one concerned with the interrelationship between body parts and the other with monitoring the location of our body and limbs in space. He suggested that receptors in the periphery provide much of the information used to determine the interrelationship between body parts, whereas exteroceptors (i.e. vision, touch and hearing) inform our positioning in extrapersonal space.

1.2 Peripheral Sources of Kinaesthesia

The general view during the first half of the 19th Century was that signaling of muscle lengthening and contraction came from sensations obtained from the brain's outflow of motor impulses, a sensation of innervation (Müller, 1837). Sherrington (1900) argued against this view and proposed that muscular senses resulted from signals generated in the periphery (Proske, 2015).

We now know that receptors sensitive to mechanical and chemical stimuli are situated in our muscles, joints, tendons and skin. They are all potential sources of kinaesthetic input (Gandevia, 1996) and changes to the mechanical or chemical state of the structures they reside in will alter the afferent information they relay to the Central Nervous System (CNS). In healthy / non-clinical populations, information from single classes of receptors are never used in isolation; rather the CNS uses information coming from a combination of different receptors to resolve a task (Proske & Gandevia, 2012). I now explore some of these different receptors and the evidence of their contribution to kinaesthesia.

1.2.1 Cutaneous Receptors

"Cutaneous receptors embedded in a multilayered glove covering the skeleton are well placed to signal movement of the underlying skeleton" (Gandevia, 1996, p.139). Located in the non-hairy or glabrous skin, cutaneous receptors can be classified into four different subtypes based on their receptive field size (type 1 = small; type II = larger) and adaptation rate (slowly and rapidly adapting) (Johnson, 2001). Hairy skin also contains the same four classes of receptors, with an additional class of nonencapsulated hair-follicle receptors (McIntyre, Proske & Tracey, 1978).

The four receptors are grouped into two slowly adapting (SA) systems and two rapidly adapting (RA) systems. The SAI system allows us to perceive different shapes and textures, whilst the SAII system's sensitivity to skin stretch enables the detection of forces acting on the skin and changes of hand postures (Johnson, Yoshioka & Vega-Burmudez, 2000). The RA systems detect minute slippage between objects and the skin (Srinivasan, Whitehouse & LaMotte, 1990), making them critical to grip control and the RAII system is sensitive to high frequency vibrations, responding to distant events transmitted by objects held in the hand (Brisben, Hsiao & Johnson, 1999). The different systems respond to many of the same stimuli, making it difficult to isolate one class of receptor (Johnson et al., 2000). But as we will see in the next section, evidence has started to accumulate for a potential role for skin in kinaesthesia.

Microneurography recordings have demonstrated that slowly adapting cutaneous receptors can signal various joint configurations in the hand (Edin, 1992) and recordings during imposed ankle movements showed SAII's to be the most responsive of the four receptors (Aimonetti, Hospod, Roll & Ribot-Ciscar, 2007). I will now present some of the additional methods that have been used to explore skin's role in signaling joint position and movement.

Joint motion causes skin to stretch on one side of the joint and slacken on the other. As a result, mechanical skin stretch administered to the back of the hand can evoke illusory movements of the finger joints (Collins & Prochazka, 1996). This effect can also be created at the knee and elbow joints, though sensations of movement at these more proximal joints are stronger when combined with muscle receptor stimulation (Collins, Refshauge, Todd & Gandevia, 2005). Muscles that cross more than one joint have been shown to provide ambiguous signals for kinaesthesia (Sturnieks, Wright & Fitzpatrick, 2007). Because many movements in the fingers are transmitted via long tendons originating from muscles located in the forearm, signals from these muscle receptors may offer a poor representation of individual finger joint angle or motion. As a result, the CNS may prioritize information from skin receptors located around the finger joints to establish which joint is moving (Collins, Refshauge & Gandevia, 2000). A recent study found that manipulating skin stretch around the elbow joint by applying elastic sports tape influenced a targeted movement of the unseen hand (Kuling, Brenner & Smeets, 2016). Surprisingly, the movement shift corresponded to a more extended elbow angle, regardless of whether the inside or the outside of the elbow joint was taped. These studies demonstrate that skin stretch alone can signal the movement and the position of our joints.

Disturbing or blocking sensory feedback from cutaneous receptors can also hamper our kinaesthetic awareness, particularly in the hand. Thresholds to detection of passive joint movement significantly increase following experimentally-induced pain to the skin overlying the thumb (Weerakkody, Blouin, Taylor & Gandevia, 2008) and when cutaneous feedback is removed from the skin surrounding an anesthetized joint in the index finger, movement of the joint goes completely undetected (Edin & Johansson, 1995). These studies emphasize the importance of cutaneous receptors in the hand.

The four cutaneous afferent groups clearly serve distinct functions. Whilst the CNS likely builds a picture of tactile perception based on their combined signals, it has been suggested that two separate channels exist to process the incoming information from the SA and the RA afferents (Johnson, 2001). In their 2012 review of proprioception, Proske & Gandevia (2012) concluded that cutaneous receptors make a significant contribution to movement sensation at most joints, but are not the primary contributors to position sense at more proximal joints. Finally, though cutaneous receptors are largely considered to be proprioceptors, their ability to detect touch means they can also act as exteroceptors as we come in to contact with external objects in our surroundings (Proske, 2015). This attribute provides the CNS with another inference of limb position and movement information.

1.2.2 Tendon Organs

Golgi tendon organs (GTOs) are situated at both the musculotendinous junction and within the tendon itself (Barker, 1974). Their primary contribution to kinaesthesia comes from their ability to sense force and heaviness (Proske & Gandevia, 2012), yet they are also ambiguously sensitive to stretch (Fortier & Basset, 2012). Their location enables them to reliably monitor whole muscle tension (Gregory, Brockett, Morgan, Whitehead & Proske, 2002), with each receptor providing force levels from the muscle units it envelops (Houk & Henneman, 1967).

Tendon organs were originally believed to function as overload sensors that prevented a muscle being exposed to excessive levels of force (Brodal, 1981). They were also thought to be responsible for a reflex evident only in individuals with upper motor neuron lesions (Fulton & Pi-Suner, 1928). These theories were largely abandoned following work that showed GTOs were sensitive to activity in a single motor unit (Reinking, Stephens & Stuart, 1975; Houk & Henneman, 1967) and after recordings in felines demonstrated their different responses to a stretch or contraction when they were elicited reflexively (Cleland, Hayward & Rymer, 1990; Cleland & Rymer, 1990). Tendon organs are now regarded as the primary receptor for sensing force within a muscle (Walsh et al., 2014) and their sensitivity improves when the force is generated actively (from within the muscle) rather than passively (imposed upon the muscle from an external source) (Houk, Singer & Henneman, 1971; Jami, Petit, Proske & Zytnicki, 1985). It has also been suggested that they are more sensitive to shortening rather than lengthening active muscle tissue (Moore, 1984), leading some authors to refer to them as “contraction receptors” (Proske & Gandevia, 2012, p.1675). It has been estimated that every motor unit within a muscle is linked to at least one tendon organ (Proske, 1993), suggesting that when the input from several tendon organs are combined, they can signal whole muscle force (Prochazka & Gorassini, 1998; Mileusnic & Loeb, 2009). Despite these examples of GTOs’ signaling attributes, it appears that their role in sensing limb position and movement is somewhat limited.

Tendon organs can provide ambiguous information related to muscle stretch under certain conditions. Though generally unresponsive during muscle stretch in humans, they can discharge if a rapid stretch is applied whilst the muscle is contracting (al-Falahe, Nagaoka &

Vallbo, 1990). Mechanically, they are ill equipped to sense changes in muscle length, but their response to the increase in muscle tension that results from a stretch might assist in informing the CNS of changes in muscle length (Prochazka & Ellaway, 2012). Ultimately, the fact that they discharge during muscle contraction and not muscle lengthening (Appenteng & Prochazka, 1984) suggests that they are unreliable length sensors.

Kistemaker, Van Soest, Wong, Kurtzer and Gribble (2013) attribute the lesser-recognized role of GTOs in movement control theories to a lack of understanding of their function. Their paper presents some interesting observations about these receptors and their potential contributions to kinaesthesia. Recognizing that their main role is to signal the degree of tension in a muscle, they go on to state that GTOs also monitor the degree of tension in the tendon, a measure that could be used to provide an indication of tendon length. They propose that as muscles spindles (covered later in this chapter) cannot signal tendon length fluctuations that result from changes in muscle force, they are incapable of representing the entire length of the muscle-tendon complex and therefore cannot provide an accurate representation of joint angle. This was the case in a grasp task where the total muscle and tendon length was poorly represented by muscle spindle discharge alone, but well represented by the combined signals from tendon organs and muscle spindles (Dimitriou & Edin, 2008a). Kistemaker et al. (2013, p.1126) further proposed that this combined muscle spindle and GTO signal could be used for low-level feedback during postural and movement tasks. Anatomical findings seem to support this theory, as GTOs and muscle spindles are sometimes found in series with one another, forming “tendon organ-spindle dyads” (Marchand, Bridgman, Shumpert & Eldred, 1971; Richmond & Abrahams, 1975).

In summary, though originally deemed “overload sensors” (Brodal, 1981), GTOs were found to accurately code for muscle force throughout the entire range of a muscle’s contractile capability (Houk & Henneman, 1967). Each receptor senses the tension of the muscle fibres they envelop, meaning a population of GTOs can signal whole muscle tension levels, which is likely used to inform the sense of force and the sense of heaviness (covered later in this chapter) (Proske & Gandevia, 2012). GTOs are more sensitive to tension resulting from muscle contraction than from passive stretch (Houk et al., 1971), though there is evidence that they can signal the magnitude of stretch a muscle is under (Gregory et al., 2002). One group have postulated that during muscle contraction, their input is combined with that of muscle spindles to form a representation of total muscle and tendon length (Kistemaker et al., 2013), and this could then provide an accurate indication of joint angle, a key element of position sense (Dimitriou & Edin, 2008a).

1.2.3 Joint Receptors

Joint receptors reside in the joint capsule, ligaments and loose articular tissue (Newton, 1982). Much like its effect on skin, joint rotation causes the joint capsule to stretch on one side whilst it becomes compressed on the other (Proske & Gandevia, 2012). The two mechanoreceptors that signal this stretch are Ruffini-like endings, similar to the SAII endings in cutaneous receptors, and Pacinian Corpuscles, which respond to compression of the capsule (Grigg, 1994). The present role that joint receptors are thought to play in kinaesthesia differs slightly from that with which they were originally attributed.

Following recordings from feline preparations (Boyd & Roberts, 1953; Skoglund, 1956), joint receptors were viewed as mid-range position sensors, playing a pivotal role in kinaesthesia. Two groups later found them to be unresponsive through the mid-range (Burgess & Clark, 1969; Tracey, 1979), with most receptors only firing at the two extremes of the joint's available motion (Burgess & Clark, 1969). Studies supporting the notion that they signaled position over the full range (Godwin-Austen 1969; Zalkind, 1971; Ferrell, 1980) were confounded by the fact that these recordings may have been from other muscle-based receptors (Clark et al., 1985; Gregory, McIntyre & Proske, 1989; McIntyre et al., 1978). Further clarity of their role was provided after recordings from a different nerve in the feline showed very few afferents firing from mid-range joint movement (Dorn, Schaible & Schmidt, 1985). Based on this work and considering the likelihood that the original feline recordings came from muscle-based receptors, it is now widely accepted that joint receptors do not play a significant role in position sense (Proske & Gandevia, 2012). So, what role do these receptors play in kinaesthesia?

When studying the various kinaesthetic sensors, it is difficult to isolate one group of receptors (be it skin, joint or muscle based) as many respond to the same stimuli and their afferents run in common peripheral nerves. An anatomical anomaly that occurs in the hand provides the opportunity to remove sensory input from muscle afferents. To take advantage of this, the index, ring and little fingers are held extended and the middle finger is flexed, this disengages the muscles that cross the middles finger's distal interphalangeal (IP) joint and leaves only skin and joint afferents to signal the joint's position and movement (Gandevia & McCloskey, 1976). Gandevia and McCloskey (1976) used this hand posture to show that subjects were poor at detecting slow and small-imposed movements at the distal IP joint in the absence of muscle afferent input. It was later demonstrated that under the opposite conditions, with muscle afferents intact but skin and joint inputs blocked, detection levels were worse than when all inputs were available (Gandevia, Hall, McCloskey & Potter, 1983), suggesting that skin and joint provided important sensory feedback in this scenario. Further work at the proximal IP joint found that position sense was unaffected when skin and joint signals were removed via digital nerve blocks (Rymer & D'Almeida, 1980), but when these same experiments were recorded over a wider range, errors were reported near the extreme ranges (Ferrell & Smith, 1988), where the CNS may rely more heavily on joint receptors. At the distal IP joint, subjects' ability to detect the direction of imposed movements decreased when the joint was anaesthetized, though there was some improvement when the joint was injected to increase intra-capsular pressure (Ferrell, Gandevia & McCloskey, 1987), suggesting joint receptors hold some level of importance in signaling movement sense. These same results however, could not be replicated when the study was later repeated (Clark, Grigg & Chapin, 1989).

Further evidence suggests that joint receptors provide ambiguous signals of joint movement. Intraneural electrical stimulation of joint receptor afferents showed some receptors can generate small sensations of joint movement. The same afferents discharged when the described movements were imposed back upon the joint (Macefield, Gandevia & Burke, 1990). Thus, the CNS would appear to receive movement information from joint receptors and unlike muscle-based receptors, the discharge from one afferent alone can cause sensation of movement. Despite this, their signal is still considered ambiguous as many joint receptors discharge when subjected to opposite directions of motion through two or three planes of movement (Macefield et al., 1990).

Ferrell, who had previously argued that joint receptors signaled joint position during the mid-range of movement (Ferrell, 1980), settled on the idea that they were best suited as limit detectors, providing positional information at the end ranges of movement (Ferrell, 1988), a role that had previously been suggested by another group (Burgess & Clark 1969; Clark & Burgess

1975). This role of limit detectors has some crossover with their suggested role in sensing noxious stimuli.

Some of the early feline recordings showed rapidly adapting joint receptors discharging when a joint was maximally extended and twisted simultaneously (Burgess & Clark 1969). Other groups recorded the receptors discharging when a joint was moved beyond its normal operating range or exposed to noxious stimuli (Schaible & Schmidt, 1983). Additional movements shown to cause joint receptors to discharge in the mid-range include loading the joint capsule in primates (Grigg & Greenspan, 1977) and inducing local inflammation to the knee joint of the cat (Grigg, Schaible & Schmidt, 1986). Later recordings in humans also captured them firing when local pressure was applied over the joint capsule in the finger joints (Burke, Gandevia & Macefield, 1988). These studies show that joint receptors can discharge when exposed to extreme movements or invasive procedures.

Initially thought to play a pivotal role in signaling position sense, joint receptors' contribution to kinaesthesia comes from their ability to ambiguously detect movement. It appears that the CNS increases reliance on them the closer a joint is to its anatomical end range, where they may possibly signal joint angle (Fuentes & Bastian, 2010). As with cutaneous afferents, their importance may be of greater importance at more distal joints, notably in the hand (Ferrell et al., 1987).

1.2.4 Small Diameter Afferents

Sensory fibers are grouped based upon their diameter and conduction velocity. Groups III and IV are considered small-diameter afferents. Sensitive to multiple forms of stimuli and comprising a large proportion of skin, joint and muscle afferents (including over 50% of all muscle afferents), small-diameter afferents supply information related to nociceptive and non-nociceptive mechanical, chemical and thermal events (Laurin, Pertici, Dousset, Marqueste & Decherchi, 2015). Both group III and IV afferents have free nerve endings located within the connective tissue of skeletal muscle and group IVs also have endings within small vessels of muscle (von Düring & Andres, 1990). Group IV fibers only innervate these free-nerve endings, whilst group III fibers can also innervate Paciniform Corpuscles (Kindig, Hayes, Hanna & Kaufman, 2006; Stacey, 1969).

Small diameter afferents can be activated by low to moderate levels of exercise. The group III fibers are more sensitive to mechanical stimuli resulting from muscle contraction (Rotto & Kaufman, 1988) and the group IV fibers appear more sensitive to the resulting metabolic changes (Haouzi, Hill, Lewis & Kaufman, 1999). Group IIIs respond vigorously at the onset of muscle contraction, their discharge rate increasing with the level of contraction and group IVs also respond to muscle contraction, albeit at longer latencies (Kaufman, Hayes, Adreani & Pickar, 2002). Their signals help ensure that adequate blood flow and oxygen is delivered to the muscles during exercise and they also play a significant role in the development of fatigue in humans (Amann, Sidhu, Weavil, Mangum & Venturelli, 2015). During higher levels of exercise-induced fatigue, muscle tissue can become ischemic and acute pain can occur. Strong evidence suggests that the group III and IV afferents relay this nociceptive information to the CNS (Laurin et al., 2015). Small diameter afferents may signal pain sensations arising from within skeletal muscle, as shown by a study in which subjects were aware of painful stimuli even after their skin had been anesthetized and group I and II afferents blocked (Graven-Nielsen, Mense & Arendt-Nielsen, 2004). Aside from this evidence of their activity during exercise, the exact role they play in regulating skeletal and autonomic function remains undetermined (Kaufman et al., 2002).

Group III or ‘A Delta’ fibers are thinly myelinated, conducting nerve impulses between 2.5 and 30 meters per second. About half of these fibers respond to contraction and many discharge when non-noxious pressure is applied to their receptive field. Their response to tendon stretch is variable, with most investigators reporting a moderate effect. Group IV or ‘C fibers’ are unmyelinated, and conduct nerve impulses at less than 2.5 meters per second. Group IV afferents are far less responsive to probing of their receptive fields, normally requiring pinching to evoke activity and rarely responding to tendon stretch, even at noxious levels (Kaufman & Rybicki, 1987; Kaufman et al., 2002).

The fact that small diameter afferents respond to many of the same stimuli as other sensory fibers makes it difficult to discern their contribution to kinaesthesia, yet there are examples in which their involvement can at least be inferred. As I covered earlier in this chapter, cutaneous receptors located in the skin are sensitive to multiple forms of input, including touch. Skin also contains group IV mechanoreceptors with limited receptive fields and low mechanical thresholds, some of these have been seen to respond to brushing of the skin and will continue to discharge until the stimulus is removed. This group IV activity enables subjects to accurately report the site of an imposed stimulus (Ochoa & Torebjörk, 1989) and provides evidence that group IV afferents could relay information pertinent to different limb positions, especially when surfaces of the body are touching each other or signaling contact with an external object.

Group III and IV fibers converge onto some of the same spinal interneurons as other afferents, indicating that they might modulate the effects of sensory input arising from cutaneous, joint and muscle receptors (Schomburg, Steffens & Kniffki, 1999). Specifically, their reinforcement of group Ib afferents implies a potential role in signaling muscle tension (Laurin et al., 2015), and recordings of group III afferents discharging in synchrony during the contraction phase of locomotion in decerebrated cats lends weight to this argument (Hayes, McCord, Koba & Kaufman, 2009). The following study illustrates the influence of small diameter afferents on signaling both muscle tension and noxious stimuli. In a two-arm force-matching task, subjects demonstrated consistent accuracy when attempting to match a low-level torque of their reference arm with their indicator arm. Following either injection of hypertonic saline or application of painful heat over the biceps of one arm, subjects consistently and significantly underestimated the force generated by the sore arm (Weerakkody, Percival, Morgan, Gregory & Proske, 2003).

Recently, two different subtypes of group III and IV muscle afferents were identified in humans (Pollak, Swenson, Vanhaitsma, Hughen, Jo, Light, Schweinhardt, Amann & Light, 2014). One subtype was found to discharge when exposed to levels of intramuscular metabolites associated with moderate to strenuous exercise. The other subtype only discharged to noxious levels of metabolites, resulting from ischemic contractions or hypertonic saline infusions (Amann et al., 2015). The diverse role of these afferents is supported by observations that they might inhibit or facilitate motor unit recruitment of both the homonymous muscle and muscles of other limbs by acting at various points within the transmission of motor signals (Laurin et al., 2015).

The study of small diameter afferents' contribution to kinaesthesia is somewhat limited by the difficulty in isolating them as well as the ethical issues involved with applying painful stimuli when attempting to activate them. Their functions are diverse and though they are often referred to collectively, they do respond slightly differently to the same stimuli. To date, the literature presents them as being pivotal in mediating exercise-induced fatigue and providing feedback resulting from both noxious and non-noxious events. Their convergence on common interneurons can strengthen the projections of other afferents and their discharge during muscle contraction could be used for determining tension levels within the muscle. The fact that they form a large proportion of total muscle afferents suggests they are important to the sensory information processed by the CNS, but evidence of their exact role is currently inconclusive.

1.2.5 Deafferented Individuals

When other kinaesthetic inputs are lost, small diameter inputs can fulfill certain requirements. The senses of itch, pain and temperature have a limited potential to act as proprioceptors in guiding movement (Proske & Gandevia, 2012). For example, "temperature changes in the armpit can signal that the arm is abducted" (Gandevia, 1996, p.143). There are few documented cases in the literature of individuals with large fiber sensory neuropathies who must rely more heavily on small-diameter afferent input. It has previously been suggested that these cases are the "purest form of loss of movement and position sensation" (Cole, 2008, p.295), and therefore reviewing them can further our understanding of kinaesthesia and how it is affected when the major afferent inputs are absent.

One of the earliest published studies on a human deafferented subject reported that the patient, 'G.O.', could perform multiple finger movements that required integrated muscle actions, as well as move his thumb to different distances at different speeds. Despite exhibiting this level of control, he was unable to perform basic everyday movements involving his hands. One reason might have been his lack of automatic reflex corrections to voluntary actions, which are normally provided by primary and secondary afferents (Rothwell, Traub, Day, Obeso, Thomas & Marsden, 1982). Subject 'A.N.' could hold various postures without the use of his visual system, but found new movements were impossible without looking at the involved body part. He could sometimes sense if his arm was moved, but not the direction it was moved in. Everyday tasks required great concentration and constant visual surveillance, for example, 'A.N.' noted that he could not daydream whilst walking. The authors commented that he was however very "adept at cheating" (Cole & Sedgewick, 1992, p.505), in other words he was proficient at using other cues to complete tasks. In a study investigating grip force control, subject 'G.L.' used excessively high levels of force to grip an object compared to control subjects. The authors attributed her inability to modulate force appropriately to the long period she had been without cutaneous and other forms of proprioceptive feedback (Nowak, Glasauer & Hermsdörfer, 2004).

These case studies highlight the impact that large fiber sensory neuropathies can have on the individuals' everyday lives. It is curious to note both the similarities and the differences these cases present, as well as the compensations each person adopts to overcome their limited sensory feedback. In summary, though small-diameter afferents are not considered principal contributors to kinaesthesia, their feedback may be especially useful to the CNS when the dominant sensory pathways are unavailable.

1.2.6 Recap of Receptors

Thus far, I have explored the receptors located in skin, tendon and joints and reviewed the evidence of their contribution to kinaesthesia. One key point to reiterate is that no single class of receptor is without limitation and a combination of their sensory feedback is needed to build an accurate picture of what the body is doing at a given moment (Proske & Gandevia, 2012). Having covered the information relayed to the CNS from receptors located in the periphery, classified as *afferent* information, I now consider *efferent* signals that originate from within the brain itself.

1.3 The Sense of Force, Heaviness and Effort

Whenever we perform a movement, whether we draw our attention to it or not, we are aware of the muscle contractions involved, the physical exertion or effort required to execute the movement and if lifting an object, a gauge of how heavy it is. The awareness of these various sensations is thought to predominantly rely on the *efferent* signals issued by the brain, plus some additional input from the peripheral receptors (Proske & Gandevia, 2012). It appears that the CNS monitors the movement commands it issues and based on previous experience of how the body responds to certain commands, the CNS predicts the consequence of its motor output. As a result, the CNS could have two ways to determine the outcome of its motor commands.

Receptors could signal the resulting changes in the periphery, or based on the signal it issued and past experiences, the CNS will know that a particular action was executed (Walsh et al., 2014).

Sense of limb position and sense of limb movement can also be influenced by centrally derived signals. For example, when we support our limbs in the vertical plane, it is thought that we draw information from both central and peripheral sources (Allen, Leung & Proske, 2010). In this setup, the CNS would have access to feedback from GTOs signaling the degree of tension in the muscles supporting the weight of the limb against gravity, in addition to the knowledge of the motor commands it issued and the prior experience of holding the limbs in that specific posture. In support of this theory, changes in the gravitational field can cause proprioceptive illusions (Lackner, James & Graybiel, 1981; Young, Oman, Merfeld, Watt, Roy, DeLuca, Balkwill, Christie, Groleau, Jackson, Law, Modestino & Mayer, 1993).

Two pivotal reports suggested that a combination of central and peripheral sources informed human proprioception. Sperry (1950) introduced his hypothesis of a *Corollary Discharge* following his study investigating the stability of the visual field during eye movements of the fish. He suggested that changes in the periphery, including postural alterations, combined with the discharge of motor commands both informed central sensory regions. He posited that the motor commands in particular might play an important "adjustor role" (Sperry, 1950, p489). The second hypothesis came from von Holst and Mittelstaedt (1950) and led them to a similar conclusion, with the addition of one key concept. They introduced the term *reafference* to denote afferent signals that were generated by the body's own actions, and the term *exafference* to denote afferent signals that arose from input generated by stimuli from outside of the body. They proposed that reafference signals are created from an *efference copy* of the motor command. It is now widely accepted that afferent signals resulting from a movement arise from a combination of both exafferent and reafferent information. It is not yet fully understood how most of the reafferent information resulting from motor commands fails to reach consciousness. But as a result, the perception and intensity of afferent signals is suppressed during movement (Proske & Gandevia, 2012).

One example of this suppression of afferent information during movement comes from a playful study involving 'tit for tat' between two participants (Shergill, Bays, Frith & Wolpert, 2003). Each pair of subjects had a force transducer, fitted to a lightweight lever of a torque motor, positioned over their left index finger while their right index finger rested on top of the force transducer positioned on their partner's left index finger. The trials began when one subject had a defined low level force applied to their finger via the torque motor, they then attempted to match that force with their right index finger by applying the perceived force back to their partner's left index finger. Unaware that they had received the same instruction, the pair then took turns to reciprocate the force they felt each time. In all cases, the forces escalated rapidly. In a second part of the study, individuals repeated a similar paradigm without a partner. In this case, the torque motor applied the force to their left index finger each time and they then attempted to recreate that force with their right hand, which this time rested on top of their own left index finger. Again, they consistently overestimated the force needed. For the final part of the study, subjects again received a force to the left index finger via a torque motor, but this time they matched the force using a joystick that controlled the torque motor. They could match the forces much more accurately under this condition. This result highlights the attenuation of sensory stimuli during movement. Perhaps this attenuation enables us to focus our attention on incoming external stimuli and avoid distraction by the signals generated from our own movements (Proske & Gandevia, 2012). It is important to note that during everyday behaviors, we switch between the performance of learned tasks during which we pay little attention to the motor commands issued and resulting reafferent signals, to the performance of demanding or new tasks during which we pay great attention to both exafferent and reafferent signals.

To assess the role of motor commands, a degree of paralysis or fatigue can be used to decrease the muscular system's force output. One method of inducing paralysis is to use an ischaemic block to prevent afferent information reaching the CNS and efferent signals from reaching the isolated body part. Studies in the blocked hand demonstrate that if subjects attempt to move their wrist, they perceive the hand to move in the same direction that they attempted to move it, without any actual motion having occurred (Gandevia, Smith, Crawford, Proske & Taylor, 2006). This demonstrates that motor commands can provide some sense of limb position. Another study that was thought to involve total body paralysis had the incapacitated subject try to dorsi-flex their foot. No movement resulted, but the subject later reported that they felt like the foot moved into plantarflexion, the opposite direction to that which they had attempted (Gandevia, Killian, McKenzie, Crawford, Allen, Gorman & Hales, 1993). It was later revealed that complete paralysis had not yet occurred and that some of the muscle afferents were still receiving efferent signals. These reverse illusions disappeared later in the experiment once the block had taken full effect.

In a series of experiments designed to investigate the origins of the senses of force, heaviness and effort, subjects used their thumb flexors in a weight-matching task (Luu, Day, Cole & Fitzpatrick, 2011). Specifically, the authors were attempting to investigate the assertion that signals from the CNS create some sense of heaviness when an object is lifted. If this was the case, weakening the muscles responsible for performing a lift should have increased the motor command issued and as a result, the subjective heaviness of the object should have increased. Three methods were employed to weaken the thumb flexors of one hand: the first involved subjects holding their thumb flexed against a load cell with 100% maximum effort (HF group), the second involved subjects holding the same position with 40% of their maximum (LF group). The first exercise method ceased when subjects' force output dropped to 40% of their maximum and the second ceased when subjects could no longer maintain their 40% force output. The third and final method involved complete paralysis of the involved muscles and then allowing recovery until subjects could achieve 40% of their previous maximal force output. After a brief rest period, subjects completed a series of force matching experiments between unseen loads held by their thumb flexors. The control thumb held a reference weight and the fatigued thumb held an indicator weight. After each lift, subjects reported whether the indicator weight felt heavier or lighter than the reference weight. The reference weight was then increased or decreased accordingly, until the subjects reported that the two weights felt equal. Following fatigue, the HF group initially perceived the reference weights to be lighter than they had felt pre-fatigue, this perception recovered to control levels over a five-minute period. The LF group felt that the reference weight was close to how it felt pre-fatigue, matching it with good accuracy. However, when vibration was applied to the thumb flexor during the LF group's fatigue protocol, the reference weight then felt light during the matching trial. Vibration was applied in an attempt to desensitize the GTOs, as their discharge rate is known to increase until a level of saturation is reached, at which point their discharge rate drops. The results lead the authors to conclude that a large contribution to the sense of heaviness comes from peripheral receptors, including a major input from muscles spindles, which they stated provide more than just information related to limb position and movement.

Following review of some of the peripheral signals that provide afferent information, we now see that afferent information can be further classified as reafferent or exafferent in nature, depending on where it originates. The research suggests that efferent signals or motor commands play a part in shaping our kinaesthetic awareness. Of the three senses covered in this section, the sense of effort appears best suited to contribute to limb position and movement sense. In the next section, I discuss the pivotal role that muscles spindles play in human kinaesthesia.

1.4 Muscle Spindles as Significant Contributors to Kinaesthesia

1.4.1 Introduction and Historical Background

There is now strong evidence of muscle spindles being our principal proprioceptors, but as mentioned earlier in this thesis, joint receptors held this mantle for a large part of the 20th century (Proske, 2015). Sherrington (1900) originally reported on the muscle spindle's ability to sense stretch in a muscle, though he believed their feedback to be unconscious and purely for reflexive control. It is generally accepted that for a receptor to contribute to conscious sensations, it needs to project to the cortex (Proske & Gandevia, 2012). Evidence that spindle afferents failed to reach the cortex (Brindley & Merton, 1960) only strengthened the argument that they were not involved in kinaesthesia. However, faulty methods were later identified in this work (McIntyre, Proske & Rawson, 1984) and further studies provided evidence that muscle spindle afferents did in fact project to the cortex (Oscarsson & Rosen, 1963; Landgren & Silfvenius, 1969). Specifically, it was shown that spindles projected to Area 3a of the primary somatosensory cortex (Phillips, Powell & Wiesendanger, 1971).

Perhaps the real turning point for muscle spindles occurred following Goodwin et al.'s (1972) seminal paper. Building on the evidence that spindles were sensitive to mechanical muscle vibration in a passive muscle (Brown, Engberg & Matthews, 1967), Goodwin et al. demonstrated that vibration of the biceps or triceps muscle tendon produced an illusion of movement at the elbow joint in a direction congruent with the vibrated muscle being stretched. This occurred when the vibrated muscles were relaxed or contracting and caused distortions to both position and movement sense. Further work by this group investigated the kinaesthetic effects of moving a finger that had been ring-blocked with lignocaine (a local anaesthetic) or by occluding circulation of the whole hand. The subjects correctly reported when a finger was being moved in both conditions. These experiments presented a clear case for the muscle spindles importance to kinaesthesia. A brief overview of the muscle spindle's morphology follows.

1.4.2 Morphology and Location

The name 'muscle spindle' was adopted by Sherrington (1894) after Kühne (1863) had originally referred to them as 'muskelspindeln' due to their spindle-like shape. Muscle spindles are encapsulated, which gives them their spindle or fusiform shape. Accordingly, their contractile regions, housed within the capsule are known as *intrafusal* fibres and the muscle fibres that spindles lie parallel to, are known as *extrafusal* fibres. During neural development, the spindles grow in the periphery and sensory axons grow out to them. As such, these axons are said to 'innervate' the spindle, even though information travels in the opposite direction, from the periphery back to the CNS. The non-contractile region of a spindle is innervated by primary (Ia) and secondary (II) sensory endings, the former being the largest axon in the mammalian nervous system (Matthews, 1972). Some mammalian muscles may contain up to 500 muscle spindles (Iles, Stoked & Young, 1990; Prochazka 1996). The ratio of the number of muscle spindles to the weight in grams of the muscle they reside in is known as *density.* The density of muscle spindles is lower in more proximal joints, whilst small muscles in the extremities have a higher density of spindles (Gandevia, 1996). The primary function of muscle spindles is to detect the rate and degree of length change of extrafusal muscle fibres. This function is used in both voluntary and reflexive motor control. In 1943, Lloyd presented evidence that muscle spindles were responsible for the monosynaptic, or 'knee jerk' reflex (Lloyd, 1943). As the name implies, one synapse occurs between the Ia afferent running from the primary endings of the spindle and the alpha motor neurons that innervate extrafusal fibres of the homologous muscle.

1.4.3 Function

Sensory endings spiral around the non-contractile region of the spindle and when the muscle they reside in lengthens, it causes the sensory endings to stretch. If the change in the resting membrane potential is big enough, an action potential will be generated, ultimately causing the receptor to discharge. Due to their structure and innervation by different classes of sensory axons, muscle spindles are sensitive to both the changes in muscle length and the velocity of muscle length change. The primary endings are more sensitive to the velocity of length change and secondary endings are more sensitive to the magnitude of length change, though there is clear overlap in their function.

Presumably, if the length of all the muscles crossing a single joint is known, the position and the velocity of that joint's movement can be determined (Walsh et al., 2014). However, their feedback of joint position is potentially ambiguous; firstly, because mechanical muscle vibration has shown them capable of signaling anatomically impossible positions, making them unsuitable joint limit detectors (Craske, 1977). Secondly, as previously mentioned, muscle spindles will discharge when their homologous muscle is stretched and, they can also discharge due to the influence of descending pathways.

1.4.4 The Fusimotor System and Alpha Gamma Co-Activation

All the receptors covered prior to the muscle spindle share one common property; they can all be considered *passive* receptors, meaning that for them to discharge, a change must occur within the environment in which they are situated. The muscle spindle can be considered an *active* receptor, as it is the only somatosensory receptor with its own motor innervation, the *fusimotor system*. As alpha motor neurons innervate extrafusal muscle fibers, gamma motor neurons innervate the intrafusal fibres of the muscle spindle and these can be categorized as *dynamic* or *static*, depending on the type of intrafusal fiber they attach to. The main function of the fusimotor system is to prevent the muscle spindle from 'unloading' or ceasing to discharge when a muscle shortens (al-Falahe et al., 1990). Thus, when a muscle contracts, the gamma motor neurons are co-activated with alpha motor neurons to prevent the spindles falling silent (Vallbo, 1974). This is known as *alpha gamma co-activation*. The overriding opinion was that this co-activation occurred every time a muscle contracted (Matthews, 1972), and indeed the *beta system* fulfills this role, via single neurons that split to innervate both intrafusal and extrafusal fibres (Bessou, Emonet-Dénand & Laporte, 1963 & 1965).

Despite there being ample evidence of gamma activation and alpha activation occurring simultaneously (Aniss, Diener, Hore, Gandevia & Burke, 1990; Burk, Hagbarth & Löfstedt, 1978; Kakuda, Vallbo & Wessberg, 1996), the sophistication of the system allows for separate activation when required. The first evidence of this was seen in recordings from the cat, in which the effects of alpha and gamma activation were shown to occur independent of one another. Gamma activity appeared to be 'set' by the CNS depending on the task at hand; the authors introduced the term *fusimotor set* to describe this (Prochazka, Hulliger, Zanagger & Appenteng, 1985). Furthermore, the dynamic and static fibres of the gamma system can also be modulated independent of one another (Murphy, Stein & Taylor, 1984), thus enabling the CNS to tune the spindles and bias their sensitivity to overall changes in muscle length or to the rate at which length changes occur.

There is evidence of both fusimotor set and dynamic and static tuning of spindles in humans. Ribot-Ciscar, Rossi-Durand & Roll (2000) showed that over half of the spindles they recorded from altered their response to imposed stretches when the subject was asked to complete mental computations. This suggests that muscle spindle sensitivity to movement can be modified in relaxed human subjects. Two further studies used the ankle joint to investigate the influence of instruction on muscle spindle sensitivity. The first used a multi-directional footplate to impose two-dimensional figures upon the ankle joint, essentially using the subject's foot to trace out a symbol (Hospod, Aimonetti, Roll & Ribot-Ciscar, 2007). Subjects were asked to either relax or to attempt to identify the letter or number that their foot motion was describing. When subjects attempted to identify the symbol, over half of the muscle spindles recorded from modified their activity. When this modified spindle activity occurred, subjects' number of correct answers increased. The second study used ramp and hold movements whilst recording from muscle spindles (Ribot-Ciscar, Hospod, Roll & Aimonetti, 2009). Once again, subjects were instructed to either relax or pay attention to the imposed movements, but this time they had the additional instruction of either reporting on the amplitude or the speed of the movement. When reporting on the speed of the movement, significant increases were seen in dynamic and static spindle responses. However, when reporting on the amplitude of the movement, spindle discharge reflected an improved sensitivity to ankle position but suppressed sensitivity to velocity. The authors concluded that gamma dynamic and static activity was being modulated depending on the aspect of the task subjects were reporting on.

Clearly the muscle spindle and fusimotor system comprise and operate at a greater level of complexity than the kinaesthetic sensors covered earlier in this thesis, but complex systems can present certain challenges and one element of muscle spindle function is still not fully understood. We know that the background discharge of muscle spindles is largely responsible for signaling limb position (Clark et al., 1985), of which the secondary endings provide the most reliable portion of the signal (Matthews, 1982). The lack of understanding arises because muscle spindles can change their discharge patterns due to both changes in muscle length and to fusimotor stimulation. Therefore, how does the CNS determine which portion of the code pertains to changes in muscle length and which is the result of increased fusimotor drive? It has been postulated that discharges resulting from fusimotor stimulation must be subtracted from the overall spindle response (Goodwin et al., 1972; McCloskey, Gandevia, Potter & Colebatch, 1983; Matthews, 1982), though there is currently no evidence of this (Walsh et al., 2014). I now present the evidence illustrating the role that muscle spindles play in kinaesthesia. The present view is that they are of primary importance (Proske & Gandevia, 2012).

1.4.5 Muscle Thixotropy and Muscle Spindles' Role in Kinaesthesia

Thixotropy refers to the friction-like behaviour exhibited by a muscle (Gandevia, 1996) according to its history of contraction and length change (Proske & Gandevia, 2012). It affects both the extrafusal and intrafusal fibres (Proske & Morgan, 1999). If the latter remain in a taught or slackened state, the resting discharge rate of the muscle spindles increases or decreases respectively (Morgan, Prochazka & Proske, 1984; Proske, Morgan & Gregory, 1993). This ability to alter spindle activity without changing the length of the homologous muscle has proven to be a useful tool when assessing muscle spindles' contribution to kinaesthesia. For example, accuracy in limb-matching and pointing tasks can be altered via a conditioning contraction of the involved muscles (Proske, Tsay & Allen, 2014). This history dependent property of muscle tissue exerts such a large influence over the spindles that it can be used to produce illusions of altered joint position (Gregory, Morgan & Proske, 1988; Wise, Gregory & Proske, 1996). This final point has caused some to question whether spindles are suitable to accurately signal joint position (Walsh et al., 2014), but in everyday occurrences, thixotropic affects are minimized as muscles are normally active (Allen, Ansems & Proske, 2007).

Thixotropy can influence subjects' ability to detect passive movements imposed at the forearm (Wise et al., 1996). Discrepancies between movement detection thresholds were observed at other joints, but these were resolved once the overall muscle length change imposed by the movement was considered and not the degree of joint angle change (Hall & McCloskey, 1983). This observation lends support for muscle spindles being the principal receptor for detecting imposed movements (Proske & Gandevia, 2012), although as mentioned earlier, skin receptors are equally sensitive to detecting the direction of imposed movements (Aimonetti et al., 2007).

Muscle spindles can create sensations of movement, provided enough of them are simultaneously stimulated. Illusory movements of the finger joints can be created by pulling on exposed tendons in the forearm (Matthews & Simmonds, 1974) and whilst electrical stimulation of single muscle spindle afferents produces no sensation of movement (Macefield et al., 1990), electrical stimulation of a population of afferents produces the expected illusions (Gandevia, 1985).

One of the simplest yet most compelling pieces of evidence for muscle spindles primary significance in kinaesthesia is that following total hip joint replacement involving removal of the entire joint capsule and all ligamentous components, the ability to sense the position and movement of the limb persists (Grigg, Fineman & Riley, 1973). Similar results have also been seen at the knee and shoulder (Cuomo, Birdzell & Zuckerman, 2005; Ishii, Terajima, Terashima, Bechtold & Laskin, 1997). Presumably in these examples, cutaneous receptors and GTOs would be the only other potential source of major kinaesthetic input.

I now briefly cover some of the literature investigating muscle spindles' role in kinaesthesia from the last 10 years. Dimitriou & Edin (2008b) recorded muscle spindles during free moving wrist and hand movements used to undertake a key-pressing task. Acceleration and velocity of the limb significantly impacted the afferents' discharge rates and these were more "phase advanced than expected," so much so that the angular velocity of the wrist could be predicted from the spindle responses. These authors continued this line of work and concluded that muscle spindles can act as "forward sensory models" to predict the future kinematic state of their parent muscle (Dimitriou & Edin, 2010). If this proposition proves correct, muscle spindles would play a vital role in correcting movements in real time (Walsh et al., 2014). An additional role for muscle spindles has also been demonstrated, in which they may contribute to the sense of exerted force and heaviness of lifted objects (see The Senses of Force, Heaviness & Effort; Luu et al., 2011). Finally, just as GTOs might serve as ambiguous detectors of length change, muscle spindles could potentially signal muscle force due to their co-activation during voluntary contraction and increased discharge rate during muscle contraction (Walsh et al., 2014).

1.4.6 Muscle Spindle Summary

Though originally viewed as being solely responsible for the stretch reflex, muscle spindles are now known to project to the cortex and should therefore be capable of producing conscious sensations. Their sensitivity adjusts depending on task demands, this being facilitated by their sophisticated fusimotor system which not only allows them to operate both in unison with and independent of their homologous muscle, but also to be preferentially tuned to relay improved velocity or length sensitive feedback. The ability to alter their signaling response via thixotropy and artificial stimulation has enabled the exploration of their contribution to the senses of position and movement. In recent years, additional information that the CNS might garner from their feedback has been proposed, serving only to further their position as a diverse receptor, vital to both voluntary and reflexive motor control (Proske, 2015).

As touched upon at the start of this section, the real turning point for the role of muscle spindles in kinaesthesia resulted from Goodwin et al.'s (1972) seminal paper, which firmly established their position as our principal receptors. Indeed, arguably the most compelling evidence of muscle spindles influence on position and movement sense comes from experiments using mechanical muscle vibration to stimulate them.

1.5 The Vibratory Illusion

Mechanical muscle vibration provides a potent stimulus for muscle spindles (Roll, Vedel & Ribot, 1989), creating illusory movements consistent with the vibrated muscle being lengthened (Gandevia, 1996). These perceived movements can occur rapidly, ceasing only upon removal of the stimulus and resultantly, anatomically impossible joint positions have been reported (Craske, 1977). As mentioned previously, this point illustrates why muscle spindles would be unsuitable limit detectors of joint motion (Proske et al., 1988).

Goodwin's original work used a vibratory frequency of 100Hz (Goodwin et al., 1972). Since then, direct recordings from muscle spindle afferents have shown them to be most sensitive to 80Hz, particularly their primary endings (Roll & Vedel, 1982; Roll et al., 1989). McCloskey (1973) found that if the vibration frequency was reduced to 30-40Hz, the sensation of limb displacement was stronger than that of limb movement, presumably reflecting decreased stimulation of primary and increased stimulation of secondary endings.

When appropriately implemented, the vibratory illusion can be used to induce any two or three-dimensional movement (Roll, Albert, Thyrion, Ribot-Ciscar, Bergenheim & Mattei, 2009; Thyrion & Roll, 2010). A series of experiments by Lackner (1988) that involved using the vibratory illusion, have offered insight into how the brain resolves conflicting sources of sensory information. One that is commonly referenced required subjects to touch their nose with their hand whilst elbow flexors of the same arm were vibrated in the absence of vision. The discharge of muscle spindles in the elbow flexors caused an illusion of the elbow straightening. Because the hand was in contact with the nose, some of the subjects reported that their nose felt as if it was telescoping out from their face, hence this study being referred to as 'Pinocchio's Nose'. Another study demonstrated the vibratory illusion's influence on visual interpretation; subjects held a torch stationary in their hand, whilst elbow muscles of the same arm were vibrated. Subjects resolved the illusory movement of their arm, by perceiving the light to move in a direction consistent with the illusion. The authors referred to this as a 'propriogyral illusion' (Lackner & Levine, 1978). These papers provide an indication of the level of reliance that the CNS places on muscle spindles in certain situations, so much so that it can resolve mismatched sensory input by distorting the size of body parts and the apparent location of visual markers.

Whilst vibration's effect on muscle spindles is quite robust, it still has certain intricacies and limitations. Experiments involving simultaneous vibration of both agonist and antagonist musculature at similar frequencies and amplitudes produces little to no sensation of movement (Gandevia, 1985; Ribot-Ciscar & Roll, 1998. This is unsurprising however, when considering that the nervous system appears to compute the difference between agonist and antagonist muscle spindle discharge rates to determine joint angle (Ribot-Ciscar & Roll, 1998). The speed of the movement illusion is also susceptible to change, with decreases occurring when the targeted muscle supports increasing loads, and when these loads exceed half of its maximal capacity, the illusion disappears completely (Ansems, Allen & Proske 2006; McCloskey, 1973). Thixotropy can also cause the illusion to disappear if slack is introduced to the intrafusal fibres (White & Proske, 2009), or it can increase the speed of the illusory movement following a conditioning contraction (Gooey, Bradfield, Talbot, Morgan & Proske, 2000). These points highlight the need to be diligent when utilizing the vibratory illusion during scientific investigations.

Mechanical muscle vibration appears to exert different effects depending on whether the experimental setup utilizes a matching task or a pointing task. Proske (2015) proposed that muscle receptors were not directly involved in pointing tasks and went on to report what happens when the vibratory illusion is used in this type of task. A study by Izumizaki, Tsuge, Akai, Proske & Homma (2010) reported a 30% decrease in the size of the vibratory illusion when assessed in a pointing task as opposed to a matching task and similar results were reported elsewhere (Kammers, van der Ham & Dijkerman, 2006), leaving Proske to conclude that during a “pointing task the vibration illusion is attenuated but not abolished” (Proske, 2015, p.181).

If applied correctly, mechanical muscle vibration can strongly stimulate muscle spindles and in the right setting, create illusions of joint movement and displacement. As a tool in the study of kinaesthesia, it offers strong evidence for the case of muscle spindles being of primary importance to our senses of limb position and limb movement. I now briefly review the susceptibility of the other kinaesthetic receptors to mechanical muscle vibration.

1.5.1 Other receptors stimulated by vibration

Thus far we have seen that if the appropriate frequency is used, muscle vibration can selectively activate muscle spindle primary endings, especially when the muscle is relaxed. When the muscle is active, GTOs and cutaneous receptors can also discharge in response to certain frequencies under the right conditions (Fallon & Macefield, 2007).

Of the cutaneous receptors, Meissner Corpuscles of the RAI system respond well to relatively low vibration, between frequencies of 20-60Hz (Mountcastle, LaMotte & Carli, 1972; Talbot, Darian-Smith, Kornhuber & Mountcastle, 1968). The detection of high frequency vibration requires Pacinian Corpuscles of the RAII system, their sensitivity peaking in between 200 and 300Hz (Johansson, Landström & Lundström,1982). SAIIs respond in a predictable fashion to high frequency vibration, provided application of the stimulus is precise (≥ 1-2mm) (Gynther, Vickery & Rowe, 1992) and the SAI system responds to very low vibration, between 0.3-3Hz (Bicchi, Dente & Scilingo, 2003).

GTO's generally show a poor response to vibration in the absence of muscle contraction (Brown et al., 1967), though they have been recorded in a passive muscle when exposed to 10-40Hz vibrations at very low amplitudes (Roll et al., 1989). Their sensitivity improves when the targeted muscle is contracting (Fallon & Macefield, 2007) and they can be driven by vibration at 100Hz frequency (Brown et al., 1967).

Despite this potential to stimulate cutaneous and tendon based receptors with vibration, it should be noted that there is little to no cross-over of their preferred frequencies with the 80Hz frequency known to maximally activate primary endings of muscle spindles (Roll & Vedel, 1982). To the best of my knowledge, there have been no studies that have recorded the response of small diameter afferents or joint receptors to mechanical vibration, though it has previously been shown that when vibration is applied to the joint, no illusion of movement occurs (Goodwin et al., 1972). When attempting to modulate muscle spindle activity, vibration is often the chosen method and though thixotropy offers a viable and simple alternative, the sense of effort is a large confounding variable. Intraneural stimulation of the receptor offers a far more invasive method.

Receptor	Vibration Frequency (Hz)	Vibration Amplitude (mm)	Additional Details
RA I Cutaneous	40 – 60 [a]	0.002 – 0.02 [a]	-
RA II Cutaneous	200 – 300 [b]	0.001 [b]	-
SA I Cutaneous	2 – 32 [c]	0.001 – 1mm [c]	-
SA II Cutaneous	50 – 1000 [d]	< 0.1 [d]	≥ 1-2mm of location [d]
Golgi Tendon Organs	10-40 (passive) [e] 100 (active) [e]	0.2 – 0.5 (passive) [e] 0.15 (active) [e]	Poor response when muscle is passive [e]

Table 1.1 Sensitivity of cutaneous receptors and GTOs to vibration. [a] Mountcastle et al., 1972. [b] Talbot, Darian-Smith, Kornhuber and Mountcastle, 1968. [c] Johansson, Landström, Lundström, 1982. [d] Gynther, Vickery and Rowe, 1992. [e] Roll, Vedel and Ribot 1989.

1.5.2 Muscle Vibration Disturbs Kinaesthesia

Following on from Goodwin, McCloskey and Matthew’s work (1972), Capaday and Cooke (1981) pioneered the use of muscle vibration during a single-arm end-point positioning task. Vibration applied to the antagonist (lengthening) rather than the agonist (shortening) musculature resulted in customary undershooting of the intended target. Inglis and Frank (1990) reported the same result when vibration was utilised during a matching task in the horizontal plane. Furthering this concept, they repeated the task to demonstrate that even with an eccentrically-controlled movement, the muscle spindle feedback from the lengthening muscles still provided the primary source of position sense (Inglis, Frank & Inglis, 1991). The literature demonstrates that concentrically and eccentrically controlled targeting tasks involving a single joint are strongly influenced by vibration, but what effect does vibration have during a movement sequence involving two or more joints?

1.6 A Kinaesthetic Movement Sequence

Noting that “most of our everyday movement repertoires fall in the category of movement sequences” (Cordo, 1988, p.40), Cordo devised a task that relied on the kinaesthetic feedback from the elbow joint to time a targeted movement at the thumb and index finger, a strategy comparable to a back-handed throw in the horizontal plane, like a Frisbee toss.

Advantages of this task include drawing participants' focus away from the body part being studied, whilst the horizontal plane movement emphasizes the role of muscle spindles (Ansems et al., 2006), reduces gravity's influence on the limb, and decreases the contribution of feedback from the sense of effort (Walsh, Allen, Gandevia & Proske, 2006). Cordo, Gurfinkel, Bevan & Kerr (1995) used vibration during this sequence for a concentrically controlled movement to induce both over and undershooting of the target, depending on the vibration frequency applied. It remained to be seen whether muscle vibration could influence task accuracy of an eccentrically-controlled movement when the muscle spindles in the lengthening musculature were discharging due to both the increasing muscle length, as well as gamma motor neuron drive (Burke, Hagbarth, & Löfstedt, 1978). Therefore, the **first objective** of this thesis was to determine whether muscle vibration would degrade task accuracy during an eccentrically-controlled movement sequence, as had been shown during a concentric movement sequence (Cordo et al., 1995) and during an eccentric targeted movement (Inglis et al., 1991).

1.7 Exercise-Induced Fatigue also Disturbs Kinaesthesia

Defining and quantifying fatigue that results from exercise is complicated by the numerous physiological mechanisms that can create it. "The ability of muscle to produce force or power whether or not the task can be sustained" (Enoka & Duchateau 2008, p.12) provides a clear definition of exercise-induced muscle fatigue and highlights the distinction between a muscle's decreasing capacity and the ability to continue a task.

Exercise-induced muscle fatigue can degrade kinaesthesia and might be responsible for some of the clumsiness often experienced after intense exercise (Proske & Gandevia, 2012). As an example, think of the final stages of a very long hike, you may have experienced increased stumbling or misplacement of your feet. This likely results in part from impaired position and movement sense. One study used isometric contractions to fatigue either agonist or antagonist muscles involved in a rapid, self-terminated movement task using flexion and extension movements of the elbow joint (Jarić, Radovanović, Milanović, Ljubisavljević & Anastasijević, 1997). They demonstrated that fatiguing the agonist muscles increased final position errors and decreased movement velocity more than fatiguing the antagonists. Another technique used to assess kinaesthetic ability is to passively position a joint and ask subjects to re-create the position after the joint has been moved to a different position, whilst minimizing visual, auditory and tactile cues. After fatiguing contractions of the internal and external rotators of the glenohumeral joint, subjects' ability to reproduce three pre-set angles of glenohumeral rotation was significantly decreased when compared to pre-fatigue levels. The performance of control subjects slightly improved during the same time frame (Myers, Guskiewicz, Schneider & Prentice, 1999).

Limb-matching tasks can also be used to assess kinaesthesia. One method to investigate the elbow joint, involves strapping both forearms to individual lightweight paddles that can be rotated about a hinge that is aligned close to the axis of the elbow joint. Potentiometers on the paddle hinges feed a voltage signal to represent the elbow joint angle. Using this setup for an active matching task in the vertical plane, a group of subjects were chosen based on their ability to achieve matching accuracy within ±2 degrees. Following concentric exercise of the elbow flexors of one arm, matching errors increased compared to control values, though they were only significant when the exercised arm acted as the indicator arm (Walsh, Hesse, Morgan & Proske, 2004). In a series of follow-up experiments, subjects initially varied in their matching accuracy, but following the exercise protocol, all of them adopted a more extended position with their indicator arm when their fatigued arm acted as the reference (Allen & Proske, 2006). This result was interpreted as a disturbance to the subjects' sense of position. To investigate possible disturbances to the sense of movement, a tracking task was used that required the subjects to match the passive movement of one arm (controlled by the experimenter) with their other arm. Interestingly, movement-tracking performance was not significantly disturbed regardless of whether the fatigued limb acted as the reference or the indicator arm.

Threshold to detection of passive motion (TTDPM) is an assessment method used to test one facet of movement sense, namely the ability to sense the onset and direction of joint movement (Riemann, Myers & Lephart, 2002). In a study employing TTDPM at the shoulder, subjects' thresholds to detection of both internal and external glenohumeral rotation increased by 73% following fatiguing exercise of both motions. Although the title of the study refers to "position sense", it demonstrates the adverse effect that fatigue can have on subjects' ability to sense movement (Carpenter, Blasier & Pellizzon, 1998). Again, testing the shoulder joint, another study investigated the effect of muscle fatigue on movement sense by assessing subjects' proficiency in discriminating different movement velocities imposed on their shoulder

(Pederson, Lonn, Hellstrom, Djupsjobacka & Johansson, 1999). Subjects were split into two groups: one group were prescribed light exercise at 10% of their maximal voluntary contraction (MVC) and the other performed repeated maximal voluntary contractions until fatigued. Post exercise, subjects in the light exercise group had significantly higher chances of distinguishing between the different velocities than the group who exercised with MVCs until fatigue. Female subjects also had a lower probability of distinguishing the correct velocities than male subjects. Subsequent investigations have also reported gender differences in kinaesthesia; a recent study observed females consistently overestimating a remembered joint position, whereas men both overestimated and underestimated the target position (Vafadar, Côte & Archambault, 2015).

These results highlight the fact that exercise-induced fatigue, like mechanical muscle vibration, has the potential to disturb kinaesthesia. This has significant implications for athletes when training and competing. It is already known that injuries occur later in a sporting event as fatigue accumulates (Woods, Hawkins, Hulse & Hodson, 2003; Fuller, Taylor & Raftery, 2016). The acute negative impact on kinaesthesia could be partly responsible for this (Proske & Gandevia, 2012). Consequently, the **second objective** of this thesis was to investigate the effect of muscle fatigue and eccentric muscle damage on an eccentrically-controlled movement sequence. To do this, I employed an exercise protocol and monitored its effect on task performance during the aforementioned eccentrically-controlled limb movement sequence (outlined in the first objective).

1.8 Eccentric Muscle Damage

A *muscle contraction* comprises activation of tension-generating sites within muscle fibers. *Contraction* is a slight misnomer, because in physiology, a muscle does not necessarily shorten when producing tension (Widmaier, Raff & Strang, 2010). There are three broad classifications of muscle contraction. A *concentric contraction* involves a muscle shortening under tension. The common description of an *isometric contraction* is a muscle generating tension without changing length, though muscle fascicles are known to shorten during isometric contractions (Héroux, Stubbs & Herbert, 2016; Ito, Kawakami, Ichinose, Fukashiro & Fukunaga, 1998). Perhaps a more accurate definition would be: when a muscle generates tension and the angle of the joint it crosses remains constant. Lastly, *eccentric contraction* is the term used to denote a muscle lengthening under tension. This contraction type is a common occurrence in everyday life, with examples that include sitting in to a chair, or walking down stairs and even the simple act of lowering a glass to a table.

Exercises involving eccentric contractions have unique effects on the body, including a degree of muscle damage (Enoka, 1996) and whilst all forms of exercise have the potential to cause fatigue and weakness, the drop in strength resulting from eccentric exercise can remain for ten days or more. Joint range of motion can also be reduced for the same duration and this duration matches the time taken for the damage to be repaired (Clarkson, Nosaka & Braun, 1992). Although exercise using either isometric or concentric muscle contractions can disturb kinaesthesia if the resulting drop in force is of sufficient magnitude (Allen & Proske, 2006), it is known that most of the force loss results from fatigue-related metabolic factors (Proske & Allen, 2005) and not muscle damage (Newham, McPhail, Mills & Edward, 1983). Once time is given to recover from the effects of fatigue (Smith & Newham, 2007), eccentric-based exercise provides an opportunity to investigate the strength deficits and kinaesthetic disruptions that result from mechanical damage to the muscles.

One study involving eccentric exercise of the elbow flexors used three assessments to observe the influence on proprioceptive function and the amplitude and frequency of physiological tremor, which relies in part on motor unit firing patterns (Stein & Lee, 1981). Joint position sense was the only dependent variable to change significantly following exercise, though the amplitude of forearm tremor did increase. In separate experiments, subjects first used their non-exercised and then their exercised arms as a reference for recreating three predetermined joint angles (a matching task and an active reproduction of joint angle task respectively), measured at 60º, 90º and 120º of elbow flexion. Joint angle position sense was unaffected after exercise when the exercised arm acted as its own reference, but when the non-exercised arm acted as the reference, the exercised arm matched it with a more flexed elbow angle. It was suggested that the increase in tremor amplitude could have been indicative of increased muscle spindle sensitivity or the increased recruitment of large motor neurons to support the load following exercise. Large motor neurons exhibit less fine motor control and this point is supported in part by the increase evident in the electromyography (EMG):force ratio observed following eccentric exercise. This could indicate additional neural activity being required to generate a given level of tension within the muscle (Komi & Viitasalo, 1977). The authors concluded that unaccustomed eccentric exercise might impair neuromuscular function and that this impairment may arise from disruptions of the afferent receptors located in the skeletal muscle and tendon (Saxton, Clarkson, James, Miles, Westerfer, Clark & Donnelly, 1995).

Eccentric exercise also disrupts kinaesthetic awareness around the knee joint. In one such study, subjects underwent a fatiguing protocol for their knee extensors on an isokinetic dynamometer. They were assessed pre and post exercise with an active repositioning task and a joint reaction to release test. For the latter, the lower leg was passively positioned at one of four different angles and once the knee extensors were confirmed to be relaxed (by manual palpation), the investigator let the limb fall. Subjects were instructed to stop the fall of the limb as soon as they perceived that is was released. The angle through which the limb fell before subjects stopped it was deemed the "knee joint reaction angle to release". After fatigue had subsided, only the reaction angle to release was impaired and only from the two angles that would have challenged the knee extensors in a shorter position and with a greater torque. The conclusion was reached that muscle damage was responsible for the persistent impairment to joint reaction angle to release. The lead author later presented a series of experiments that provided evidence of eccentric exercise exerting greater detrimental influences in the upper limbs than the lower limbs, though the upper limb sustained greater damage from the initial exercise bout in each experiment (Paschalis, Nikolaidis, Theodorou, Giakas, Jamurtas & Koutedakis, 2010).

Further investigation in to the effects of eccentric exercise of the knee extensors presented impaired joint position sense up to 48 hours post exercise, as assessed via a passive positioning and active repositioning test, though TTDPM tests were only effected at the one and 24-hour time point. The authors suggested that future studies should attempt to differentiate whether exercise interfered with muscle spindle function and/or the spinal cord circuitry (Torres, Vasques, Duarte & Cabri, 2010).

As mentioned in the earlier section on fatigue, a limb-matching task is a common method of assessing joint position sense, although it largely relies on the difference in muscle spindle feedback coming from each limb (Tsay, Savage, Allen & Proske, 2014), which makes the interpretation of results more complicated (Proske & Gandevia, 2012). It is now known that for a limb-matching task in the vertical plane, if the fall in force after the fatiguing protocol is of sufficient force magnitude, then exercise using any of the three main contraction types can be used to impair matching accuracy. This was the first study to reassess joint position sense 24 hours after the initial eccentric exercise protocol when deficits in strength were still evident, thereby controlling the possible confounding effects of fatigue on position sense, such as the accumulation of metabolites (Tsay, Allen, Leung & Proske, 2012). Previous studies had shown that when the elbow flexors from one arm were exercised and used as the reference arm, subjects matched the position with their unexercised arm in a more extended position (Walsh et al., 2004). When the same method is used at the knee, with the knee extensors of one of the legs being fatigued and then acting as the reference limb, the non-exercised leg also adopts a more flexed position (Givoni, Pham, Allen & Proske, 2007). These two studies led to the explanation that the damaged muscles were being perceived as being longer than they actually were and that perhaps the effects of exercise had increased the muscle spindle discharge rate, leading to this perception of the muscles being at an increased length (Proske & Gandevia, 2012). To test this, the antagonist muscles were exercised (the elbow extensors and the knee flexors) (Allen et al., 2010). In both instances, the results ruled out the previous assertion, with the non-exercised arm still adopting a more extended position than the exercised arm and the non-exercised leg still adopting a more flexed position than the exercised leg. If the matching errors had resulted from signaling disruptions originating in the muscles, the opposite postures should have been observed. Instead, these results lent weight to the hypothesis that changes had occurred to a central map, causing the brain to compensate for the weakened limbs by placing them in a posture that required less effort to sustain the position of the limb, a more "gravity-neutral posture" (Proske & Gandevia, 2012). In both postures, the limb's line of force from its centre of mass falls closer to its associated joint, and thereby creates less torque. They might also place the muscles at a more favourable point of the length-tension relation curve (Walsh et al., 2004).

Exercises requiring eccentric contractions can create initial deficits like those that result from isometric or concentric contractions and, depending on the exercise prescription, all have the potential to disrupt kinaesthesia. However, the deficits created by eccentric contractions can remain for ten days or more. This time frame grants an opportunity to investigate exercise effects without the influence of fatigue-related metabolic factors, provided that two hours are given after the initial exercise event (Proske & Allen, 2005). Therefore, the **third objective** of this thesis was to investigate the effect of muscle fatigue and eccentric muscle damage on an eccentrically-controlled movement sequence and the response of the damaged muscles and the nervous system to muscle vibration. The application of muscle vibration allowed us to probe changes that might have occurred to muscle spindle sensitivity and/or the nervous system's interpretation of the spindle feedback.

It has previously been suggested that the lasting effects from eccentric exercise may result from changes having occurred within the brain. Allen et al. (2010) stated that whilst the effects of exercise had a "peripheral origin", the disruption of position sense occurred centrally, "perhaps at the level of the sensorimotor cortex". The 2012 study reviewed in this section (Tsay et al., 2012) arrived at a similar conclusion, proposing that the fall in muscle force after exercise had altered the "body schema", one of many somatosensory maps of the body, represented in the brain. They suggested that the altered representation would persist until some sensory cues indicated that recovery of muscle function was complete.

1.9 Somatosensory Representations

What purpose do these representations play and how do they relate to kinaesthesia? Receptors located in the periphery provide detailed information regarding muscle length, tension, skin and joint strain, yet all this incoming code must be combined with some form of reference for it to be useful. None of these receptors tell us the dimensions of our limbs. As a result, somatosensory representations housed within the brain, form frames of reference to discern exactly where our limbs are. Additionally, we need to differentiate between body parts that are our own and those that are foreign. We now know that there are multiple somatosensory representations of the body and though purely conceptual for many years, modern research has increased our understanding of these representations (Harris, Carnevale, D'Amour, Fraser, Harrar, Hoover & Mander, 2015). As referenced earlier in this thesis, Tsay et al. (2012) proposed that if the fall in force resulting from exercise reaches a certain level, it might be enough to signal a change in one of these somatosensory representations.

1.10 Possible Sites of the Kinaesthetic disturbance

> *"... it remains controversial to explain how exercise affects limb position sense and more research is needed to achieve an agreement."* - Fortier & Basset, 2012, p.801.

Clearly questions remain over how exercise affects kinaesthesia and the degree to which the source of the disruptions occur centrally or peripherally. For many years, damage in the periphery to the muscle-based receptors was suspected. Evidence of extrafusal fiber damage following eccentric contractions (Proske & Morgan, 2001) led to the suggestion that intrafusal fibres might also be damaged (Saxton et al., 1995; Brockett, Warren, Gregory, Morgan & Proske, 1997) or fatigued (Bongiovanni & Hagbarth, 1990), thus implicating muscle spindles. It was also postulated that GTOs could be sensitized by eccentric exercise, in turn leading to overestimation of tension levels within the muscle (Brockett et al., 1997). These proposals were largely disregarded when single afferent recordings in feline GTOs and muscle spindles failed to show significant changes in their signaling properties following eccentric muscle damage (Gregory et al., 2002; Gregory, Morgan & Proske, 2004). Electrically evoked muscle contractions produce different contractile responses than those produced voluntarily, therefore the results from these animal studies are not definitive in a human model (Malm, 2001).

As previously mentioned, vibration can preferentially activate muscle spindles and invoke illusory limb movements consistent with perceived lengthening of the targeted muscle (Goodwin et al., 1972). To the best of my knowledge, the one study that attempted to quantify changes to the vibratory illusion following eccentric exercise provided ambivalent results, with the reported size of the illusion increasing at some frequencies whilst decreasing at others. The authors posited that the sensitivity of muscle spindle primary endings had decreased (Regueme, Barthèlemy, Gauthier & Nicol, 2007). Proske & Gandevia (2012) reference this as the only study proposing that the source of the kinaesthetic disturbance lies within the muscle. The original authors noted that using the non-vibrated limb to report the size of the illusion did not help answer whether changes to the illusion had occurred peripherally within the exercised limb or centrally where the proprioceptive information was being processed. In any event, it has since been suggested that the limb matching method may not involve reference to a somatosensory representation (Proske, 2015), thereby offering no indication of whether central changes have occurred.

1.11 Summary and Significance

Our ability to detect the position and movement of our bodies, known as kinaesthesia, relies on the combination of accurate signaling from peripheral receptors being referenced against perceptual body maps. One of these receptors, the muscle spindle, can be stimulated by mechanical muscle vibration, which if applied correctly can disrupt kinaesthesia. Exercise-induced fatigue also disrupts kinaesthesia and muscle damage from eccentric exercise prolongs this effect; however, it currently remains unclear exactly how or where this disruption occurs.

To my knowledge, this study is the first to use an eccentrically-controlled movement to perform Cordo's (1988) kinaesthetic movement sequence and the first to vibrate eccentrically lengthening muscles in a single limb-targeting task. It is also the first time that performance of an eccentrically-controlled single-limb task is assessed following an eccentric exercise protocol.

1.12 Summary of Objectives

The overall objective of this thesis was to further our understanding of the effects that fatigue and eccentric muscle damage have on kinaesthesia. Firstly, I aimed to determine whether muscle vibration would degrade task accuracy during an eccentrically-controlled movement sequence, as had been shown during a concentric movement sequence (Cordo et al., 1995) and during an eccentric targeted movement (Inglis et al., 1991). Secondly, I investigated the effect of muscle fatigue and eccentric muscle damage on an eccentrically-controlled movement sequence and the response of the damaged muscle and nervous system to muscle vibration.

1.13 Task Outline

Participants performed a slow eccentric extension of the right elbow through the horizontal plane without vision of the right arm (see Figure 2.1). One of two light emitting diodes (LEDs), situated along the lever arm's path of motion, illuminated prior to movement and served as the target for the given trial. The participant's task was to open the right hand when they judged it to be passing through the target position (e.g. "release the Frisbee" at the target position). On half of the trials the elbow flexor muscles of the right arm were vibrated. An exercise protocol comprised of eccentric contractions was employed to fatigue and damage the elbow flexors before the task was repeated both immediately after the exercise and following a two-hour rest.

1.14 Hypotheses

Inglis et al. (1991) and Cordo et al. (1995) both observed that the application of muscle vibration caused participants to underestimate their arm position during their respective tasks. As such, the **first hypothesis** was that muscle vibration would decrease task accuracy, causing participants to undershoot the targets (e.g. open their hand short of the target).

The **second hypothesis** was that exercise would decrease task performance after exercise-induced fatigue and eccentric muscle damage. There are two measures for task performance, accuracy (constant error) and consistency (variable error). My sub-set of hypotheses for the second hypothesis were as follows:

i) Accuracy (constant error) would not be affected by the exercise protocol. I formed this hypothesis following work showing that errors in joint position sense were not directionally dependent upon the exercised muscle (Allen et al., 2010).

ii) Consistency (variable error) would increase after the exercise protocol. I hypothesized that participants' mean hand opening would be centered about the target, but with increased variable error after the exercise protocol. This was based on previous work showing that the amplitude of limb tremor rises following eccentric exercise (Saxton et al., 1995). Significant increases in variable error following eccentric exercise had also been reported by others (Tsay et al., 2012).

iii) Two hours post-exercise, performance would improve for the trials compared to the immediate post-exercise trials, but not to the same level of performance as prior to exercise. This pattern of improved performance following a period of rest has previously been reported (Allen & Proske, 2006; Tsay et al., 2012).

The **third hypothesis** was that immediately following exercise and after two hours of recovery, muscle vibration would continue to cause participants to undershoot the targets (e.g. open their hand short of the target). This hypothesis was established following previous work showing the persistence of a vibratory illusion following eccentric exercise (Regueme et al., 2007).

Chapter 2: Methods

2.1 Participants

Twelve male participants were recruited from the University of British Columbia and surrounding area. The participants' mean (± standard deviation) age, height and weight were 25.1 ±3.4 year, 180.2 ± 6 cm and 72.4 ± 8.8 kg, respectively. Only males were studied, due to previous work showing sex-specific differences in response to fatiguing protocols (Wüst, Morse, De Haan, Jones & Degens, 2008; Sewright, Hubal, Kearns, Holbrook & Clarkson, 2008; Pederson et al., 1999). Right-hand dominant individuals (Tidoni, Fusco, Leonardis, Frisoli, Bergamasco & Aglioti, 2015) (determined by participants' hand they used for writing) were invited to participate. Individuals with known neurological deficits and any existing right upper limb orthopedic injuries sustained during the previous 12 months were excluded from the study. Six of the participants regularly partook in resistance training, though all had abstained from any upper body exercises for the week prior to the study. Three of the participants were familiar with studies involving mechanical muscle vibration. Participants received a $40 payment for their involvement in the complete study. The University of British Columbia Clinical Research Ethics Board approved all procedures and all participants gave their written informed consent prior to participation.

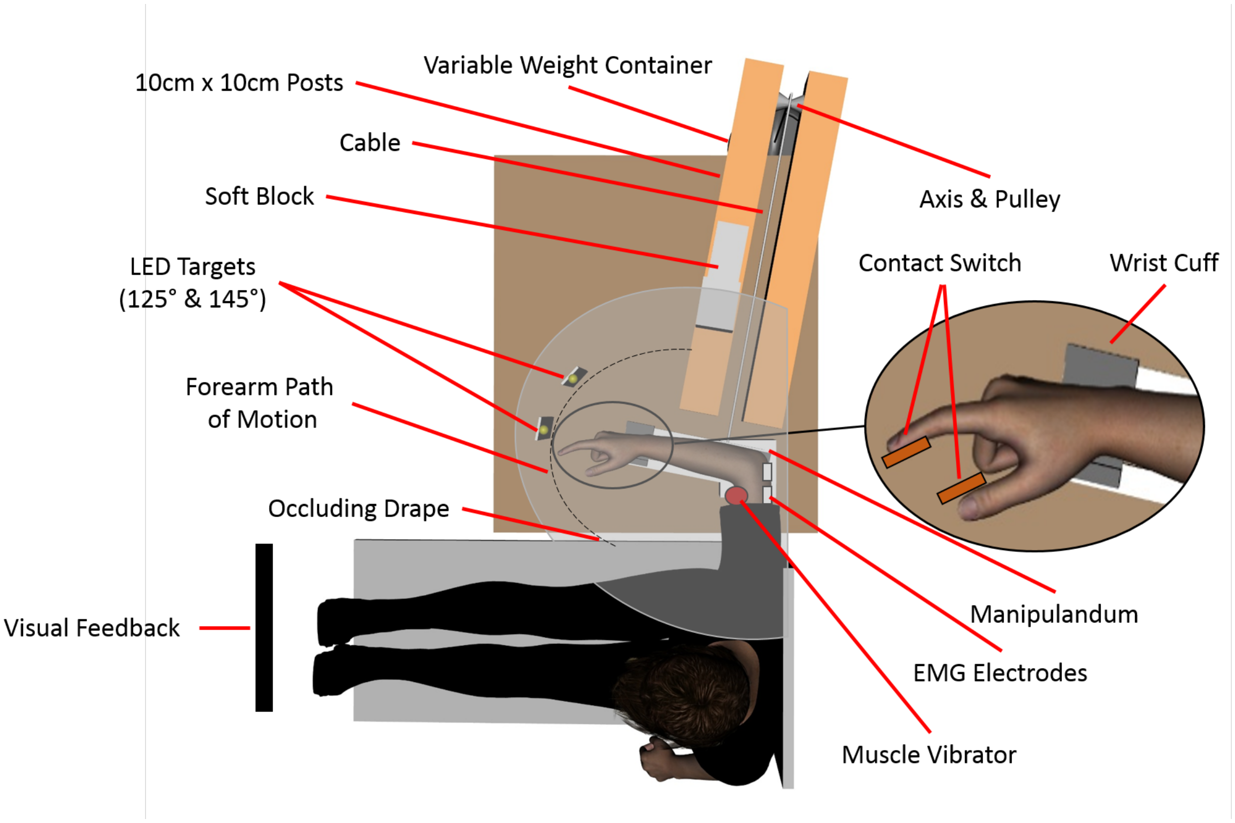

Figure 2.1 Apparatus

2.2 Apparatus

2.2.1 Custom-Built Apparatus

The apparatus is schematically depicted in Figure 2.1. A custom built manipulandum was mounted on top of a sturdy table, with two 10cm x 10cm posts fixed to the tabletop, extending approximately 30 centimeters from its edge. A modified skateboard wheel mounted on an axis at the end of the posts served as a pulley. A cable was attached to the lever arm (≈20 cm from the axis), and ran over the skateboard wheel, where it attached to a container of variable weights via a carabiner. This setup rotated the lever arm about its axis and required participants to perform an eccentrically-controlled extension of the elbow joint during the task. The changing moment arm of the cable to the axis of the lever arm provided variable torque throughout the movement. Peak torque occurred during the mid-range of the movement and decreased as the elbow neared both full flexion and full extension. This setup was designed to match the ascending-descending strength curve of the elbow flexors (Kulig, Andrews & Hay,

1984) and provided a consistent challenge throughout the range. An adjustable padded block served as a hard-stop for preventing any over-extension of the elbow joint during testing.

2.2.2 Targets and Starting Position

Assigning 180º to denote a straight-armed, full elbow extension posture, two targets were situated at 125º and 145º of the lever arm's arc. Two LEDs were visible above the occluding screen, indicating each target. Previously, eccentrically controlled targeted movements were only effected by muscle vibration on trials involving a target located 60º from the starting position (though the speed used for this movement was almost three times as fast) (Inglis et al., 1991). Therefore, the use of two targets rather than one allowed us to investigate the effect of muscle vibration on varying target distances. For each trial, the lever arm was held at a variable starting position between 55º and 60º to dissuade participants from relying on timing cues to trigger their responses. It has previously been shown that subjects are more accurate at judging angular distance than joint angle (Bevan, Cordo, Carlton & Carlton 1994), hence the need for this starting range.

2.2.3 Potentiometer

A single-turn linear potentiometer (Vishay Spectrol 157, linearity ±2.0%) was fitted to the axis of the lever arm, allowing measurement of the elbow joint angle. The voltage from the potentiometer was also patched to an oscilloscope (BK Precision, model 2522B) so that the lever arm position could be represented on the screen. The assistant used this when positioning the arm for each trial, but it was not visible to participants.

2.2.4 Muscle Vibrator

A mechanical muscle vibrator (custom-built DC motor, measuring 24mm x 52mm) was positioned over the distal biceps brachii of the right arm just proximal to the elbow joint and fixed in place with a compression bandage and Velcro^{TM} strap. A semi-permanent marker pen was used to outline the vibrator's position on the arm and this was used as a reference when repositioning it after the rest period. Variable voltage from a DC power supply (Zhaoxin PS-

3005D) drove the vibrator at a frequency of 85 Hz and vibration amplitude of approximately 1-2mm. This frequency and amplitude were chosen based on previous microneurography research that demonstrated preferential activation of the primary endings of muscle spindles using these parameters (Burke, Hagbarth, Löfstedt & Wallin, 1976; Roll et al., 1989; Roll & Vedel, 1982). Furthermore, previous work had found that similar frequencies evoked the largest perception of illusory movements (Regueme et al., 2007).

2.2.5 Fingertip Switch

Contacts were fitted to the thumb and index finger of the right hand and linked to a simple battery circuit to serve as an 'on / off' switch that monitored hand opening. When the thumb and index finger touched, the circuit was closed and gave a voltage of 1.5V indicating the 'on' position. When they separated, the circuit broke and resulted in 0V being recorded, indicating the 'off' position.

2.2.6 Analog Load Cell

An analog load cell (Artech Industries Inc., 20210-500) was fastened via a carabiner to a steel eyelet mounted on one of the 10x10cm posts. When required, the main cable was detached from the weight container and a loading cable was used to attach the variable load to the gauge via its carabiner. The load cell could also be attached directly to the lever arm, preventing elbow flexion beyond 80º, and this enabled us to record maximal voluntary contractions (MVCs) in this position.

2.2.7 Computer Interface and Visual Feedback

Custom applications designed in LabVIEW (Version 8.0, National Instruments, USA) on an Intel™ computer (Pentium D CPU 3.4GHz with 2 GB of RAM running Microsoft Windows XP, Version 2002 with a ViewSonic VA1912wb-3, VS10866 monitor) were used to select the target for each trial and activate the vibrator when required. A computer monitor (ViewSonic VX715 VS10057), situated at eye level two meters in front of the participants, provided visual feedback during the training trials and recordings of MVCs.

2.2.8 Sampling (Analog to Digital Conversion)

An analog to digital converter (National Instruments, USA) sampled the signals from the potentiometer of the manipulandum, break switch from the thumb and index finger, load cell (via a Micron Series 2 Digital Panel Meter, model M200000WMI) and two channels of EMG. These signals were sampled at 1000 Hz using LabVIEW (National Instruments, USA) for data collection and later analysis. Surface EMG was amplified (x10K), bandpass filtered between 30 and 3 KHz (Grass Instruments P511) and digitally sampled at 1000 Hz.

2.3 Procedures

After a brief familiarization with the apparatus and a verbal explanation of the experiment and the risks involved, participants read and signed the consent form. All procedures were conducted in the Neurophysiology Laboratory at The University of British Columbia.

2.3.1 Surface Electromyography (EMG) Setup

To assess the relative contribution of elbow flexors and extensors to the performance of the eccentrically-controlled movement sequence, surface EMG was collected to monitor the elbow musculature activity. Alcohol wipes were used to clean the skin before pairs of surface electrodes were placed over the right biceps brachii and triceps brachii (lateral head) muscle bellies, spaced 2 cm apart. Ground electrodes were placed on the right sterno-clavicular joint and right acromion process.

2.3.2 Seating Position and Restraint

Participants sat upright in an adjustable chair next to the table, with their right arm positioned in the manipulandum. A five-point racing harness stabilized their torso and restricted trunk rotation, flexion and side-bend, thereby minimizing any changes in shoulder position. Seat height, seat back inclination and proximity to the table were adjusted until the medial and lateral condyles of the right humerus (indicative of the elbow’s axis of extension and flexion) were coincident with the axis of the manipulandum and the upper arm was located 30º anteriorly from the frontal plane of the body, as measured by a protractor. The upper arm's degree of glenohumeral abduction fell between 75º and 90º. A moveable lever arm supported the forearm and hand, incorporating an adjustable wrist cuff to prevent flexion and extension movements at the wrist. The proximity of the wrist cuff to the lever arm's axis was adjusted based on the length of the participants' forearm and the distal radio-ulnar joint was braced in a semi-supinated position (also assessed for each participant). Once participants were comfortable in the seat and the manipulandum, the fingertip switch, EMG wires and mechanical muscle vibrator were all positioned accordingly. Finally, a black occluding screen was placed over the forearm and hand to block participants' vision. The assistant ensured that the arm did not come in to contact with the occluding screen at any point during the range of arm movement, as this could have provided cues via cutaneous and visual feedback.

2.3.3 Assessment of Elbow Extension

Participants were asked to fully extend their elbow on three separate occasions prior to commencing any trials. The hard stop was adjusted to rest against their forearm and the lever arm in this fully extended position. This action safe-guarded against over extension of the elbow joint. This assessment was repeated during each rest interval of the exercise protocol. This was to ensure that participants were only being fatigued through their active range of motion and to minimize any undue strain on passive structures of the elbow joint.

2.3.4 Maximal Voluntary Contraction (MVC)

Maximal Voluntary Contractions (MVCs) determined the amount of load that participants used during the trials and acted as a reference value when determining eccentric muscle damage. With the load cell attached to the lever arm and the elbow at an 80-90º angle, participants were instructed to try and flex their elbow as strongly as possible for three seconds. This was repeated twice, following 30-second rest intervals. The average of the second and third recorded values served as the MVC for that time point. Verbal encouragement was strongly provided during each attempt. This same format was used to determine participants' MVC prior to the second and third blocks of trials.

2.3.5 Setting of the Load

The container of variable load was detached from the main cable and connected to the loading cable. This was then put in place of the main cable over the pulley and attached to the analog load cell. Weight was added until 10% of the participant's MVC was achieved. This percentage was chosen to minimise fatigue during the targeting trials, prevent the influence of contraction history and avoid abolishing the vibratory illusion effect, which occurs with loads of 25 to 30% of MVC (Ansems et al., 2006; Goodwin et al., 1972). With the manipulandum lever arm blocked at full extension, the container was then reattached to the main cable.

2.3.6 Thixotropy and Contraction History

Thixotropy is a property of both intrafusal and extrafusal muscle fibres and can alter the discharge rate of muscle spindles (Proske et al., 2014). In pointing and limb matching tasks, thixotropy has been shown to cause both undershoot and overshoot, depending on the muscle's contraction history before the task (Walsh, Smith, Gandevia & Taylor, 2009; Walsh, Proske, Allen & Gandevia, 2013). To control for this, the limb was randomly moved back and forth in a passive state by the assistant, before positioning it at the pseudo-random start position between each trial. As mentioned in the previous paragraph, controlling the 10% of MVC load also served to remove any errors induced by contraction history.

2.3.7 Training

The assistant positioned the lever arm and held it within the starting range of 55-60º. Visual feedback on the monitor showed a red vertical line moving from left to right, representative of the lever arm's position. When triggered, a green vertical line moved in the same direction, representing a lever arm speed of 22º per second. This velocity was chosen to allow for adequate time for the muscle vibration to have a perceptual effect (Cordo et al., 1995). Participants were asked to control the speed of their arm so that the vertical lines tracked each other. Once participants could match the prescribed average velocity within ±2º for five consecutive trials (Carlsen, Hunt, Inglis, Sanderson & Chua, 2003), the experiment began. These training periods lasted no more than 5 minutes in total.

2.3.8 Experimental Protocol and Order of Events

The study consisted of three blocks, each consisting of 40 trials. This comprised 20 trials using the 125º target (10 trials with elbow flexor vibration/10 without) and 20 trials using the 145º target (10 trials with elbow flexor vibration/10 without). The four different trial types were presented in a semi-randomized fashion, whereby each trial type could not be presented consecutively more than once. After every 10 trials, a training trial was performed to help participants maintain the desired movement velocity. For all trials, the arm was passively positioned within the starting range by the assistant in the same manner used during the training paradigm. Participants were informed that one of the two target LEDs would illuminate at the start of each trial, and they were instructed to open their thumb and index finger when they judged their thumb and index finger to be passing through the target position. On trials with vibration present, the vibrator was turned on approximately 500ms before the lever arm was released by the assistant. Following completion of the eccentric elbow extension, a 'wash out' movement was performed in which the assistant randomly moved the passive elbow joint through flexion and extension to prevent participants using start and end point positioning cues on subsequent trials. On trials with vibration present, the vibrator was manually turned off approximately 500ms after the elbow had reached full extension. Upon completion of each block, a MVC was recorded to ensure that the forty trials had not induced any fatigue, and this was determined by making sure that the value had not dropped by more than 10%.

Each block of trials took approximately 20 minutes to complete. *Block One* acted as a control, *Block Two* followed an exercise protocol and finally *Block Three* was completed following a two-hour rest period. Subjects were instructed to refrain from partaking in any further exercise or recovery strategies (such as icing or massage) during the rest period, but were free to leave the testing area. EMG electrodes remained in place on their arm.

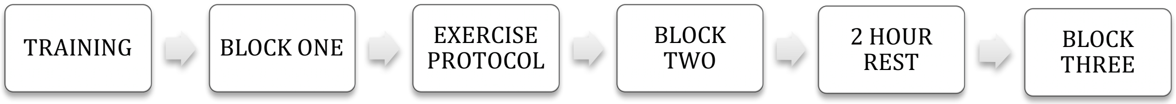

Figure 2.2 Order of Events. Participants underwent training, completed the first block of 40 trials (Block One), went through the exercise protocol and completed the second block of 40 trials (Block Two). Following 2 hours of rest, they completed the final block of 40 trials (Block Three).

2.3.9 Exercise Protocol and Determining Eccentric Damage

Eccentric contractions, in which a muscle lengthens under tension, have the potential to cause muscle damage (Proske & Allen, 2005), hence the term *eccentric muscle damage* (Prasartwuth, Allen, Butler, Gandevia & Taylor, 2006). It can occur following a bout of unaccustomed activity, such as walking or running downhill, which are often used to induce eccentric muscle damage (Maeo, Yamamoto & Kanehisa, 2016; Ely, Romero, Sieck, Magnum, Luttrell & Halliwill, 1985; Starzak, Semple, Smith & McKune, 2016). ‘Eccentric training’ is a method employed to increase strength and muscle growth in exercise programs (Douglas, Pearson, Ross & McGuigan, 2016). In this task, participants only had their right arm exposed to an eccentric training protocol. The aim of the exercise protocol was to create a 40% deficit in participants’ originally recorded MVC. MVC has been shown to be one of the most reliable markers of eccentric muscle damage (Warren, Lowe & Armstrong, 2009) while a 40% drop from pre-exercise levels is commonly used as a threshold (Prasartwuth et al., 2006; Turner, Tucker, Rogasch & Semmler, 2008) and has also been shown as an average reduction following a bout of eccentric exercise (Proske, Gregory, Morgan, Percival, Weerakkody & Canny, 2004). The container of weight was again detached from the main cable and connected to the loading cable and additional weight was added to attain 50% (Nosaka & Newton, 2002) of the participant’s original MVC. A submaximal load was chosen due to the similarity in deficits initially created by a supra-maximal load, but with the benefit of an accelerated and more comfortable recovery (Nosaka & Newton, 2002; Peake, Nosaka, Muthalib & Suzuki, 2006). A submaximal load is also more likely to be encountered in everyday life or a sporting context and central and peripheral fatigue both develop more slowly when compared to using a maximal load (Taylor & Gandevia, 2008).

Once reattached to the lever arm, the assistant positioned the arm back into the same starting position as used during the trials (55º-60º) via the end of the lever arm. The participant was informed of the additional load and instructed that upon release they must attempt to move their arm into extension in a controlled fashion at the same testing speed of 22º per second. Visual feedback was made available in the form of the training screen to facilitate this. Participants performed the exercise protocol on the same apparatus they had performed the task on, because inducing fatigue and testing on the same device increases the specificity of the testing protocol (Warren et al., 1999).

Elbow angle range and muscle lengths challenged during an exercise influence the extent of muscle damage, with longer muscle lengths previously being shown to cause more damage than shorter lengths (Nosaka & Sakamoto, 2001). However, a greater magnitude of damage to elbow flexors has been induced from 120º of elbow motion rather than 60º of motion, even when both ranges are performed at long muscle lengths (Fochi, Damas, Berton, Alvarez, Miquelini, Salvini & Libardi, 2016). As such, the aim was to equally fatigue the elbow flexors throughout the entire range used during the targeting task. To accomplish this, ten repetitions were performed for each set, with each repetition taking approximately 5.5 seconds; a similar time was taken to reposition the arm after each repetition. Two-minute rest intervals were given between sets, with an MVC reassessment performed at the one-minute mark. If the initial MVC showed a decrease of 40% or more from the pre Block One MVC value, a second MVC was performed 30 seconds later to confirm the drop below this level. When participants' MVC had dropped by 40% or more of their pre Block One (pre-exercise) value, the exercise protocol was stopped (see Figure 2.3). Active range of motion was also reassessed during each rest interval and the hard-stop adjusted accordingly, this was done to prevent over-extension of the elbow joint if the participants' available range of motion started to decrease. Although set and repetition configuration has shown to have no effect on the degree of muscle damage induced (Chan, Newton & Nosaka, 2012), the chosen scheme avoided excessive set duration, which could have led to lapses in concentration, and it allowed for reassessment of the initial MVC every three minutes (approximately two-minute set duration, plus a minute of the rest interval). Previously, Nosaka and Newton (2002) needed 3 sets of 10 repetitions with 3-minute rest intervals to induce an average MVC drop of 40%, albeit with a faster repetition speed (3 seconds per repetition). In this study, participants completed between 3 and 10 sets of the exercise protocol.

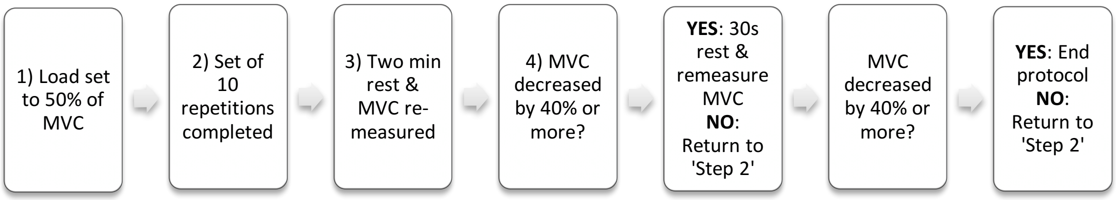

Figure 2.3 Exercise Protocol. Participants performed sets of ten eccentric repetitions between 2 minute rest intervals. During the intervals, they performed an MVC. If their MVC had decreased by 40% of more, they rested 30 seconds and completed a further MVC to confirm the decrease. Once the decrease was confirmed, the exercise protocol ended. Sets were performed until this 40% drop occurred.

2.3.10 Block Two (Post Exercise)

Before beginning the next block of trials, the elbow extension active range of motion assessment was performed and after 4 minutes had elapsed since the cessation of the final rep of the exercise, participants' MVC was reassessed. At this point, participants' elbow flexors were fatigued and damaged, therefore the load used during the experimental protocol had to be adjusted accordingly for each individual. If this measure were not taken, participants would have performed the task with a load greater than 10% of their MVC at that time point; therefore following reassessment, 10% of their new MVC was added to the container. Participants then repeated the experiment as performed during the Block One (pre-exercise) trials. Another MVC was recorded upon completion of the block to ensure that the trials did not induce any further fatigue. Following instructions not to partake in any recovery strategies or further exercise, participants then returned 2 hours later. This period of time was chosen to allow local metabolites accumulated during the exercise to subside (Smith & Newham, 2007). Any force deficits evident after this period are likely the result of muscle damage and not fatigue (Proske & Allen, 2005; Prasartwuth, Taylor & Gandevia, 2005) and it is also long before any delayed onset muscle soreness (DOMS) occurs (MacIntyre, Reid & McKenzie, 1995). DOMS could have acted as a confounding variable due to its effect on the sense of force (Weerakkody et al., 2003) and the sense of effort (Proske, Weerakkody, Percival, Morgan, Gregory & Canny, 2003). Furthermore, in a study using flexion-targeted movements, the highest deterioration in performance was seen 2 hours post exercise (Bottas, Miettunen, Komi & Linnamo, 2011).

2.3.11 Block Three (2-Hours Post Exercise)

Following reassessment of the active extension of the elbow joint for the final time, participants' MVC was recorded again. 10% of this MVC value was added to the container. Participants then completed five training trials and the experimental protocol one last time. A final MVC was recorded to ensure that the trials did not induce any further fatigue.

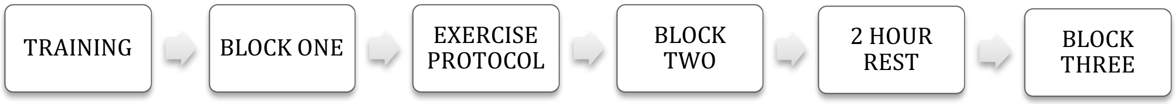

Figure 2.4 Summary of the Experimental Protocol.

2.4 Data Analysis

2.4.1 Performance Accuracy

Task accuracy or constant error was determined by finding the lever arm angle (converted from the potentiometer's voltage) at the time of fingertip contact switch break. This was then compared to the angle of the target designated for the given trial, either 125º or 145º. The difference was presented as ± degrees. Variable error was calculated from the position of mean hand opening (degrees). Constant error and variable error were calculated for all conditions. MVCs collected at all time points including measures made between sets of the exercise protocol are reported. Mean values (± SEM) were calculated and presented. Movement onset of the arm was visually identified from the lever arm position data for each trial. Movement Time (milliseconds), was defined from the movement onset to the time of hand opening. The position data were filtered with a dual pass, 2nd order, Butterworth filter with a cut-off of 5Hz. Instantaneous velocity was calculated using a central finite difference calculation. Mean velocity (degrees per second) was calculated over the same interval as the movement time, as were the RMS (root mean squared) EMG signals from the biceps and triceps.

2.5 Statistical Analysis

To analyze performance accuracy (constant error / CE) and variability (variable error / VE), separate 3 Block (Block One, Block Two and Block Three) x 2 Target (125º and 145º) x 2 Vibration Condition (control, vibration) repeated-measures ANOVAs were conducted. The same ANOVA designs were applied to mean velocity and movement time.

RMS of EMG activity (volts) for the biceps and triceps were analyzed using a 3 Block (Block One, Block Two, Block Three) x 2 Target (125º, 145º) x 2 Vibration Condition (control, vibration) x 2 Muscle (biceps, triceps) repeated-measures ANOVA.

Statistical significance was set at $p < .05$ and for all significant main effects and interactions. If sphericity was violated (based on Mauchly's test of sphericity), the p-value for the effect was adjusted with Greenhouse-Geisser correction (uncorrected degrees of freedom are reported in the text). Where required, post-hoc analyses were performed using additional repeated-measures ANOVAs to decompose the simple main effects.

Chapter 3: Results

3.1 Participant and Trial Exclusions

Trials that fell ±2 SD's from the mean hand opening were removed. This accounted for 3.8% of the total data collected. The data sets from two of the participants were not included in the analysis. One of these omissions was due to the participant's inability to perform the task correctly and the other because the participant lacked sufficient accuracy during the initial block of control trials. This left ten participants to be included in the final data analysis.

3.2 General Task Performance

Following training, participants' mean velocity during the control trials of Block One was close to the prescribed velocity (22.26 ± 1.70 degrees/second). Participants' performance during the initial block showed that they were slightly more accurate when aiming to the second target (1.35 ± 1.99 degrees) than the first target (-5.74 ± 2.24 degrees) (see Table 3.1). This trend continued for the two remaining blocks following the exercise protocol.

3.3 Vibration's Effect on Task Performance

Overall, vibration caused participants to undershoot (mean negative constant error) and open their hand short of the intended target. Participants undershot the targets during Block 1, showing that this effect was evident from the beginning of the protocol (see Figure 3.2 for a representation of the mean undershoot for the two conditions and Figure 3.1 'Block One, Control' for an example trial from a single participant). This was confirmed by a main effect of vibration on constant error (CE), F(1, 9) = 43.820, p < .001, η_p^2=.830 as well as a subsequent post-hoc comparison of constant error between control and vibration trials during Block 1 (p = .001). Unlike these constant error results, vibration had no influence on the variability of task performance (variable error of position at hand opening) during any of the blocks, F(1, 9) = 1.166, p = .308.

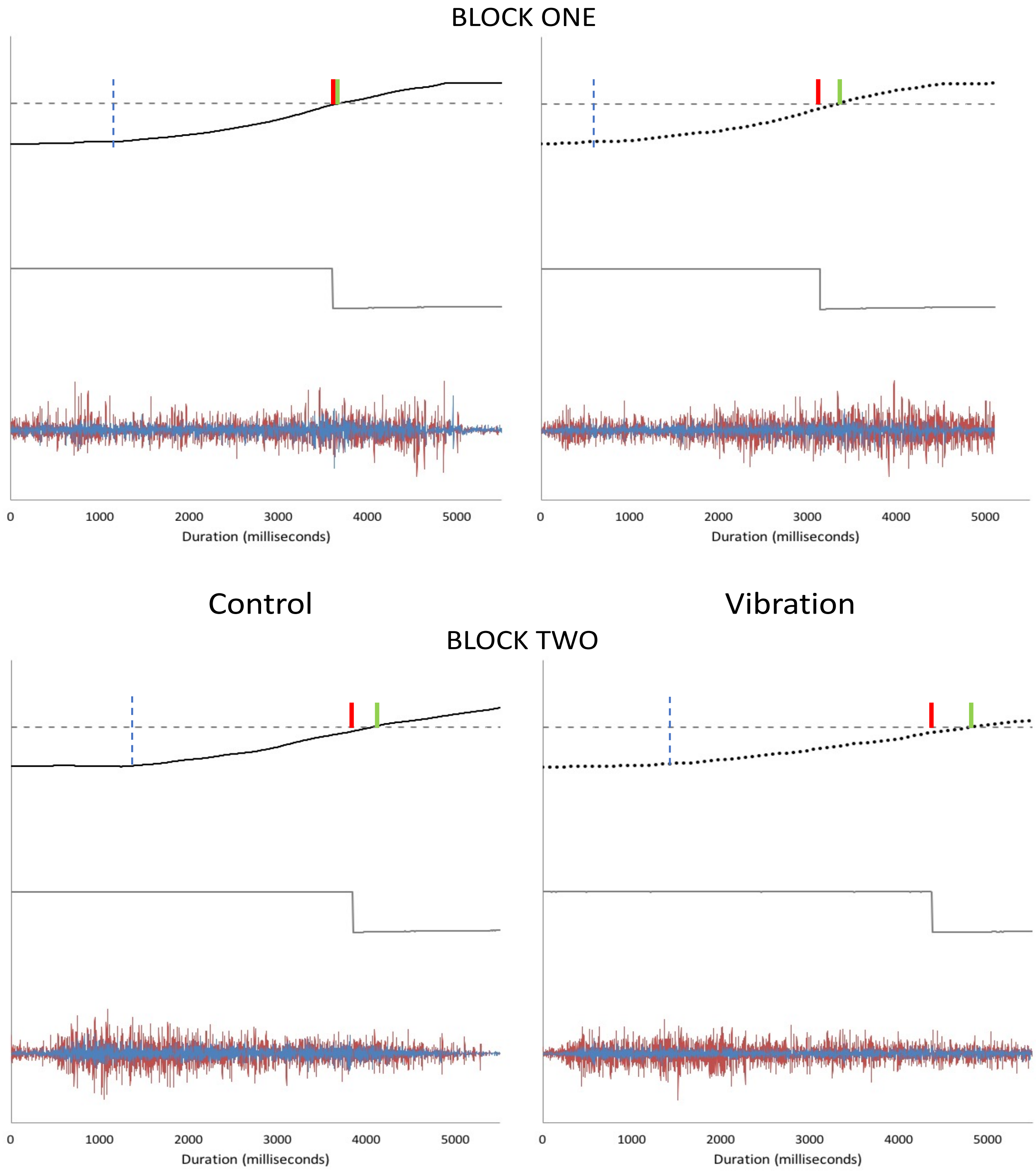

Figure 3.1 The effect of vibration and exercise on task performance. Four trials of data from one participant. Solid line = lever arm position on control trials. Dotted line = lever arm position on vibration trials. Vertical Blue Dashed Line = movement onset. Green line = target location. Red line = hand opening. Red Trace = biceps EMG. Blue Trace = triceps EMG. Both EMG traces are scaled to the biceps EMG maximum to show the relative magnitude of the more active muscle (biceps in red).

Target	Condition	Block One	Block Two	Block Three
One (125º)	Control	-5.74 ± 2.24	-12.29 ± 3.91	-10.82 ± 3.26
	Vibration	-12.56 ± 2.64	-16.90 ± 4.60	-15.83 ± 3.46
Two (145º)	Control	1.35 ± 1.99	-3.12 ± 2.52	-0.83 ± 2.81
	Vibration	-5.01 ± 1.93	-8.84 ± 2.47	-5.41 ± 2.12

Table 3.1 Mean constant error of hand opening and SEM in degrees.

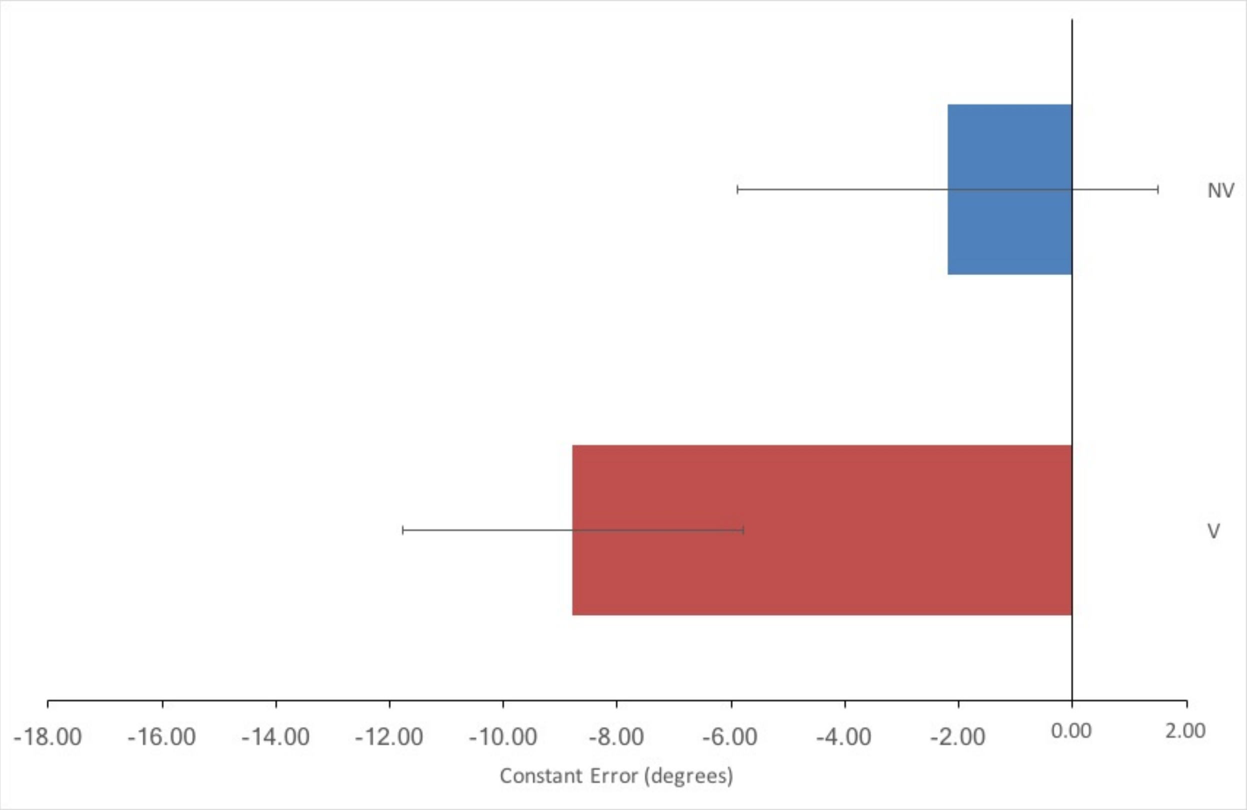

Figure 3.2 The effect of vibration on mean hand opening (targets collapsed) during Block One. '0' degrees represents target position. 'NV' is the mean of the control trials, 'V' is the mean of the vibration trials. Vibration caused participants to undershoot the targets. Error bars represent within subjects 95% confidence intervals.

3.4 Exercise's Effect on Task Performance

In general, the exercise effects led to increased undershooting of the targets (see Figure 3.1 'Block Two, Control' for an example trial from a single participant). The main effect of Block was near conventional levels of significance, F(2, 18) = 3.198, p = .065. This effect was mediated by an interaction with Vibration condition, F(2, 18) = 3.917, p = .039, η_p^2=.303. Subsequent analyses of the effects of exercise on performance showed that the exercise-induced undershooting effect was significant during the control trials, F(2, 18) = 4.786, p = .022, η_p^2=.347, but not for the vibration trials, F(2, 18) = 1.999, p = .164. Thus, whereas the effects of exercise increased the extent of undershooting during control trials (see Figure 3.3), it did not significantly affect the extent of undershooting during vibration trials. There was also a Block x Target interaction, F(2, 18) = 24.074, p < .001, η_p^2=.728. This resulted in the exercise protocol causing participants to undershoot the first target (125º) more than they undershot the second target (145º). The effects of exercise did not significantly change the level of variability in hand-opening position, with the main effect of Block failing to reach significance, F(2, 18) = 1.675, p = .215.

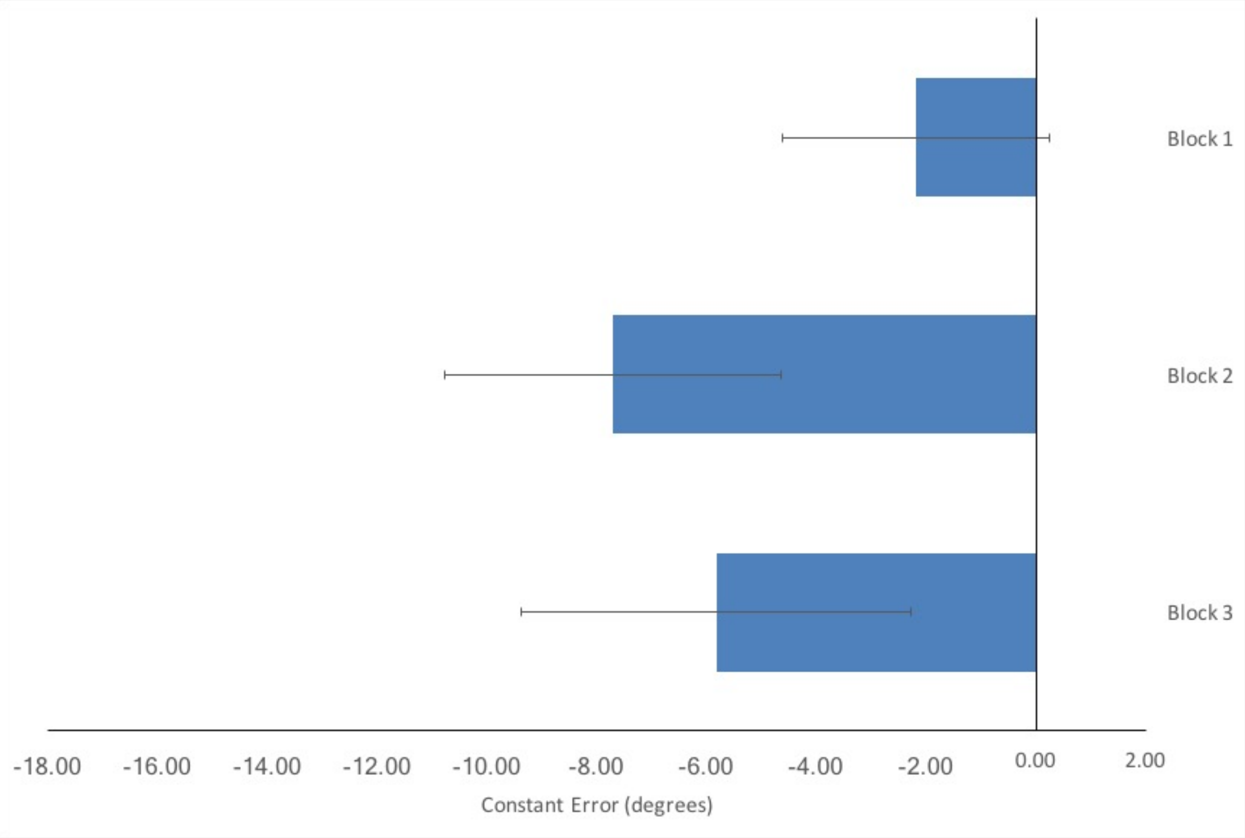

Figure 3.3 The effect of the exercise protocol on mean hand opening of the control trials (targets collapsed) during Blocks One, Two and Three. Following the exercise protocol, participants undershot the targets during the control trials. Error bars represent within subjects 95% confidence intervals.

3.5 Vibration's Effect Across Blocks

The main effect of Vibration Condition (see Section 3.3) was also affected by Block, as shown in the Block x Vibration Condition interaction (see Section 3.4). Post-hoc analysis showed that the effect of vibration (greater undershooting of the targets during vibration trials compared to control trials) was significant during all three blocks ($p < .001$). This was true for movements to both targets. Thus, the vibration effect was present for each of the blocks (see Figure 3.4 for an overview and see Figure 3.1 'Block Two, Vibration' for an example trial following the exercise protocol from a single participant). To further evaluate whether the magnitude of the vibration effect changed across blocks, the difference scores were calculated between the vibration trials and the control trials. These values were analysed with a 3 Block x 2 Target repeated-measures ANOVA. There was a main effect of Block, $F(2, 18) = 3.917$, $p <$

.039, η_p^2=.303. Post hoc analysis revealed that the magnitude of the vibratory effect did decrease from block to block, though this decrease was only statistically significant between Block One and Block Three (p = .005). It is not possible to conclude that this was a result of the exercise protocol (see Discussion for further details).

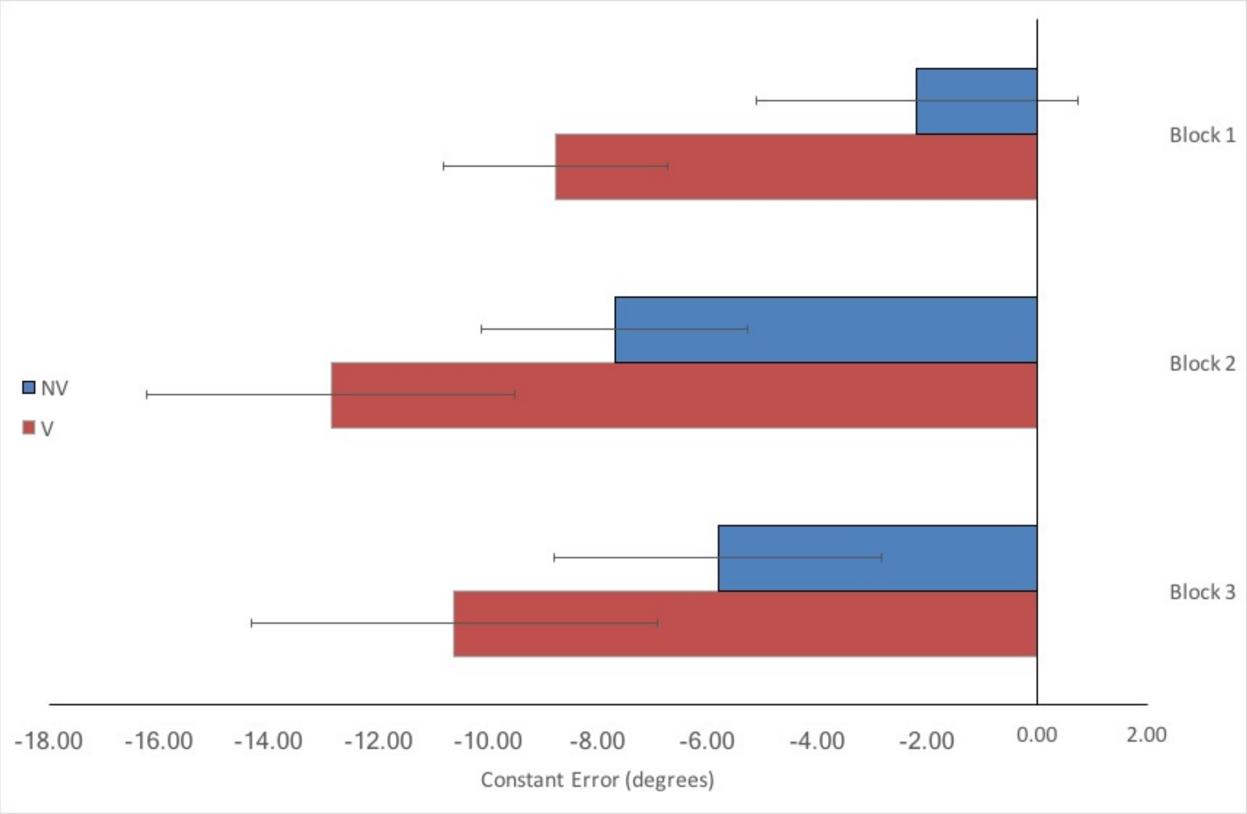

Figure 3.4 The effect of the exercise protocol on mean hand opening (targets collapsed) for both the control trials and the vibration trials during Blocks One, Two and Three. The vibration effect was significant during each of the blocks. Error bars represent within subjects 95% confidence intervals.

3.6 Velocity

Participants moved at a lower mean velocity during vibration compared to control trials, F(1, 9) = 38.631, p < .001, η_p^2=.811. This main effect of Vibration Condition was mediated by an interaction with Target, F(1, 9) = 22.706, p = .001, η_p^2=.716. This interaction was a result of the vibration-induced slowing (lower mean velocity) affecting movements to the short target more than movements to the long target. While mean velocity also appeared to decrease following exercise, this effect did not reach significance, ($p = .156$).

3.7 Movement Times

Not surprisingly, participants took longer to move to the second target, $F(1, 9) = 140.656$, $p < .001$, η_p^2=.940. There were no effects of the exercise protocol, $F(2, 18) = 0.036$, $p = .965$, nor vibration, $F(1, 9) = 2.750$, $p = .132$, on the average movement time.

3.8 Biceps and Triceps EMG

The effects of exercise led to a general increase in activity, $F(2, 18) = 22.711$, $p < .001$, η_p^2=.716, with EMG RMS being higher during Blocks Two and Three compared to Block One for both trial conditions. Furthermore, there was a Block x Muscle interaction, $F(2, 18) = 15.163$, $p = .002$, η_p^2=.628, with the EMG RMS increase following exercise being much greater for biceps than for triceps. Vibration led to a slight increase in EMG RMS activity for both muscles and this was statistically significant, $F(1, 9) = 32.454$, $p < .001$, η_p^2=.783. As expected, the biceps' activity was generally greater than that of the triceps', $F(1, 9) = 26.401$, $p < .001$, η_p^2=.746.

	Block One				**Block Two**				**Block Three**			
	T1 (125º)		T2 (145º)		T1 (125º)		T2 (145º)		T1 (125º)		T2 (145º)	
	NV	V	NV	V	NV	V	NV	V	NV	V	NV	V
Velocity	22.26 ± 1.70	18.6 ± 1.16	21.70 ± 1.61	19.74 ± 1.25	18.40 ± 1.04	16.94 ± 1.35	18.69 ± .93	17.57 ± .94	19.90 ± .94	17.93 ± .97	19.62 ± 1.05	18.25 ± 1.10
Movement Time	3074.22 ± 349.42	3280.25 ± 372.11	4435.27 ± 401.43	4518.31 ± 361.76	3150.05 ± 355.33	3150.02 ± 373.38	4642.88 ± 341.51	4619.04 ± 352.05	3037.11 ± 330.07	3087.32 ± 338.06	4604.17 ± 366.17	4723.52 ± 363.17
Biceps RMS of EMG	.42 ± .08	.48 ± .08	.50 ± .07	.59 ± .08	1.49 ± .27	1.56 ± .25	1.38 ± .25	1.47 ± .26	1.56 ± .28	1.64 ± .28	1.52 ± .26	1.64 ± .28
Triceps RMS of EMG	.16 ± .02	.17 ± .03	.17 ± .03	.18 ± .03	.39 ± .06	.42 ± .06	.36 ± .05	.41 ± .05	.40 ± .05	.44 ± .05	.39 ± .06	.42 ± .06

Table 3.2 Mean values and SEM's for Velocity (degrees/second), Movement Time (milliseconds) and Biceps and Triceps RMS of EMG (volts). T1 (125º) = Target One. T2 (145º) = Target Two. NV = Control Condition. V = Vibration Condition

Chapter 4: Discussion

The overall objective of this thesis was to further our understanding of the effects that fatigue and eccentric muscle damage have on kinaesthesia. I employed an eccentrically-controlled movement sequence and measured the impact of muscle vibration and exercise effects on task performance. Participants conducted a slow eccentric extension of the right elbow through the horizontal plane without vision of the right arm. The participants' task was to open their right hand when they judged it to be passing one of two targets, designated at the start of each trial. On half of the trials the elbow flexor muscles of the right arm were vibrated. An exercise protocol comprised of eccentric contractions was applied in order to fatigue and damage the elbow flexors. The task was then repeated both immediately after the exercise and following two-hours of rest.

4.1 Vibration led to Greater Undershooting

The first objective of this thesis was to determine whether muscle vibration would degrade task accuracy during an eccentrically-controlled movement sequence. I hypothesized that muscle vibration would decrease task accuracy and specifically, cause participants to undershoot the targets (i.e., open their hand before reaching the targets). The results confirm that this was the case. Specifically, during the Block One trials in which vibration was applied, participants undershot both targets (see Table 3.1). This result is consistent with previous findings in which muscle vibration caused participants to undershoot during both a concentric movement sequence (Cordo et al., 1995) and an eccentric targeted movement (Inglis et al., 1991). The magnitude of the undershoot that was observed is comparable to those previously reported (Inglis & Frank, 1990; Cordo et al., 1995). What can be inferred from this finding?

Muscle spindles within the lengthening musculature are thought to provide the primary source of kinaesthetic input during a movement in the absence of vision (Capaday & Cooke, 1981; Inglis & Frank, 1990). This result reaffirms previous conclusions that when these lengthening muscles are active, as required in an eccentrically-controlled movement, their spindles still provide pertinent information of limb position and movement (Inglis et al., 1991). Previous work had investigated whether fusimotor coactivated spindles (in muscles supporting a load) could create illusions of limb position during vibration. No differences were observed in subjects' tracking performance when vibration was applied to the active lengthening muscles. However, the load being controlled equated to 25% of subjects' MVC, a threshold known to abolish the vibratory effect when the limb is static (Ansems et al., 2006).

During the vibration trials in this study, at least three factors would have caused spindles of the elbow flexors to discharge: the increase in muscle length from the elbow extension, alpha-gamma co-activation from controlling the load, and lastly, artificial stimulation from the mechanical vibration. In addition, some gamma tuning might have caused increased activity in the primary or secondary endings, due to the target-oriented nature of the task (Ribot-Ciscar et al., 2009). The presence of multiple factors that could have activated spindles during the task, suggests that the CNS must have been performing a subtraction of fusimotor activity whilst attempting to resolve the ensemble of muscle spindle feedback (Goodwin et al., 1972; McCloskey et al., 1983; Matthews, 1982).

4.2 Exercise Effects also led to Greater Undershooting

The second objective of this thesis was to investigate the effect of muscle fatigue and eccentric muscle damage on an eccentrically-controlled movement sequence. Like vibration, the exercise protocol also degraded kinaesthesia, causing participants to undershoot the targets. This result supported my general second hypothesis: that exercise would decrease task performance for the Block Two (post-exercise) trials. However, it opposed my suggestion that accuracy (constant error) would be unaffected by the exercise protocol. This finding somewhat contrasts previous evidence showing that movement tracking accuracy, when assessed in a limb-matching task, is not significantly reduced following fatigue of elbow flexors (Allen & Proske, 2006). I propose that these contrasting results are due to the differences between the targeted movement sequence used in this thesis and the limb-matching task used in the aforementioned study. Principally, the movement sequence that I employed avoided any involvement of the non-exercised limb.

For participants to undershoot the targets following exercise, they might have perceived their elbow flexors to be at a greater length (and therefore the elbow at a more extended joint angle) than they really were at the time of hand opening. Studies utilizing limb-matching assessments have also reported results suggestive of a skewed perception of muscle length (Allen

& Proske, 2006; Walsh et al., 2004; Givoni et al., 2007; Saxton et al., 1995). As I addressed in the introduction, this theory has since been refuted, following studies involving exercise of the antagonist muscles (Allen et al., 2010). The working hypothesis from Proske and Gandevia (2012) is that these matching errors suggest the exercised limb adopts a more gravity-neutral posture, regardless of whether the flexors or extensors of the limb are exercised. Because the task in this thesis involved a horizontal plane movement with a low-level and consistent torque, this same line of reasoning does not apply for the results in this thesis. If the characteristic posture that an exercised limb adopts is indeed one of gravity-neutral, then changing the elbow angle whilst the arm is supported in the horizontal plane will not alter the effort required to hold it there. Physical changes within the limb however, might have affected task performance in this thesis.

As mentioned in Section 1.4 on muscle spindles, thixotropy refers to the history dependent property of muscle tissue. Thixotropy can be used to change the resting discharge rate of muscle spindles (Morgan et al., 1984; Proske et al., 1993) and influence accuracy in limb-matching and pointing tasks (Proske et al., 2014). Passive tension levels rise within a muscle after it is exposed to eccentric exercise, and are thought to result from the forming of injury contractures in damaged fibres (Whitehead, Weerakkody, Gregory, Morgan & Proske, 2001). If we assume that this increase in whole muscle passive tension would also affect the intrafusal fibers, it might raise the resting discharge rates of muscle spindles and exert similar effects on kinaesthesia as thixotropy does. Gregory et al. (2004) reported slight, albeit insignificant increases in mean discharge rates of primary and secondary endings from the medial gastrocnemius of the cat following a series of eccentric contractions. In this preparation, all the surrounding musculature was removed. At the elbow joint, four muscles can resist elbow extension (the action controlled during the movement sequence used in this thesis). Perhaps, following the exercise protocol, the rise in passive tension from these muscles compounded to produce higher discharge rates of muscle spindles for a given muscle length and for a given rate of muscle length change. This would have led participants to feel that their elbow was more extended than it was and subsequently undershoot the targets.

It has been suggested that following muscle fatigue and damage, elevated EMG signals result from larger motor units being recruited earlier in a graded contraction (Weerakkody et al., 2003). Larger motor units exhibit less fine motor control than smaller motor units (Saxton et al., 1995). I observed increases in both biceps brachii and triceps brachii mean EMG RMS signals following exercise. If these increases resulted from a higher proportion of larger motor units being recruited, it offers another reason why task performance might have decreased following the exercise protocol. Increased activity in triceps brachii (antagonists in this study's task) has also been observed previously, with an accompanying fall in elbow extensor force output after exercise of elbow flexors (Dundon, Cirillo & Semmler, 2008). During this thesis, MVCs were not recorded from elbow extensors, thus I cannot comment on the second part of this finding. Another plausible explanation for the increased triceps activity following the exercise protocol, is that it might be indicative of a motor strategy deployed to increase joint stability in the presence of increased flexor muscle weakness (Turner et al., 2008).

The level of triceps activity during the slow eccentric elbow extension was equivalent to levels reported in the literature (Ansems et al., 2006; Sampson, Donohoe & Groeller, 2014). Mechanical muscle vibration caused a slight increase in signal levels of both the biceps brachii and triceps brachii surface EMG. The fact that this increase was evident in both muscles, suggests that it resulted from some form of electrical interference as opposed to activation of the tonic vibration reflex (Hagbarth & Eklund, 1966).

Another consequence of eccentric muscle damage can be reduced range of motion of the involved joint. At the elbow, this causes a reduction in the resting angle when the arm is held at the side of the body (Jones, Newham & Clarkson, 1987). The recovery of these deficits matches the time taken for muscle damage to be repaired (Clarkson et al., 1992). Following the exercise protocol in this thesis, I observed a reduction in participants' resting elbow angle (unrecorded observations). This reduction in actual available range could have caused participants to underestimate how far they could extend their elbow. For example, participants might have perceived movements through a portion of their range to represent a greater percentage of their actual available range, which in turn could have caused them to undershoot the targets. However, neither this justification nor that of passive muscle tension changes can explain why a difference was observed between the accuracy to the two targets (see Section 4.6). If the undershooting of the targets had resulted from a change to participants' perceived range of motion, they should have undershot the second target more than they undershot the first.

The effects of exercise impacted task performance in the same way as mechanical muscle vibration, by causing participants to undershoot the targets. The vibratory illusion is believed to result from a change in the perceived velocity of muscle length changes, which in turn creates kinaesthetic illusions (Roll & Vedel, 1982). When reviewing the mean velocities in Table 3.2, it is notable that those for the vibration trials are always lower than those for the control trials (for each block and target respectively). Following the exercise protocol, the mean velocities initially decreased and then increased slightly after the rest period, though not to the pre-exercise levels. This pattern of decrease post exercise and then partial recovery to pre-exercise levels following the rest period, mirrors that of the MVC values recorded (see Table 5.1 in Appendix A). Thus, it appears that the exercise caused participants to undershoot via the same method that vibration did, by making them move slower. Accordingly, the combination of exercise effects and vibration resulted in the lowest velocities and greatest undershooting of targets observed during this study. As the magnitude of the vibratory illusion is dependent on the vibration frequency used, the magnitude of the exercise effect appears to be dependent on the force deficit created.

4.3 Variable Error was not significantly affected by Exercise or Vibration

I hypothesized that consistency (variable error) would decrease following the exercise protocol (i.e., participants' mean hand opening being centered about the target, but with increased variable error). This hypothesis was not supported, as variable error was unaffected following the exercise protocol. This finding was unexpected. A prior study had reported decreased limb steadiness during both eccentric and concentric movements following an eccentric protocol (Turner et al., 2008), and others had observed increased variability in a limb-matching task 2 hours after a bout of eccentric exercise (Tsay et al., 2012). The latter study reasoned that matching errors had occurred due to the resulting fall in force from exercise, in turn creating a shift in one of the somatosensory representations or central maps of the body. This reasoning opposes a recent proposal that limb-matching tasks might only require the CNS to match the muscle spindle input from both arms without referencing a central map (Proske, 2015). In contrast, locating a limb's position in space (as in the task of this thesis) might require the CNS to reference afferent input against a central map. If this proposition is correct, it could explain why exercise failed to influence participants' consistency in this thesis.

Variable error was also unaffected by the presence of mechanical muscle vibration. In all but one of the conditions (Block Three trials to the first target) there was a trend for participants to be slightly more consistent during trials involving vibration. Perhaps vibration's artificial driving of the muscle spindles was over-riding their naturally occurring discharge, resulting in a more uniform spindle signal being received during the vibration trials. The lack of influence of muscle vibration on variable error aligns with reports from previous studies using similar paradigms (Inglis et al., 1991; Cordo et al., 1995).

4.4 Performance after the 2 Hours Rest Period

Following the 2-hour rest period, participants completed the final block of trials, Block Three. I had hypothesized that task performance would improve for this third block compared to Block Two, but not to the level of Block One. The results reflected this, as participants' mean hand opening fell closer to the targets than they did during Block Two, but not as close as during Block One. As previously mentioned, it has been proposed that errors seen in limb-matching paradigms result from the fall in force following exercise (Tsay et al., 2012). One group calculated that each percentage drop in MVC correlated with a 0.053° error in their limb-matching task (Walsh et al., 2004). I observed a similar correlation in this study, with the margin of undershoot (constant error) following the same pattern as the deficits to pre-exercise MVCs. In other words, the further participants were from their pre-exercise MVC, the further they undershot the targets. This pattern of MVC levels post-exercise and post-rest has been reported previously (Allen et al., 2010; Tsay et al., 2012) and was also found to correlate with the errors observed.

The most plausible justification for the errors seen following exercise, appears to relate to the ensuing force deficits. I agree with the hypothesis of Proske and Gandevia (2012): that the drop in force signals a change in one or more of the somatosensory representations of the body, which then results in kinaesthetic disturbances. If it were the force deficit only exerting an influence within the limb, then the fact that participants used a scaled load for each block (based on their pre-block MVC), would have prevented any errors being observed.

4.5 The Decreasing Influence of Vibration

The third objective of this thesis was to investigate the effect of muscle fatigue and eccentric muscle damage on an eccentrically-controlled movement sequence and the response of the damaged muscles and the nervous system to muscle vibration. The application of muscle vibration allowed us to probe changes that might have occurred to muscle spindle sensitivity and/or the nervous system's interpretation of the spindle feedback. I hypothesized that the effect of muscle vibration (i.e., target undershoot) would persist for blocks 2 and 3. Muscle vibration did continue to cause participants to undershoot during blocks 2 and 3, thereby compounding the undershoot already created by the exercise protocol.

Despite the persistence of the vibratory effect throughout the experiment, there was a reduction in the magnitude of the vibratory illusion between blocks. The reduction between blocks one and two did not reach statistical significance, but the reduction between blocks one and three did. Further clarification would be required to determine whether this resulted from the exercise protocol or whether it was due to some form of learning adaptation or desensitisation to the vibratory stimulus.

Previously, Regueme et al. (2007) had attempted to measure the velocity of the vibratory illusion following a stretch-shortening cycle exercise protocol (in the form of single leg rebounding movements on a sled). Two days after the exercise, subjects perceived vibratory illusions to be slower (as reported via their non-fatigued legs) when 80 and 100 Hz frequencies were applied and faster when 40Hz was applied. The authors chose not to report perceptual changes immediately following the exercise due to confounding metabolic influences, but unlike the findings in this thesis, their exercise protocol failed to induce a significant drop in subjects' MVCs. Prior work has demonstrated that when vibration is applied to a fatigued muscle during a limb-matching task, the same errors occur as when it is applied to an unfatigued muscle (Allen & Proske, 2006). The fact that vibration continued to cause constant errors during both the second and third blocks suggests that following exercise induced muscle-damage the CNS continues to be strongly influenced by muscle spindles.

4.6 Participants' Performance to the First and the Second Target

During each of the three blocks, participants were always more accurate when aiming to the second target. One possible reason for this could have been the situation of this target, at 35° from the 180° used to denote a straight-arm posture (which varied from person to person). It has been suggested that as joints approach end range, the signaling of joint angle may be biased by feedback from joint receptors (Fuentes & Bastian, 2010). It is possible that the additional input from joint receptors within the range of the second target, may have served to improve participants' accuracy. To clarify this, further studies involving removal of joint receptor input (i.e. joint anaesthesia) would be required, and these are beyond the scope of this thesis.

Another possible rational relates to the hard stop used to protect participants from over-extending their elbow. The original plan was to bring the load to a gradual stop by placing a sponge underneath it, and in turn, minimize end-point positioning cues. Because each participant achieved a varied degree of elbow extension, the load finished at a varied height from the floor. This led to us removing the sponge. As a result, instead of bringing subjects' arms to a gradual stop, the hard stop was used to block the elbow from being pulled any further in to extension. It is possible that for trials to the second target, participants had an expectation of when their arm was going to be stopped following hand release and used this feedback to time their release point on subsequent trials. I will explore this possibility in the next section (4.7).

The exercise protocol also appeared to affect accuracy to the first and second targets differently, causing participants to undershoot the first target more than they undershot the second. Once again, the end cue provided by the hard block is one possible reason for this finding. Additionally, previous work has shown that eccentric exercise can result in impaired motor performance at shorter muscle lengths and the impairment is most pronounced with loads equivalent to 10% of MVC (the amount used in this study) (Turner et al., 2008). Others have also reported that 2 hours after exercise, voluntary muscle activation is particularly impaired at short muscle lengths and the optimal angle for generating force shifts acutely to longer muscle lengths (Prasartwuth et al., 2006). Finally, increases in passive tension as the elbow joint approached extension might have served as an additional source of positional information. Any of the aforementioned reasons, either in isolation or combination, offer potential rational for the performance differences observed between the first and the second targets.

4.7 Methodological Issues

If I was to run the experiment again, the primary design issue I would improve upon would be the removal of any positional cues from the movement end point. This could take the form of a spring mechanism or valve to gradually stop the arm prior to reaching full elbow extension. The starting range could also be increased from 5 degrees to provide additional discrepancy to participants' position sense. To improve the efficacy of the elbow flexor exercise and remove opportunities for compensation, I would place some form of restraint on the posterior distal humerus. Increasing wrist stabilization would also prevent participants from moving their elbow joint away from the axis of the manipulandum and reducing the torque provided by the load. Another potential improvement to the procedure could involve the method of applying the vibrator to the arm. For all participants, a compression bandage and Velcro™ strap held the vibrator in place. Although the same person applied this at the start of the study and after the rest period, using an elasticated compression support would improve consistency of the vibrator amplitude being transferred to the arm.

Regarding other sensory endings, I recognise that cutaneous receptors are activated by mechanical muscle vibration (especially those of the RA systems), though they are not believed to be responsible for the vibratory illusion. This was clearly demonstrated by Goodwin et al., (1972). They observed no illusory movements when the vibrator was moved away from the tendon and onto an area of skin overlying the elbow joint. Finally, the increases in passive tension following exercise would have been signalled by GTOs, which are known to monitor changes in passive tension following eccentric contractions. Their sensitivity to vibration combined with stretch (as would have occurred during the vibration trials of this thesis) also increases following eccentric contractions (Gregory, Morgan & Proske, 2003). Despite these limitations, muscle vibration still offers a non-invasive indication of muscle spindle activity.

One strength of the experimental design of this thesis was the timing of the blocks around the exercise protocol. Assessing performance following two-hours rest after the exercise protocol, ensured that local metabolites had been removed from the muscle (Smith & Newham, 2007) and DOMS were not present (MacIntyre et al., 1995). These factors can both act as confounding variables. Another strength of the design was that the exercise protocol was delivered via the same apparatus as participants used to perform the task. This point is known to increase the specificity of the exercise intervention (Warren et al., 1999). The apparatus design also provided a consistent challenge throughout the entire range of motion, rather than fatiguing one portion of the range more than another.

4.8 Further Research

Although the effect of vibration did not change to a statistically significant extent from one block to the next, there was a significant decrease between Blocks One and Three. To ensure that this decrease resulted from the exercise protocol, a sample of participants would need to complete the study (starting each block at the same time points) without the exercise protocol and use the same load throughout the trials. Though beyond the scope of this thesis, these findings would then determine whether the decreased effect of vibration resulted from some desensitization to muscle vibration or from the use of different loads for each block of trials. Regarding potential learning effects, Bevan et al., (1994) tracked subjects' performance of this movement sequence over 3 days and found the only effect of practice was on consistency during the first 30-40 trials of day one and only at the fastest velocity (76º/s). Accordingly, this makes it unlikely that a learning effect was responsible for the observed decrease in the vibration effect.

Another variation to this study would be to assess participants passively. Vibration would still be applied on half of the trials and participants would still complete the exercise protocol, but, their arm would be moved passively for them during each trial. This would control the mean velocities and total movement time, remove any sense of effort involved in the task, and decrease the influence from GTOs. The task would solely rely on peripheral kinaesthetic input and allow further probing of muscle spindle function following muscle fatigue and damage. To tease out the impact of vibration and exercise on primary and secondary endings of muscle spindles, a Ribot-Ciscar et al. (2009) inspired approach could be used to try and evoke tuning of the gamma system. Participants could be instructed to focus on the speed of their movement for some trials and on the target location for other trials. One addition to the protocol used in this thesis could be a task designed to measure whether participants' perception of their available range of motion changes. The overriding opinion in the literature is that the effects of exercise signal a change to one or more of the somatosensory representations of the body and I believe that measuring perceived range of motion offers a viable option to begin investigating these changes.

Finally, studies involving manipulation of skin strain have provided contradictory findings. Some have shown that it can influence movement sense (Collins & Prochazka, 1996), whilst others report that it creates no detectable change in a matching or pointing task at the elbow (Tsay, Allen & Proske, 2016), and others still have found that taping either the inside or outside of the elbow joint results in subjects judging the joint to be more extended than it is (Kuling et al. 2016). The apparatus I have assembled could be used to investigate the influence of skin strain on this movement sequence and further our understanding of cutaneous receptors' contribution to kinaesthesia.

Chapter 5: Conclusion

For this study, participants performed a slow eccentric extension of the right elbow through the horizontal plane without vision of the right arm. Their task was to open the right hand when they judged it to be passing through the target position (e.g. “release the Frisbee” at the target position). Errors induced by mechanical muscle vibration of the elbow flexors led to earlier hand openings than during control trials and ranged from 4º to 6º. This range accounts for approximately 5% of the entire range of motion at the elbow joint, therefore errors of this magnitude would be detrimental in everyday activities, especially those involving skilled motor tasks (Tsay et al., 2012). This finding confirms that muscle spindles of the lengthening musculature are highly involved in providing kinaesthetic input during an eccentric movement. It also demonstrates that these spindles remain susceptible to vibratory illusions when their homologous muscle is lengthening under tension.

Exercise-induced muscle fatigue and damage had a similar effect as vibration on task performance, causing participants to further undershoot the targets. Like vibration, this undershoot appeared to result from a disturbance to either participants’ limb position sense or movement sense. Furthermore, the degree of undershoot appeared to correlate with the MVC deficit present at the time of testing. The drop in force following exercise might signal a change to one or more of the body’s somatosensory representations, leading to kinaesthetic disturbances (Proske & Gandevia, 2012). In terms of sporting performance, these kinaesthetic disturbances could have negative repercussions on skilled movements and more importantly, likely contribute to the higher incidence of injuries seen to occur later in sporting events as fatigue accumulates (Woods et al., 2003; Fuller et al., 2016). This has led some to suggest that fatigue can be considered a risk factor for ligament injuries (Miura, Ishibashi, Tsuda, Okamura, Otsuka & Toh, 2004).

During this task, the effect of vibration was observed prior to, immediately after and following two hours of rest from the exercise. The preservation of the vibratory illusion suggests that the CNS continues to heavily rely on muscle spindles to signal limb position and movement in the absence of vision, even when the muscle they reside in has been exposed to damaging eccentric contractions. As a result, following the exercise protocol, the effects of exercise and muscle vibration combined to create the largest undershoot observed in this study. This finding contrasts those from limb-matching studies where the effects of vibration and exercise appeared to differ (Allen et al., 2010).

Applying the significance of these findings to the general population, it is worth considering that the senses of limb position and movement decline with age (Proske & Gandevia, 2012). Exercise can slow this decline and offers an effective strategy to reduce the risk of falling in the elderly (Lee & Kim, 2016) and prolong independent living. This thesis demonstrates that the acute effects of exercise can be detrimental if the exercise prescription is too severe. Studying the effect of exercise on kinaesthesia can further our understanding of the senses of limb position and movement and inform the intervention strategies designed to assist elderly and patient populations (Fuentes & Bastian, 2010).

The overall objective of this thesis was to further our understanding of the effects that fatigue and eccentric muscle damage have on kinaesthesia. The findings demonstrate that fatigue and eccentric muscle damage can impair the performance of an eccentric movement sequence. Because muscle vibration (known to stimulate muscle spindles) impaired task performance both before and after exercise it is unlikely that this impairment occurs due to changes within the spindles or the CNS' reliance on their input. This result leaves open the possibility that central changes occur following exercise, perhaps to one or more of the somatosensory representations of the involved body parts. Following exercise, any changes to these representations might remain until new sensory information indicates that recovery from the exercise is complete (Proske & Gandevia, 2012). Investigating different techniques to elicit novel sensory input to the nervous system might allow us to manipulate these representations, and in turn accelerate recovery times and reduce injury rates.

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Appendices

Participants' MVCs

Participant	Block One	Block Two	Block Three
1	104.70	62.55	80.04
2	71.32	51.99	48.05
3	90.02	53.33	54.39
4	91.72	57.00	79.46
5	117.54	82.77	94.41
6	98.92	76.87	89.75
7	78.21	52.48	51.86
8	148.63	88.68	111.72
9	125.28	67.25	99.01
10	110.02	54.94	77.85

Table 5.1 Participants' MVCs (Nm), recorded before Blocks One, Two and Three.