Physiological Studies Investigating Neurological Adaptations to Resistance Training.

By

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ABSTRACT

The effect of different strength training paradigms on corticospinal excitability and inhibition was studied throughout this thesis. The primary aim was to investigate the corticospinal responses following isometric, isotonic, cross-education and whole-body vibration (WBV) strength training, and to determine if any observed differences in corticospinal parameters (excitability, inhibition, and motor unit synchronisation) influenced the development of strength.

Study 1 investigated the effect of four-weeks of isometric strength training of the first dorsal interosseous (FDI) muscle. Strength increased by 54%, however, cross-correlation analysis revealed no significant difference in the strength of motor unit synchronisation following training, suggesting that correlated motor unit activity is not important in the expression of muscle strength.

As corticospinal inputs are important for motor unit synchronistaion, transcranial magnetic stimulation (TMS) was used in study 2 to measure corticospinal excitability and inhibition following isometric strength training of the FDI. Following training, index finger isometric abduction strength increased by 34%; however strength training did not influence corticospinal excitability and this was associated with a significant reduction in corticospinal inhibition.

In study 3, increases in strength (28%) were observed following four-weeks of heavy load controlled isotonic strength training of the biceps brachii (BB). No change in muscle girths were observed following training. There was also a significant increase in corticospinal excitability; however, contrary to isometric strength training of an intrinsic hand muscle, there were no differences in corticospinal inhibition. Using a similar training load to study 3, four-weeks of cross-education strength training of the right BB (study 4) resulted in a 19.2% increase in contralateral strength and an increase

in corticospinal excitability in the non-trained limb, in the absence of muscular girth changes in the untrained arm. The final project investigated the acute effect of upper body whole body vibration (WBV) on corticospinal excitability and inhibition (study 5). Previous studies have demonstrated that high frequency local vibration increases motor unit synchronisation and corticospinal excitability, however no studies have investigated the corticospinal responses following WBV applied to the upper body. Using a vibration intensity that has customarily been used in previous studies that have reported significant effects did not affect corticospinal excitability and inhibition when compared to a control condition.

Results from this thesis support the view that corticospinal excitability and inhibition are identified neural adaptations to strength training. However, the corticospinal responses appear to be influenced by the type of strength training performed and muscles trained.

DECLARATION

"I, Dawson John Kidgell, declare that the PhD thesis entitled "**Physiological Studies Investigating Neurological Adaptations to Resistance Training"** is no more than 100,000 words in length including quotes and exclusive of tables, figures, appendices, bibliography, references and footnotes. This thesis contains no material that has been submitted previously, in whole or in part, for the award of any other academic degree or diploma. Except where otherwise indicated, this thesis is my own work".

Signature Date

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PUBLICATIONS AND AWARDS

Chapter 3

Kidgell, D.J., Sale, M.V., & Semmler, J.G. (2006). Motor unit synchronisation measured by cross-correlation is not influenced by short-term strength training of a hand muscle. *Experimental Brain Research*, 175: 745-753.

Chapter 4

Kidgell, D.J & Pearce, A.J. (in press). Corticospinal properties following short-term strength training of an intrinsic hand muscle. *Human Movement Sciences (2010) doi:10.1016/j.humov.2010.01.004.*

Chapter 5

Kidgell, D.J., Stokes, M.A., Castricum, T.J., & Pearce, A.J. (in press). Neurophysiological responses following short-term strength training of the biceps brachii muscle. *Journal of Strength and Conditioning Research.*

Chapter 6

Kidgell, D.J., Stokes, M.A, & Pearce, A.J. (in press). Strength training of one limb increases corticomotor excitability projecting to the contralateral homologous limb. *Motor Control.*

Awards

Glen-Cross Young Scholar Award for best student presentation at the 9th Motor Control and Human Skills Conference, Hobart, Tasmania.

Publications currently in review arising from this thesis

Chapter 2

Kidgell, D.J., & Pearce, A.J. (submitted for publication). The use of single pulse TMS to investigate the neural adaptations to strength training. *Journal of Science and Medicine in Sport.*

Chapter 7

Kidgell, D.J., & Pearce, A.J. (submitted for publication). Acute upper-body vibration does not alter the functional properties of the corticospinal pathway in healthy humans. *Journal of Science and Medicine in Sport.*

Book Chapters

Kidgell, D.J., & Pearce, A.J. (2010). Motor Control Studies in Skill and Strength training, Muscle Soreness and Fatigue. In *Fundamentals of Exercise and Sport Science* (2nd Ed.), pp. 353-442. Sydney, Australia: McGraw-Hill. ISBN: 978-0-07-028824-9.

Pearce, A.J., & **Kidgell, D.J.** (2009). Chapter 2: Neuroplasticity following skill and strength training: Evidence from transcranial magnetic stimulation studies. In *Horizons in Neuroscience Research, Vol 3, ed.* Costa, A & Villalba, E, New York: Nova Science. ISBN: 978-1-61728-027-6.

Abstracts

Chapter 3

Semmler, J.G., Sale, M.V, & **Kidgell, D.J** (2006). Motor unit synchronisation measured by cross-correlation is not influenced by short-term strength training of a hand muscle. *Australasian Winter Conference on Brain Research, pg*: 24

Chapter 4

Kidgell, D.J., Hunter, S., & Pearce, A.J. (2009). Effect of strength training on the cortical control of movement. *The 9th Motor Control and Human Skills Conference, pg:* 66.

Chapter 6

Kidgell, D.J., & Pearce, A.J. (2009). Neural adaptations following cross-education strength training: A pilot study. Australian Conference of Science and Medicine in Sport. *Journal of Science and Medicine in Sport, 12*(6):52-53.

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CHAPTER ONE - INTRODUCTION

Strength can be broadly defined as the maximal force or torque that can be developed by the muscles performing a specific movement. It has been demonstrated that training-related changes in muscle strength are accompanied by adaptive alterations in the neuromuscular system during the early phases of a strength training program (Carroll et al., 2001a; Enoka, 1988). Evidence for changes in neural function following strength training has been provided through the use of surface electromyography (sEMG), evoked spinal reflex recordings and via single motor unit recordings (Del Balso and Cafarelli, 2007; Duchateau et al, 2006; Narici et al., 1989). Changes in the amplitude of the sEMG signal have, by default, been interpreted as increases in neural drive, therefore contributing to the increase in force (Davies et al., 1985; Narici et al., 1989). Measurement of evoked spinal reflexes, such as the Hoffman reflex (H-Reflex) and volitional wave (V-wave) have been shown to increase following a period of strength training, possibly contributing to early strength development (Aagaard et al., 2002b; Del Balso and Cafarelli, 2007; Fimland et al., 2009a).

Alterations in motor unit behaviour, such as increased motor unit discharge rate and motor synchronisation have been suggested to account for the rapid increases in strength (Kamen and Knight, 2004; Milner-Brown et al., 1975; Van Cutsem et al., 1998). Although there is good evidence for changes in motor unit discharge rate following strength training (see Duchateau et al., 2006 for review), there is very little evidence to demonstrate how changes in motor unit synchronisation may increase strength (Griffin et al., 2009; Milner-Brown et al., 1975). The most direct method to quantify motor unit synchronisation is by the cross-correlation of individual discharge times from pairs of concurrently active motor units, where the discharge times of one motor unit are used as a reference, and a histogram is constructed of the peri-event discharge times of the other motor unit (Datta and Stephens, 1990). There are a number

of cross-sectional studies that have suggested that increases in motor unit synchronisation may be an important neural mechanism for strength development (Fling et al., 2009; Semmler and Nordstrom, 1998b; Semmler et al., 2004). However, there has only been one training study (Milner-Brown et al., 1975) which used a sEMG technique to quantify motor unit synchronisation and this technique has since been shown to be inadequate (Semmler and Nordstrom, 1999; Yue et al., 1995). Therefore, the first set of experiments within this thesis examined the effect of short-term isometric strength training of an intrinsic hand muscle on the strength of motor unit synchronisation.

Recently, it has been suggested that adaptive changes in corticospinal excitability may also contribute to the early phase of strength development (Carroll et al., 2002; Griffin and Cafarelli, 2007). Changes in corticospinal excitability can be investigated using non-invasive transcranial magnetic stimulation (TMS). Stimulation over the primary motor cortex (M1) can induce a series of descending volleys in the corticospinal pathway, which in turn, cause a muscle response referred to as a motor evoked potential (MEP). When controlled for torque and type of motor task, the MEP is a reliable intra-participant measure (Kamen, 2004; van Hedel et al., 2007), allowing for confident interpretation of changes following acute or chronic interventions. Adjustments in MEP amplitude are thought to reflect changes in the strength of corticospinal cell projection onto spinal motoneurons innervating target muscles. Although MEP amplitude is reflective of the excitability of corticospinal cell projection, changes in corticospinal inhibition may also be important for voluntary muscular activity and therefore a potential mechanism underpinning changes in strength. Corticospinal inhibition can be measured from single pulse TMS, determined by the duration of the silent period (SP) and refers to the neural mechanisms by which output

from the M1 is attenuated by inhibitory γ-aminobutryic acid (GABA) receptor mediated interneuron transmission (McCormick, 1989; Werhahn et al., 2007).

Recently, a number of investigations have used TMS to determine the effect of short-term strength training on corticospinal excitability (Beck et al., 2007; Carroll et al., 2001a; Griffin and Cafarelli. 2007; Jensen et al., 2005; Lee et al., 2009a). For example, Carroll et al. (2001a) observed that short-term strength training of the first dorsal interosseous (FDI) muscle did not alter the size of the TMS evoked MEP at rest and at higher force levels, observing a significant reduction in the size of the MEP, despite reporting a large increase in strength following training. Similarly, Jensen et al. (2005) reported a significant reduction in the size of the maximal MEP and slope of the stimulus-response curve at rest following four-weeks strength training of the biceps brachii (BB). Further, Lee et al. (2009a) observed that four-weeks of strength training of the wrist abductors did not modify the size of the TMS evoked MEP. However, in contrast, Griffin and Cafarelli (2007) observed a 32% increase in MEP amplitude following isometric strength training of the tibialis anterior (TA). Despite these recent studies, there are no reports within the literature regarding changes in corticospinal inhibition following a period of strength training.

The potential for different methods of strength training to alter corticospinal excitability and inhibition were investigated throughout the majority of this thesis. Whilst chapter 3 investigated the effect of isometric strength training on motor unit synchronisation, in chapter 4, TMS was used to determine the corticospinal responses to short-term isometric strength training of an intrinsic hand muscle (FDI).

Most studies that have investigated the corticospinal responses to strength training have used muscles that are not associated with common strength training practices. Therefore, chapter 5 investigated the corticospinal responses following heavy

load controlled isotonic strength training of the elbow flexor muscle (BB). As it has recently been suggested that strength training is a form of skill training and/or motor learning (Carroll et al., 2002; Farthing, 2009; Zhou, 2000), the timing to perform each repetition throughout the training period was deliberately and purposefully controlled to make the strength training exercise more challenging for participants.

The practice of strength training one limb has shown to increase the strength of the opposite homologous limb and, as such, is termed cross-education (Zhou, 2000). The magnitude of the cross-transfer of strength is proportional to the quantity of strength achieved in the trained limb. The neural mechanism underpinning this contralateral transfer of strength is poorly understood, therefore, this issue was addressed in chapter 6 by using TMS and quantifying the corticospinal responses to the untrained homologous limb.

It has been suggested that whole-body vibration (WBV) exercise may be a superior form of strength training due to its acute and chronic effects on the neuromuscular system (Carson et al., 2009; Delecluse et al., 2003; Dolny and Reyes, 2008). Although it has been reported that WBV exercise increases neural excitability, no studies have investigated the corticospinal responses following an acute bout of upper body WBV exercise, despite a number of studies demonstrating improved muscular output as a result of adaptive changes in the neuromuscular system (Bosco et al., 1998; Cochrane and Stannard, 2005; Cormie et al., 2006). Therefore, chapter 7 examined the corticospinal responses following a single bout of WBV exercise.

Whilst the neural adaptations that occur during the initial phase of a strength training program have proven difficult to identify, the purpose of this thesis was to systematically investigate the corticospinal responses to various strength training practices (isometric, isotonic, cross-education and WBV) to provide evidence for a

corticospinal mechanism (one of several potential mechanisms) for strength development.

1.1 Primary aim of the research

1. To determine the corticospinal responses following different methods of strength training (isometric, isotonic, cross-education and WBV).

1.2 Specific aims of the research

1. To determine the effect of isometric strength training on the strength of motor unit synchronisation and coherence (Study 1).
2. To determine the corticospinal responses (latency, MEP amplitude and SP duration) following isometric strength training of an intrinsic hand muscle (Study 2).
3. To determine the corticospinal responses (latency, input-output properties and SP duration) following heavy load controlled strength training of the elbow flexor muscles (Study 3).
4. To determine the corticospinal responses (latency, input-output properties and SP duration) of the contralateral untrained limb following cross-education strength training (Study 4).
5. To determine the corticospinal responses (latency, MEP amplitude and SP duration) following an acute bout of upper body WBV exercise (Study 5).

1.3 Primary hypothesis of the research

1. It was hypothesised that different forms of strength training would increase corticospinal excitability and reduce corticospinal inhibition and this would be reflected by an increase in strength.

CHAPTER TWO – REVIEW OF LITERATURE

It is well established that the human nervous system is able to modify its function in response to activity or experience. This response has been termed 'plasticity' and involves reorganisation of neural assembles that control movement. Recent evidence suggests that the M1 can experience plasticity following various types of physical activity (Jensen et al., 2005; Katiuscia et al., 2009; Remple et al., 2001; Rogasch et al., 2009; Sanes, 2003; Sanes and Donoghue, 2000). Whilst plasticity is stimulated in a variety of ways, recently it has been shown in participants undertaking skill and strength training (Beck et al., 2007; Jensen et al., 2005; Pascual-Leone et al., 1995; Pearce et al., 2000). The use of TMS is a non-invasive technique that can quantify such changes within the corticospinal pathway following specific training interventions. This review will discuss the functional organisation of the human corticospinal system and how it adapts to various forms of resistive exercise.

2.1 Organisation of the cerebral cortex

The cerebral cortex is a structure within the human brain approximately 3-4 mm thick that plays a central role in many complex brain functions including memory, attention, perceptual awareness, and motor control (Mountcastle, 1997). The human cerebral cortex is composed almost entirely of neocortex (about 90%), with the archicortex and paleocortex constituting the remaining small fraction of the cortex (DeFelipe et al., 2002; Fatterpekar et al., 2002; Haines, 2006; Nolte, 2002; Rothwell, 1994). The following will briefly review the cytoarchitecture of the human cerebral cortex.

2.1.1 Structure of the cerebral cortex

The cerebral cortex is well endowed with neurons, neuroglia, and blood vessels (Haines, 2006; Nolte, 2002). The structural organisation of the three types of cells that populate the cortex; being pyramidal cells, stellate neurons and fusiform neurons; enable the classification of the cortex into three types: allocortex, mesocortex and the neocortex (DeFelipe et al., 2002;, Fatterpekar et al., 2002; Haines, 2006; Luppino and Rizzolatti, 2000). The allocortex is the oldest region and is composed of only three layers and is located in the limbic system. The mesocortex is younger and is composed of three to six layers and is predominantly located in the insula and cingulate gyrus. The neocortex, is the youngest region of the cortex and is composed of six layers that comprises the bulk of the cerebral cortex (Rothwell, 1994). Whilst the cerebral cortex is structurally organised into layers, it also has organisation through functional connections (Mountcastle, 1997).

Most corticospinal output is mediated through pyramidal neurons and stellate (or granule) cells. The cellular organisation of pyramidal and stellate cells within the cortex gives it a characteristic layered or laminar appearance that can be identified as six distinct layers:

I. **Molecular layer.** A layer lying immediately inferior to the pia matter and containing very few cell bodies.

II. **External granular layer.** A layer of densely packed small cells including small pyramidal and stellate cells.

III. **External pyramidal layer.** A layer consisting of medium to large sized pyramidal cells.

IV. **Internal granular layer.** This layer is predominantly composed of densely packed stellate and pyramidal cells.

V. **Ganglionic layer**. This layer contains large pyramidal cells (Betz cells) (Fatterpekar et al., 2002; Mountcastle, 1997; Nolte, 2002).

VI. **Multiform layer.** This layer is relatively thin and mostly composed of densely packed, spindle-shaped cells, many with axons leaving the cortex (Fatterpekar et al., 2002; Mountcastle, 1997; Nolte, 2002).

Layer 1 contains mainly long horizontal dendrites and axons in deeper layers as well as thalamic afferents. The medium to large pyramidal cells in layer III and V contain long corticocortical connections. In addition, pyramidal cells in layer V also project to sub-cortical areas such as the basal ganglia, brain stem and to the spinal cord (Mountcastle, 1997; Porter and Lemon, 1993). Layers II and IV receive afferent inputs, with inputs from the thalamus generally terminating in layer IV (Jones, 1975a). Layer VI contains small pyramidal cells which exhibit greater morphologic variability than the pyramidal cells located in other layers and they have corticocortical and corticothalamic projections (Rothwell, 1994). Layers II through VI all contain stellate cells, some of which form excitatory connections onto pyramidal cells and some of which form inhibitory synapses (Feldman, 1984; Haines, 2006; Hof et al., 1995a; Hof et al., 1995b; Jones, 1975b).

There are horizontal and vertical connections of neurons within the cortex (Passingham, 1993; Porter and Lemon, 1993). Pyramidal cells have axons which leave the cortex, whereas stellate cells are classed as true interneurons as their axons do not leave the cortex (Porter, 1985; Porter and Lemon, 1993; Mountcastle, 1997; Luppino and Rizzolatti, 2000). Pyramidal cells, located in all layers of the neocortex, have

vertical dendrites that extend into layer 1. Further, the dendrites of pyramidal cells give the cortex strong perpendicular projections. Studies have demonstrated a columnar functional organisation and within these columns, the cells share common input and output connections (Keller, 1993b; Szentagothai, 1975; Mountcastle, 1997; Keller, 1993a). Pyramidal cells also form horizontal plexuses of dendrites in layers II, III and IV of cortex (Porter, 1985; Porter and Lemon, 1993; Luppino and Rizzolatti, 2000) which have been measured up to 3 mm in the primary motor cortex (M1) and excite other intercolumnar pyramidal neurons (Ghosh and Porter, 1988a; Ghosh and Porter, 1988b).

The neural connections within the cerebral cortex have been identified based upon the neurotransmitters used by the cortex. For example, inhibitory γ-aminobutryic acid (GABA) has been demonstrated to form columnar patterns (DeFelipe and Jones, 1985). In addition, inhibition has been demonstrated horizontally over long distances following excitation of pyramidal axon collaterals, probably via inhibitory interneurons to other pyramidal neurons (Ghosh and Porter, 1988a; DeFelipe and Jones, 1985; Porter and Lemon, 1993; Ghosh and Porter, 1988b). Inhibitory GABA terminals have been located on the initial segments of pyramidal cell axons, with such modulations being placed to control the output of pyramidal cells (Mountcastle, 1997; Fatterpekar et al., 2002). This data provides support for vertical and horizontal patterns of connectivity for both excitation and inhibition within the M1.

2.2 Corticospinal pathway

The spinal cord is under the control of a number of neurons that descend from the M1. The largest of these are the corticospinal neurons that form the bulk of the corticospinal or pyramidal tract (Porter and Lemon, 1993; Weber and Eisen, 2002).

Corticospinal neurons have their origins in layer V of the cerebral cortex. Although corticospinal neurons are located within six cortical regions, the M1 has the largest concentration (Porter, 1985). Within the M1, these corticospinal neurons are functionally organised to project to motoneurons that control specific muscle groups (Porter and Lemon, 1993; He et al., 1993; Rothwell, 1994).

Corticospinal neurons that arise within the M1 descend through the internal capsule, brainstem, and medulla oblongata to continue on to the spinal cord as the corticospinal pathway (Porter, 1985; Porter and Lemon, 1993; Phillips and Porter, 1964). In humans, 90% of the axons of the corticospinal pathway are small (5 μm), lightly myelinated with slow conduction velocities (14 $m.s^{-1}$). Less than 10% are classified as fast conducting (70 $m.s^{-1}$) and large in diameter (12-15 μm) (Phillips and Porter, 1964; Porter and Lemon, 1993; Porter, 1985; Rothwell, 1994).

As the corticospinal neurons leave the M1 and descend to the medulla, they are organised somatotopically. At the medullary spinal junction, approximately 85-90% of the corticospinal neurons cross the midline to form the motor pyramidal decussation (Rothwell, 1994), where they continue as the lateral corticospinal pathway and converge onto motoneurons within the ventral horn of the spinal cord that innervate limb muscles (Porter, 1985). The remaining uncrossed corticospinal neurons continue as the ventral corticospinal pathway and terminate at the thoracic spinal cord where they innervate predominantly trunk musculature (Porter, 1985). The important difference between these corticospinal projections is that the origin of each projection corresponds to a different terminal territory in the spinal cord (He et al., 1993; He et al., 1995). There is good evidence for a functional role of the corticospinal system in the control of the upper limb and changes in its functional organisation following skill training (Perez et al., 2004; Pascual-Leone et al., 1995; Pearce et al., 2000; Katiuscia et al., 2009).

However, functional changes within the corticospinal pathway projecting to the spinal motoneurons innervating the FDI and BB following a period of strength training remain unclear, despite the importance of this musculature in positioning and controlling the hand in space.

2.3 Techniques to investigate the functional properties of the motor cortex

The ability to examine the human central nervous system (CNS) has developed remarkably over the last 30 years. Imaging techniques such as functional Magnetic Resonance Imaging (fMRI) and positron emission topography (PET), indirectly measure the changes in blood flow associated with neural activity while participants perform a particular motor task (Jenkins et al., 1994). A number of investigations have demonstrated modifications in cortical activity during various movements. For example, there is a strong relationship between isometric force production, pre-movement activity and actual movement execution that results in increased cortical activity in the M1, supplementary motor area (SMA) and the dorsal portion of the anterior cingulate cortex (Dettmers et al., 1995; Thickbroom et al., 1999b; Farthing et al., 2007). Although these studies demonstrate changes in blood flow during movement preparation and execution, they do not provide any objective data concerning the excitatory and inhibitory synaptic events specific to the M1 during movement.

2.3.1 Transcranial stimulation

There are a number of techniques available to investigate human corticospinal function and these include non-invasive transcranial magnetic stimulation (TMS) and to a lesser extent transcranial electrical stimulation (TES). Both these techniques provide excellent temporal resolution and both are able to identify the functional class of the

neurons contributing to motor activity by providing a quantitative measure of neuron excitability by allowing the investigation of both excitatory and inhibitory processes. TES is a technique that uses a single electrical pulse that is applied through the scalp over the M1. It is thought that TES directly activates fast-conducting, large-diameter corticospinal neurons located within the M1 (Rothwell, 2003; Rothwell, 1994; Hallett, 2007). Such stimulation evokes short-latency contralateral muscle twitches. Since TES employs a short (100μs) yet strong (0.5 A) stimulus, only a small proportion of the stimulus actually activates the brain, most of the stimulus travels along the surface where it causes significant pain and activation of the scalp musculature (Rothwell, 2003). An alternative technique that is TMS.

TMS is a non-invasive tool that makes it possible to activate the corticospinal pathway by inducing an electrical field in a relatively small part of the brain in conscious human participants (Weber and Eisen, 2002; Hallett, 2000; Curra et al., 2002; Chen, 2000). TMS allows an indirect assessment of human corticospinal activity during voluntary contractions, making it possible to measure the cortical control to a muscle in humans. TMS works by eliciting a magnetic field by the use of a magnetic coil that is positioned over the motor strip of the skull. A large, brief current is passed through the coil, which causes a large magnetic field, which induces an electrical current in the brain (Chen, 2000; Hallett, 2000; Terao and Ugawa, 2002). If the intensity of the current is large enough, it will depolarize presynaptic neurons that project onto corticospinal neurons, resulting in a number of descending volleys along the corticospinal pathway which synapse with corresponding motoneurons, resulting in the activation of the muscle of interest (Anand and Hotson, 2002;, Chen, 2000; Weber and Eisen, 2002). The resulting transient muscle response can be recorded by sEMG and

quantified as the MEP (Figure 2.1) (Darling et al., 2006; Kobayashi and Pascual-Leone, 2003).

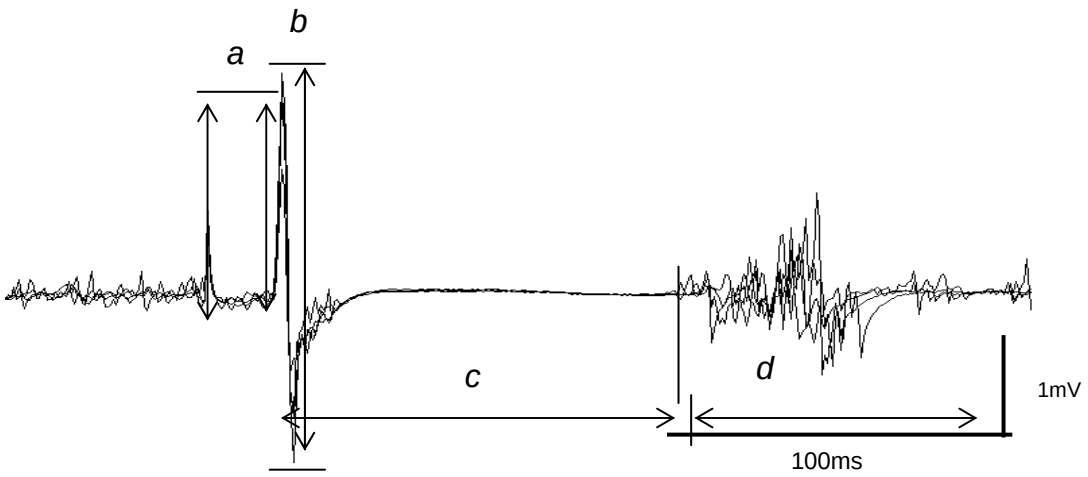

Figure 2.1. Descending corticospinal volleys recorded from the BB and the resultant MEPs after TMS. Latency duration is measured from stimulus artifact to MEP onset and is shown at (a), peak to peak MEP amplitude is shown at (b). Silent Period duration is measured from onset of MEP to return of EMG at (c). Return of EMG activity is shown at (d).

When single pulse TMS is applied over the M1, a number of variables can be measured, representing the corticospinal function, such as; latency, motor threshold (MT), MEP amplitude, and SP duration (Kobayashi and Pascual-Leone, 2003; Rothwell, 2003; Weber and Eisen, 2002).

The latency of the MEP is a reproducible measure of the corticospinal conduction time and is measured from the time of stimulation to the onset of the MEP (Byrnes et al., 1999; Pearce et al., 2000; Pearce and Kidgell, 2009). For example, the conduction time from stimulation to a hand muscle is approximately 20 ms of which 13 ms is from peripheral mechanisms with the remaining time comprising of central conduction, synaptic delay at the motoneuron and conduction down a short intradural segment of the motor root (Hess et al., 1987). In healthy individuals, latency is a reliable measure; however, in people with neurological conditions, latency is variable and often longer, suggestive of demyelination of descending pathways (Kobayashi and Pascual-Leone, 2003). Further, it is also well known that tonic voluntary activation can reduce the corticomotor conduction time of an average of 2 – 3 ms due to facilitation of spinal motoneurons (Rossini et al., 1994).

MT can be determined during rest (i.e. resting MT) or during voluntary contraction (i.e. active MT). Resting MT (RMT) is simply the lowest TMS stimulus intensity required to produce an MEP above a certain (arbitrary) amplitude in a given number of trials (Rothwell, 2003; Rossini and Rossi, 2007; Curra et al., 2002). RMT provides information about the excitability of a central group of neurons controlling specific muscle representations (Hallett, 2000; Hallett, 2007). RMT is also believed to reflect the membrane excitability of interneurons projecting onto corticospinal neurons, as well as the excitability within the spinal cord, neuromuscular junction and muscle (Curra et al., 2002; Kobayashi and Pascual-Leone, 2003).

The threshold to elicit a MEP is lower in smaller distal hand muscles (i.e. FDI) compared to larger proximal limb muscles (i.e. biceps brachii, BB) (Chen, 2000; Hallett, 2000). Differences in MT across muscle groups are most likely related to the degree of corticospinal projection to the spinal motoneuron pool innervating those muscles (Porter, 1985; Perez et al., 2004). However, when establishing MT, it is essential to report the recording conditions in which MT is established (i.e. resting or during low levels of voluntary muscle activation). Establishing RMT requires that there is no background EMG activity present prior to and during stimulation (Curra et al., 2002). Whereas, active MT (AMT) is assessed during low levels of voluntary muscle activation (usually 2-10% of MVC), and since voluntary muscle activation increases the excitability of cortical and spinal neurons, the stimulus intensity required to produce an MEP is lower, thus AMT is lower than RMT (Carroll et al., 2001b; del Olmo et al., 2006; Rogasch et al., 2009). The criterion for establishing RMT and AMT is different and usually involves a number of trials (usually 10). For example, Rossini et al. (1994) suggested that the criterion for determining RMT required five out of 10 MEPs above 50 μV be used, however, recently Carroll et al. (2001b) demonstrated a high degree of correlation of RMT in participants across three experimental sessions when measuring three out of five MEPs above 50 μV as the criterion for establishing RMT.

The amplitude of the MEP is quantified as the degree of corticospinal excitability (Rossini and Rossi, 2007; Hallett, 2000; Anand and Hotson, 2002) and is influenced by different types of physical activity and disease states. There are a number of techniques that can be employed to measure the amplitude of MEPs. However, a significant problem with MEP measurement is the inherent variability of MEP amplitude (Burke et al., 1995; Lorenzano et al., 2002) in relaxed muscles. However, it has been demonstrated that increasing the probability of the motoneuron pool

discharging, via a low level contraction of the target muscle, can reduce this variability (Kiers et al., 1993).

There are a number of different methods of analysis that can be used to determine the amplitude of MEPs. Because MEPs vary considerably in amplitude from trial to trial, it is common to evoke a number of MEPs within a trial. Once a trial has been completed, the peak-to-peak amplitude and area of each MEP are identified and then averaged to provide a mean value of the individual trials (Carroll et al., 2001b; Magistris et al., 1998; Ridding and Rothwell, 1997). Also, a collection of the averaged MEPs can be calculated and thus the peak-to-peak amplitude and area of the MEP can be quantified (Pitcher et al., 2003; Bastings et al., 2002). There has been very little research to date, to demonstrate if there are any meaningful differences in the methods used to analyse MEP amplitude. McDonnell et al. (2004) demonstrated that the reliability between all three methods (mean MEP, ensemble average, and maximum MEP) was comparable, noting that no single method is more reliable than another. In light of this, there are other factors that can influence the variability of MEPs, such as level of alertness, muscle relaxation and attention of the participants, anatomical differences and electrode placement (Carroll et al., 2001b; Koski et al., 2005) therefore, these factors must be controlled for during TMS application in order to obtain a reliable within MEP amplitude (Thickbroom et al., 1999a; Kiers et al., 1993).

The excitability and physiological strength of corticospinal projections can be investigated by constructing a stimulus-response curve, which is produced by stimulating the M1 at the optimal site with a range of TMS intensities, and requires plotting MEP amplitude against TMS intensity (Ridding and Rothwell, 1997; Carroll et al., 2001b). The relationship between TMS intensity and MEP amplitude is sigmoidal and the peak slope of the curve is a measure of the physiological strength of

corticospinal projection onto the motoneuron pool (Carroll et al. 2002). The stimlus-response curve also reflects the balance between inhibitory and excitatory inputs to the M1 and motoneuron pool.

Following the MEP there is a period of interrupted EMG known as the cortical SP (Figure 2.1) and it is an electrical silence in EMG activity that commences just after MEP onset lasting from 50 ms to 300 ms, ending with the recurrence of EMG activity (Chen, 2000; Uncini et al., 1993; Curra et al., 2002; Tinazzi et al., 2003). It should be noted that there are differences in the way in which the SP is measured. For example, some researchers will measure the duration of the SP by visual inspection of the EMG activity from the end of the MEP to the return of the EMG activity (Berardelli et al., 1999), whilst others will measure the duration from MEP onset until the return of EMG (Pearce et al., 2000; Sale and Semmler, 2005).

It has been recognised that the duration of the SP is a measure of inhibition originating within the M1 mediated by activation of cortical inhibitory neurons (Chen, 2000; Di Lazzaro et al., 1998; Di Lazzaro et al., 1999; Bertasi et al., 2000; Werhahn et al., 1995). Experimental data demonstrates that the SP is predominantly of cortical origin (Roick et al., 1993;, Classen and Benecke, 1995; Schnitzler and Benecke, 1994), although, the initial portion (i.e. first 50 ms) reflects inhibition within the spinal cord (Curra et al., 2002; Hallett, 2000; Hortobágyi and Bonato, 2005; Fuhr et al., 1991; Ni et al., 2007; Kimiskidis et al., 2005). Whist the exact physiological mechanism underlying the SP are not completely understood, the duration of the SP provides useful information about the excitability of the corticospinal pathway as a result of neurotransmitter function (Hortobágyi and Bonato, 2005; Curra et al., 2002; Sale and Semmler, 2005; Siebner et al., 1998; Werhahn et al., 1999; Pearce and Kidgell, 2010). The excitability of inhibitory cortical circuits can be investigated with paired and single

pulse TMS. Paired pulse TMS measures short interval intracortical inhibition (SICI) that is mediated by $GABA_A$ receptors (Kujirai et al., 1993), whereas the single pulse technique measures inhibition mediated by $GABA_B$ (Siebner et al., 1998). Evidence suggests that a prolonged SP is due to increased activity of inhibitory interneurons (as a result of increased $GABA_B$), thus inhibiting corticospinal activity, whilst a reduced SP reflects reduced activity of cortical inhibitory interneurons (due to reduced $GABA_B$ mediated inhibition) (Haug et al., 1992; Sale and Semmler, 2005). Further, there are several lines of evidence demonstrating that corticospinal inhibition is reduced prior to and during voluntary movements (Ashby, 1995; Ridding et al., 1995b; Wilson et al., 1993a). It is well supported that the duration of the SP is proportional to the TMS stimulus intensity (Schnitzler and Benecke, 1994; Weber and Eisen, 2002; Wilson et al., 1993a). Increasing the TMS stimulus intensity from 10% to 50% above MT, increases the duration of the SP from a mean of 50ms to 185ms, despite the amplitude of the MEP saturating (Kimiskidis et al., 2005; Hallett, 2007). Further, several lines of evidence demonstrate that corticospinal inhibition is modulated based upon the type of motor task performed (Tinazzi et al., 2003; Datta et al., 1989; Flament et al., 1993; Pearce and Kidgell, 2009; Pearce and Kidgell, 2010). Sale and Semmler (2005) demonstrated an increase in SP duration with a precision task compared to a power grip. These data demonstratethat the duration of the SP is important for shaping the output of the M1 (Fuhr et al., 1991; Roick et al., 1993; Sale and Semmler, 2005). In light of this, there is no data that has examined the effect of different methods of strength training and/or WBV exercise on changes in corticospinal inhibition.

2.4 Motor Unit Physiology

2.4.1 Organisation of motor units

A motor unit consists of a motoneuron in the ventral horn of the spinal cord, its axon and all the muscle fibres it innervates, and is considered the final common pathway of the neuromotor system (Enoka and Fuglevand, 2001). The fundamental function of a motor unit is to convert synaptic input received by a motoneuron into mechanical output by the muscle (Fang et al., 1997). The number of muscle fibres per motor unit varies and to a certain extent, will determine the motor performance of the muscle. The number of muscle fibres per motor unit can vary from as little as four for ocular muscles, 100 for small muscles involved in fine motor performance to as many as 1000 or more for larger muscles involved in gross motor patterns (Henneman et al., 1974; Fang et al., 1997; Duchateau et al., 2006).

A group of motoneurons located in the ventral horn of the spinal cord and the muscle they innervate are known as a motor unit pool. The motor units that form a motor unit pool are diverse in regard to the intrinsic properties of the motoneurons and the muscle fibres that they innervate (Duchateau et al., 2006). A motoneuron is typically characterised by its structure, excitability and distribution of synaptic input, whilst muscles fibres are classified based upon their contractile speed, force generating capacity, and resistance to fatigue (Fuglevand et al., 1999; Burke et al., 1970; Kernell, 1966; Burke et al., 1973; Kernell et al., 1999).

Most muscles in the human body contain muscle fibres that have differing contractile speeds. Given that all muscle fibres comprising a single motor unit have identical metabolic properties, muscles that have dissimilar contractile speeds, therefore must belong to a different type of motor unit subtype. Evidence now suggests that

motor units have specific physiological and biochemical properties, and therefore can be categorised based upon these properties (Kernell et al., 1999). The most generally accepted physiological classification for motor unit types are slow contracting, fatigue resistant (S); fast contracting, fatigue resistant (FR); and fast contracting, fast to fatigue (FF) (Burke and Tsairis, 1973; Burke et al., 1973; Enoka and Fuglevand, 2001; Kernell et al., 1999). Based upon this classification, it has been identified that S units have slow contraction times (i.e. time to peak force), produce a relatively small amount of tension, are recruited earlier, have slow conducting motor axons and have a greater resistance to fatigue, whilst the FR units have intermediate properties, for example has a fast twitch, produces moderate tension, are recruited later, have faster conducting motor axons and are resistant to fatigue. In contrast to the S and FR unit properties, FF units have a fast twitch, develop large tension, and are vulnerable to fatigue (Belanger and McComas, 1981; De Luca et al., 1982; Bigland-Ritchie et al., 1998). In addition to this classification, motor unit subtypes have also been classified based upon their histochemical, biochemical, and molecular properties of the muscle fibres (Pette et al., 1999; Enoka and Fuglevand, 2001). For example, histochemical analysis has identified three types of muscle fibres; type I, type IIa and type IIx (Kernell et al., 1999). Type I fibres are often referred to as slow-twitch fibres, whilst type II are fast-twitch muscle fibres, however, they can be further categorised as Type IIa and IIx (Brooke and Kaiser, 1974).

2.4.2 Motor unit synchronisation

Motor unit synchronisation is a time domain measure of the correlated activity of pairs of active motor units (Sears and Stagg, 1976). Motor unit synchronisation provides information on the strength of branched common input to motoneurons that is

modulated by the corticospinal pathway (Figure 2.2) (Nordstrom et al., 1992; Kirkwood and Sears, 1978). The most direct method used to determine motor unit synchronisation in humans is cross-correlation analysis of individual discharge times from pairs of concurrently active motor units (Semmler, 2002; Myers et al., 2004; Fling et al., 2009; Griffin et al., 2009). This procedure requires identifying the discharge time of one motor unit, which is used as a reference, and a histogram is constructed of the peri-event discharge times of a second motor unit (Farmer et al., 1997; Sears and Stagg, 1976; Ellaway, 1978). If a tendency towards synchronisation exists, there will be a peak in the cross-correlation histogram around the time of firing of the reference motor unit (Moore et al., 1966). The presence of a peak in the histogram is due to common input from branched corticospinal axons of single last-order neurons (Farmer et al., 1997; Datta and Stephens, 1990; Nordstrom et al., 1992) and represents the common input strength (CIS)(Ellaway, 1978; Wiegner and Wierzbicka, 1987). This common input is thought to increase the probability of simultaneous discharge in the motor units sharing these inputs (Kirkwood et al., 1982; Datta and Stephens, 1990).

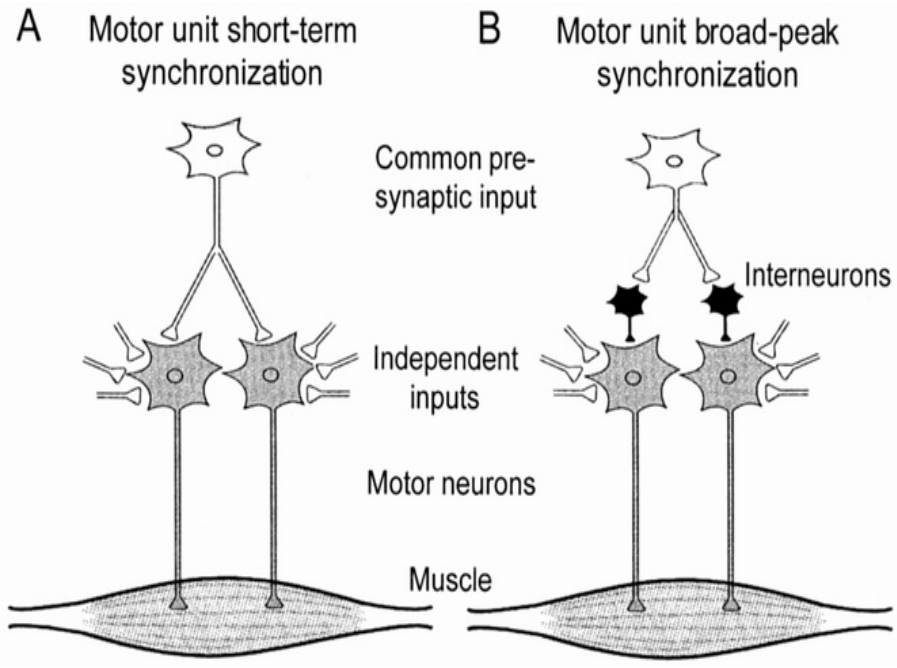

Figure 2.2. Mechanisms of motor unit synchronisation. **A**. Short-term synchronisation is demonstrated by a narrow peak in the cross-correlation histogram and is produced by a common presynaptic input. **B**. Broad-peak synchronisation is caused by inputs (interneurons) that are themselves synchronised by a common presynaptic input (Semmler, 2002).

The presence of correlated activity (i.e. synchronisation) appears as a peak in the centre of the histogram (Figure 2.3). The size of the peak in the histogram reflects the amount of common input that is shared between the neurons (Sears and Stagg, 1976; Nordstrom et al., 1992; Kirkwood et al., 1982; Farmer et al., 1997) whilst the width of the peak is used to distinguish between direct and indirect common input onto motoneurons (Nordstrom et al., 1992; Farmer et al., 1997). Direct common input produces a narrow peak in the cross-correlation histogram and is known as short-term synchronisation of motor units (Moritz et al., 2005; Ellaway and Murthy, 1985; Semmler and Nordstrom, 1999). In contrast, indirect common input produces a broader peak in the histogram and is known as broad-peak synchronisation (Farmer et al., 1997; Nordstrom et al., 1992; Lowery et al., 2007). As a result, the width of the peak can discriminate between direct cortical connections to motoneurons and those with an interposed neuron. Experimental recordings in humans suggest that the histogram peaks usually encompass a mixture of direct and indirect common inputs (Farmer et al., 1997; Nordstrom et al., 1992).

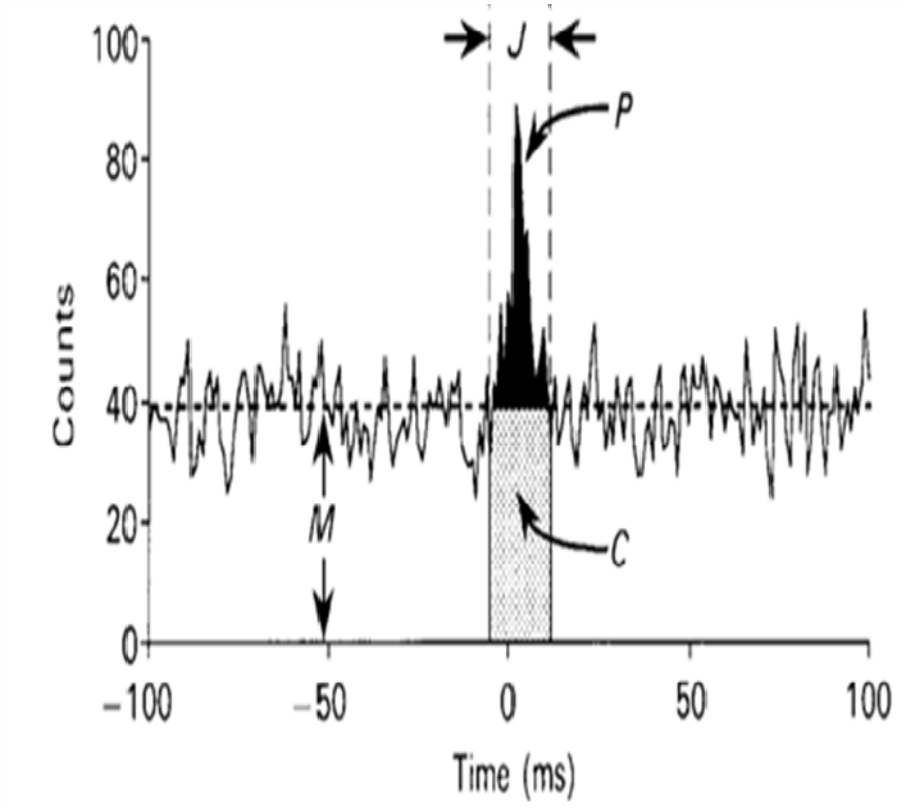

Figure 2.3. Quantification of motor unit synchronisation. An example of a cross-correlation histogram constructed from a two min recording of single motor units (Nordstrom et al., 1992).

2.4.3 Quantification of motor unit synchronisation

Motor unit synchronisation is quantified by applying the cumulative sum technique to identify statistically significant peaks, as well as significant peak widths within the cross-correlation histogram (Ellaway, 1978; Wiegner and Wierzbicka, 1987). Once peaks have been identified in the cross-correlogram, synchronisation indices can be calculated for all peaks within the histogram (Nordstrom et al., 1992). For example, the *K* index is defined as the ratio of total counts in the peak region to chance in the cross-correlogram (for review see Nordstrom et al. 1992). It has been shown that this synchronisation index tends to be smaller with higher motor unit discharge rates, therefore making it a sensitive measure for quantifying motor unit synchronisation at high force levels (Connell et al., 1986; Nordstrom et al., 1992). The common input strength (CIS) is another index often used to measure the magnitude of motor unit synchronisation. CIS is estimated from the cross-correlogram as the number of extra counts in the synchronous peak above that expected by chance, which is normalised to a trial (Nordstrom et al., 1992). Therefore, the CIS is a representation of the frequency of synchronised motor unit discharges. Another index used includes the *E* index. The *E* index quantifies the magnitude of motor unit synchronisation by counting the number of synchronous events normalised to the number of discharges of the reference motor unit (Datta and Stephens, 1990).

2.4.4 Motor unit synchronisation during motor tasks

Using cross-correlation analysis, several studies have demonstrated that motor unit synchronisation is modulated by the motor task performed (Semmler and Nordstrom, 1998b; Bremner et al., 1991a; Fling et al., 2009; Griffin et al., 2009). For example, motor unit synchronisation is less during index finger flexion, but greater during index finger abduction (Bremner et al., 1991b). Further, synchronisation is 35% greater during eccentric contractions compared to isometric and concentric (Semmler et al., 2002). There is also evidence to suggest that the strength of motor unit synchronisation is modulated by regular physical activity. However, how motor unit synchronisation is altered following motor training is not clear. In light of this, Semmler and Nordstrom (1998b) demonstrated that the strength of motor unit synchronisation was largest for the dominant and non-dominant hands in weightlifters, and was the lowest in both hands of a group of highly skilled musicians. Recently, Fling et al. (2009) have also demonstrated that the strength of motor unit synchronisation was greatest in the FDI and BB in weightlifters compared to a control group. It must be noted, as no training intervention was performed in these studies, it is not known if the difference in synchronisation are related to some aspect of muscle strength, or more closely associated with skilled motor performance. Whilst there is limited data that has examined the effect of strength training on motor unit synchronisation, it is a common impression that increases in motor unit synchronisation lead to an increase in strength.

2.4.5 Motor unit coherence

Additional information can be gained about the common input to motoneurons by examining the correlated activity from pairs of motor units in the frequency domain. This procedure, known as motor unit coherence analysis, is a measure of the strength of common oscillatory input to the motoneurons. The typical pattern of coherence that is observed during isometric contractions of hand muscles includes a large amplitude, low frequency (0–10 Hz) peak and a small amplitude, high frequency (10–30 Hz) peak (Figure 2.4). The high frequency component of coherence is thought to originate in various cortical structures that includes the M1 (Farmer et al., 1993a), whereas recent evidence suggests that stretch reflex mechanisms may contribute to low frequency (6–12 Hz) coherence (Christakos et al., 2006; Farmer et al., 1993a).

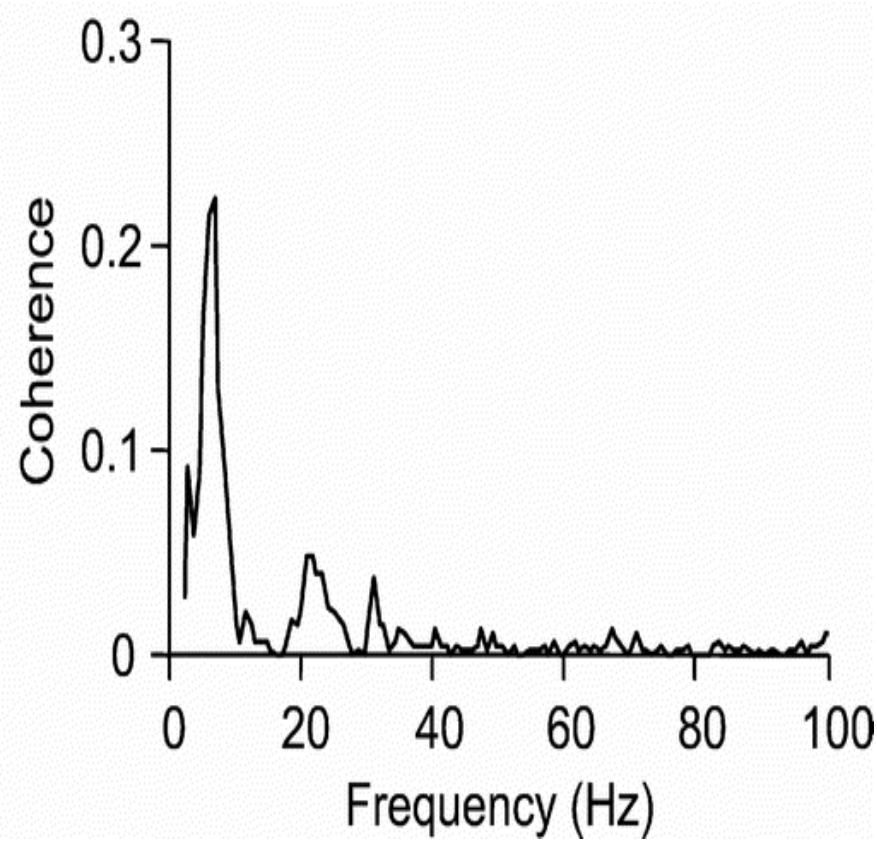

Figure 2.4. A typical pattern of coherence analysis from pairs of currently active motor units during a low level isometric contraction of a hand muscle. The typical pattern of coherence involves a large amplitude low frequency peak (0-10 Hz) and a small amplitude high frequency peak (10-30 Hz) (Semmler et al., 2002).

Similar to synchronisation, motor unit coherence is also modulated based on the requirements of the task, which includes reduced coherence at 5–10 Hz during shortening contractions (Kakuda et al., 1999) and alterations in coherence at 15–30 Hz based on the compliance of a manipulated object during a precision grip (Kilner et al., 2002). Several studies have shown a strong association between motor unit synchronisation and high-frequency (15–30 Hz) coherence, suggesting that these two measures of common input share similar mechanisms (Farmer et al., 1993a; Kilner et al., 2002). Semmler and Nordstrom (1998b), used their original motor unit sample and found that motor unit coherence was greatest in the weightlifters (at 3–9 and 21–27 Hz) and least in the musicians (at 21–27 Hz) compared with untrained participants, with a strong correlation between motor unit synchronisation and high-frequency (15–30 Hz) coherence, particularly for broad synchronisation peaks in the strength-trained participants (Semmler et al., 2004). However, this cross-sectional data again fails to provide information on the short-term adjustments in correlated motor unit activity that may occur as a direct consequence of strength training.

2.4.6 Motor unit synchronisation in upper and lower limb muscles

Given that the general line of evidence for motor unit synchronisation stems from last order common pre-synaptic input from descending corticospinal neurons to motoneurons (Bremner et al., 1991a; Datta et al., 1991; Farmer et al., 1997), the degree of synchronisation between muscles varies (Kim et al., 2001; Gibbs et al., 1997; Reilly et al., 2004; Bremner et al., 1991c; Fling et al., 2009; McKiernan et al., 1998). Motor unit synchronisation is greater in the FDI, compared to the more proximal BB and the vastus medialis muscles, suggesting that the strength of motor unit synchronisation is influenced by the type of muscle (i.e. gross vs. fine) (Kim et al., 2001). Recently, Fling

et al. (2009) assessed the magnitude of motor synchronisation of the BB and FDI in a group of strength-trained participants. These results are in accordance with previous research (Semmler and Nordstrom, 1998b), demonstrating that the magnitude of motor unit synchronisation was greater in the FDI when compared to the BB. A possible mechanism that may account for this difference in motor unit synchronisation may simply be a result of differences in the physiological strength of the corticospinal pathways monosynaptic connections onto the spinal motoneuron pool that controls the FDI being stronger compared to the BB (Kim et al., 2001; Clough et al., 1968; Fling et al., 2009). Furthermore, McKiernan et al. (1998) demonstrated that individual corticomotoneuronal cells have more recurrent and more effective terminal connections onto the motoneuron pools of distal muscles compared to proximal muscles. Support of a corticospinal origin for motor unit synchronisation has stemmed from research in patients with corticospinal lesions (Datta et al., 1991; Farmer et al., 1993a; Semmler, 2002). In patients with amyotrophic lateral sclerosis which is a progressive degenerative disease affecting large diameter corticospinal cells, motor unit synchronisation is almost absent (Schmied et al., 1999).

2.5 Neural adaptations to strength training

It has been proposed that when an individual participates in a strength training program, much of the initial increase in strength is attributed to adaptations in the nervous system (Moritani and deVries, 1979; Griffin and Cafarelli, 2005; Del Balso and Cafarelli, 2007). This is based on studies showing that in the early stages of strength training, the increase in strength precedes an increase in muscle mass (Folland and Williams, 2007; Duchateau and Enoka, 2002). There are at least two areas discussed that support a role for the CNS contributing to the early development of strength. First,

much of the initial increase in strength is attributed to changes in motor unit activity, for example increased synchronisation, rate coding and improved recruitment of fast twitch motor units, altering the manner in which trained muscles are recruited by the CNS (Kamen and Knight, 2004; Enoka, 1988; Duchateau and Enoka, 2002). Second, there is functional evidence showing that strength training of one limb can increase the strength of the contralateral untrained limb (Munn et al., 2004; Carroll et al., 2006; Munn et al., 2005b; Hortobágyi, 2005; Farthing, 2009). The sites in which these adaptations occur are unclear, but implicate a cortical, spinal and motor unit level. The following will review the effect of various methods of strength training (i.e. isometric and isotonic strength training, cross-education and vibration training) on corticospinal excitability and motor unit discharge behaviour.

2.5.1 Strength training and CNS changes

In humans, motor skill training induces changes in the M1 in the form of increased excitability of the cortical representation of populations of muscles involved in the skill task (Pearce and Kidgell, 2010; Pascual-Leone et al., 1995; Pearce et al., 2000; Perez et al., 2004; Pearce and Kidgell, 2009). Further, skill training has shown to increase the complexity and density of forelimb motor cortical dendritic projections and synapses per neuron (Adkins et al., 2006; Sanes and Donoghue, 2000; Wolpaw and Carp, 2006). These synaptic changes are thought to represent changes in cortical circuitry, thus resulting in cortical plasticity. Whilst there is good evidence for the muscle morphological changes that occur with strength training there is limited data concerning neural adaptations, in the M1 and corticospinal pathway. Proposed sites and mechanisms of neural adaptation following strength training can be seen in figure 2.5.

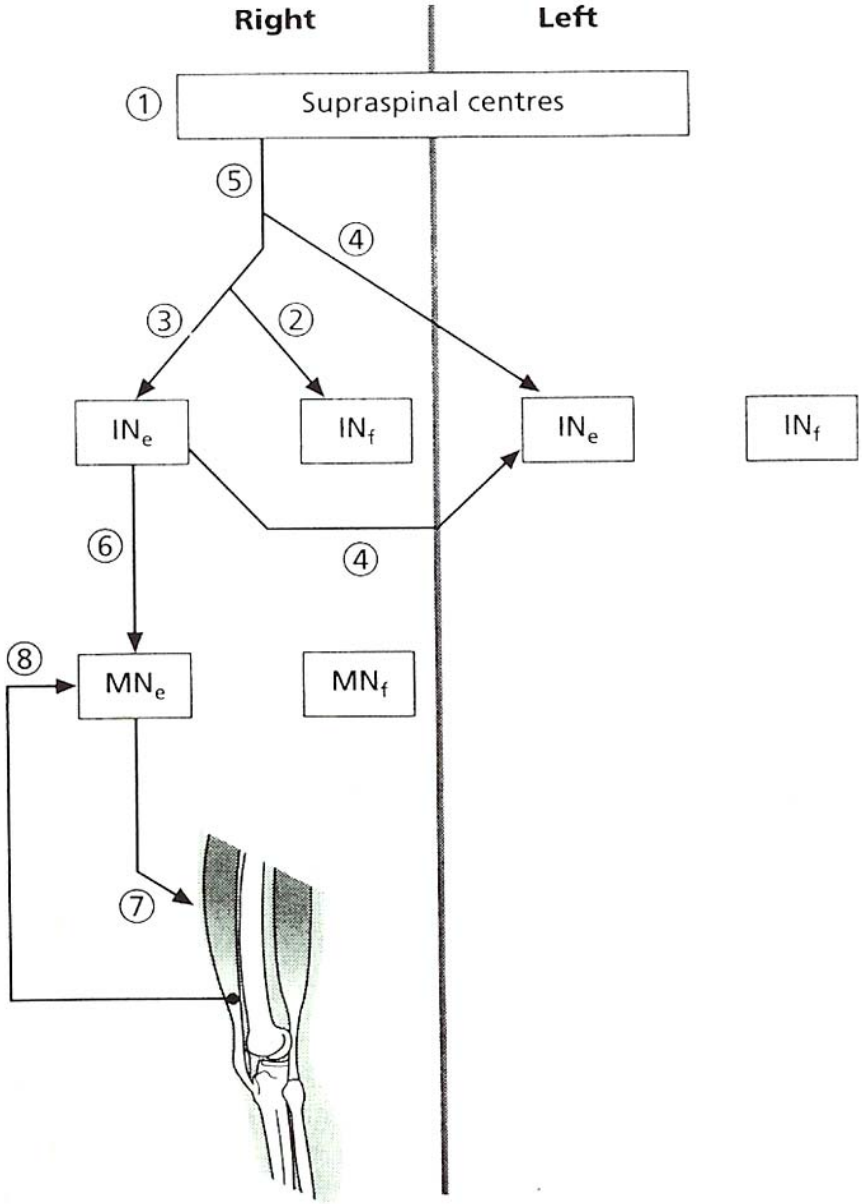

Figure 2.5. Potential sites of adaptation in the nervous system following strength training include: (1) cortical reorganisation, (2) reduced co-contraction of antagonists, (3) increased descending drive from supraspinal centres, (4) cross-education (spinal interneuronal coupling), (5) changes in the bilateral deficit, (6) changes in motor unit behaviour, (7) increased muscle activation, and (8) increased motoneuron exctiability. (Semmler and Enoka, 2000).

TMS has been used to assess CNS adaptations following strength training; however, unlike skill training research, results have been inconsistent (Beck et al., 2007; Carroll et al., 2002; Jensen et al., 2005; Lee et al., 2009a; Griffin and Cafarelli, 2007). Carroll et al. (2002) found no change in corticospinal excitability following four-weeks of strength training of the FDI muscle, despite a 33% increase in muscle strength. Although there was an increase in muscle strength, there were no associated changes in corticospinal excitability as quantified by MEP amplitude. Similarly, Jensen et al. (2005) had participants perform heavy load dynamic strength training of the BB three times per week for four-weeks. Participants completed five sets of six to ten repetitions over a four-week training period with the application of progressive overload. MEP amplitude at 5% of isometric muscle background activity and stimulus-response curves were constructed prior to and after the four-week training intervention. Following training, dynamic muscle strength increased by 31%, however this was accompanied by a decrease in MEP amplitude. In contrast to these findings, Beck et al. (2007) demonstrated a 9.5% increase in MEP amplitude following four-weeks of ballistic strength training of a tibialis anterior (TA). In support of this, Griffen and Cafarelli (2007) following four-weeks of strength training of the TA muscle, found a 32% increase in MEP amplitude at day six and a 16.2% increase at day 12 with no change in peripheral nerve excitability.

However, it is very difficult to compare this data, as the training employed (training design, muscles trained) and the protocols used to assess M1 and corticospinal excitability were different between the studies, therefore limiting our understanding on how the nervous system responds to strength training at present. For example, the work by Carroll et al. (2002) strength-trained a hand muscle requiring a fine movement, whereas Griffen and Cafarelli (2007) trained a leg muscle. Isolated isometric strength

training of the FDI with low task complexity (i.e. low precision and fine control), may have contributed to the results. In addition, research also demonstrates that movement repetition does not lead to functional changes within the M1 in the absence of skilled acquisition (Jensen et al., 2005; Farthing, 2009). On the basis of this finding, it appears that learning is a prerequisite or factor in modulating neural adaptations (Katiuscia et al., 2009). Therefore, using intrinsic muscles that are used in fine motor skill activity on a regular basis (such as the FDI) may have already undergone some form of adaptive plasticity as a result of habitual use and it may be necessary that strength training exercises prescribed should have some element of task complexity and skill.

Although these previous TMS strength training studies have measured corticospinal excitability, there are currently no strength training studies that have measured corticospinal inhibition. The duration of the SP is an example of an inhibitory phenomenon within the corticospinal pathway. The mechanism of the SP is complex and not well defined, although, some spinal and cortical mechanisms have been suggested. It has recently been demonstrated that prior to and during voluntary contractions that inhibition within the M1 is reduced and this reduction has been hypothesised to increase corticospinal drive by "releasing" corticospinal cells from inhibition (Ashe, 1997; Ridding et al., 1995b). Therefore, there is a need to assess the effect of strength training on corticospinal inhibition.

A common explanation for neural adaptations to strength training is increased neural drive (Aagaard et al., 2002a; Aagaard, 2003; Holtermann et al., 2007; Jensen et al., 2005) and motoneuron excitability. Adaptations in motoneuron excitability are often assessed by testing electrically evoked reflexes, such as the Hoffman reflex (H-reflex). Modifications in reflex physiology, provides evidence of changes in spinal cord

circuitry following training (Maffiuletti et al., 2001; Del Balso and Cafarelli, 2007; Holtermann et al., 2007; Fimland et al., 2009a;). The H-reflex is often used to assess the excitability of the spinal α-motoneuron pool (and synaptic efficacy of Ia afferents), whilst the volitional wave (V-wave) measures the magnitude of the efferent drive from the α-motoneuron pool, thus reflecting corticospinal drive (Palmieri et al., 2004; Zehr, 2002; Fimland et al., 2009a; Del Balso and Cafarelli, 2007; Aagaard et al., 2002b; Sale et al., 1983). Aagaard et al. (2002b) demonstrated a significant increase in evoked H-reflex and V-wave responses following 14 weeks of strength training of the quadriceps and suggested that these changes reflected an increase in descending drive from the corticospinal pathway leading to increased α-motoneuron excitability. This finding is further supported by Holtermann et al. (2007) and Fimland et al. (2009a) who also demonstrated enhanced H-reflex following three to four-weeks of strength training. Further, Sale et al. (1983) and Aagaard et al. (2002b) both reported increased V-wave amplitudes in strength-trained athletes. Conversely, Maffiuletti et al. (2001) demonstrated a reduction in H-reflex excitability in strength-trained athletes compared to endurance athletes. These data imply that strength training alters the circuitry of the spinal cord, via changes in α-motoneuron excitability (increase or decrease) and increases corticospinal drive (Aagaard et al., 2002b). More recently, elevated H-reflexes and V-wave amplitudes have been reported following maximal dynamic and isometric strength training (Fimland et al., 2009a; Del Balso and Cafarelli, 2007). However, changes in H-reflex and V-wave amplitude following strength training may arise as a result of changes in the intrinsic properties of Ia afferents, such as presynaptic inhibition from Ia afferent terminals, intrinsic motoneuron properties, and changes in motorneuron firing rate (Hortobágyi et al., 2009; Duchateau et al., 2006; Palmieri et al., 2004). A limitation of these techniques is the difficulty in quantifying the site of

adaptation (i.e. supraspinal or spinal) as neither technique directly measures the involvement of the M1 or corticospinal pathway. The M1 and corticospinal pathway are perhaps the primary supraspinal structures that are involved in modulating voluntary force production (Ashe, 1997), therefore changes in descending pathways should be measured with the appropriate technique (Hortobágyi et al., 2009).

Based upon the available datum, it appears that skill training induces cortical reorganisation in the form of cortical plasticity (Perez et al., 2006; Pascual-Leone et al., 1995' Pearce et al., 2000; Remple et al., 2001; Kleim et al., 2004; Adkins et al., 2006; Wolpaw and Carp, 2006), while strength training stimulates changes within spinal cord circuitry (Carroll et al., 2002; Del Balso and Cafarelli, 2007; Fimland et al., 2009a; Lee et al., 2009a). Although, these studies demonstrate changes in cortical and spinal cord activity following strength training, there is limited data to date that has systematically assessed the effect of strength training on the functional properties of the corticospinal pathway following isometric, dynamic and cross-education strength training.

2.5.2 Motor unit synchrony and strength training

Neural adaptations in motor unit discharge behaviour as a result of strength training have frequently been observed within the literature (Kamen, 2005; Duchateau et al., 2006; Van Cutsem, 1998; Kamen and Knight, 2004; Pucci et al., 2006). Changes in activation level (Knight and Kamen, 2004), motor unit firing rate (Kamen and Knight, 2004) and increases in doublet firing (Van Cutsem et al., 1998) have been reported. As discussed in more detail in section 2.4, the correlated discharge of two active motor units, known as motor unit synchronisation, is also believed to enhance

muscle force following a period a strength training (Milner-Brown et al., 1975). Milner-Brown et al (1975) provided the first line of evidence that short-term isometric strength training of the FDI resulted in increased motor unit synchronisation. Semmler and Nordstrom (1998b) demonstrated that the strength of motor unit synchronisation was largest for the dominant and non-dominant hands in weightlifters, and was lowest in both hands of a group of highly skilled musicians. Recently, Fling et al. (2009) measured the magnitude of motor unit synchronisation of the BB and FDI of strength-trained and untrained participants. In accordance with previous research, greater levels of motor unit synchronisation were noted in the strength-trained group compared to the control group for both the BB and FDI. However, since the Fling et al. (2009) study and that of Semmler and Nordstrom (1998b) did not involve a training intervention, it is not known if these synchronisation differences were related to some aspect of muscle strength, or more closely associated with skilled motor performance.

2.5.3 Cross-education phenomena

There is compelling evidence to support that a change in habitual physical activity, such as strength training, can evoke adaptations in the nervous system (for review sees Duchateau et al., 2006). One common observation within the scientific literature that underscores the complexity of neural interactions following a period of strength training is the phenomena of cross-education. This effect refers to the performance enhancement of muscles in one limb as a result chronic physical activity of the opposite homologous limb. Scripture et al. (1894) provided the first set of observations for the cross-transfer of strength. In this particular study, strength training of the right limb increased strength of the left untrained limb by 43%. Since this

original study, there have been several reported increases in muscle strength following unilateral strength training (Shaver, 1975; Brown et al., 1990; Cannon and Cafarelli, 1987; Hortobágyi et al., 1999; Scripture et al., 1894; Fimland et al., 2009b; Lee et al., 2009b). This phenomenon has also been demonstrated following skill training in the form of bilateral transfer (Lee et al., 2010; Carroll et al., 2008; Perez et al., 2007). The following will provide a review of the evidence for a cross-education effect along with the possible neural mechanisms mediating this cross transfer in strength.

2.5.3.1 Evidence for cross-education

Cross-education of muscle strength has been demonstrated comprehensively using isometric, dynamic and imagined muscle contractions (Shaver, 1975; Brown et al., 1990; Cannon and Cafarelli, 1987; Hortobágyi et al., 1999). The exact physiological mechanism for this interlimb interaction remains unclear, however the fact that this occurs in the absence of muscle hypertrophy implicates some type of neural adaptation. The traditional view suggests that some form of adaptive plasticity within the organisation of the contralateral elements of the CNS, such as the corticospinal pathway may be the locus of adaptation (Carroll et al., 2006; Farthing, 2009). However, to date, there are few studies that have assessed the effect of cross-education of strength on corticospinal excitability and spinal cord circuitry (Fimland et al., 2009b; Lee et al., 2009b; Lagerquist et al., 2006). Recent neurophysiological investigations suggest that motor irradiation may be involved in the cross-transfer of strength (Carson, 2005). There are several lines of evidence to support the notion that the contraction of muscles (i.e. > than 40% of MVC) on one side of the body leads to an increase in the excitability of the contralateral homologous motor pathway (Perez and Cohen, 2008; Cernacek, 1961; Carson, 2005; Hortobágyi et al., 2008; Todor and

Lazarus, 1986), and this has been identified as motor irradiation. Experimental data from Todor and Lazarus (1986) supports the notion that the degree of motor irradiation to the contralateral limb is conditional to the level of neural drive directed to the muscles undergoing the movement. This suggests that the degree of cross-education maybe influenced by training intensity.

Several studies have shown a strong association between the magnitude of the cross-transfer of strength and the degree of strength gained in the trained limb (Hortobágyi et al., 1997; Hortobágyi et al., 1999; Hortobágyi et al., 2003; Carroll et al., 2006; Munn et al., 2004; Munn et al., 2005b). Studies have demonstrated on average a 7.8% increase in muscle strength of the contralateral homologous muscle (Munn et al., 2004; Munn et al., 2005b; Carroll et al., 2006; Zhou, 2000; Hortobágyi et al., 1999; Hortobágyi, 2005). Munn et al. (2004) recently reported that most studies have questionable flaws in methodology, namely lack of a control group, and based upon this data it was suggested that definitive evidence for cross-education effects maybe elusive due to insufficient control measures, however, since this meta-analysis, several studies have since been published that have included a control group, and as such, the original meta-analysis conducted by Munn et al. (2004) has been adjusted and the effects of a lack of a control group appears to be minimal (Carroll et al., 2006).

Several weeks of strength training with concentric voluntary contractions increases contralateral strength by 30%, compared with strength gains of 77% after six weeks of eccentric training (Hortobágyi et al., 1997). Hortobágyi et al. (1997) also demonstarted increased cross-strength transfer following eccentric training compared to concentric training. Further, the cross-education effect has been demonstrated with electrical muscle stimulation (EMS). One study reported that EMS induced a contralateral

increase in strength of 21% after four-weeks of isometric training, which was comparable to that induced by voluntary isometric training alone (Hortobágyi et al., 1999). Further, six weeks of eccentric strength training with EMS induced an increase in strength of 104% compared to 23% of voluntary eccentric training alone (Hortobágyi et al., 1999; Oakman et al., 1999). Cross-education of strength has also been demonstrated to be specific to contraction type and velocity. For example, Farthing and Chilibeck (2003) demonstrated that the cross-transfer of strength was greatest when participants trained eccentrically at a fast speed, following isokinetic strength training of the BB.

Most cross-education training interventions have utilised a training duration of 4-12 weeks with a training intensity of 60% MVC (Zhou, 2000; Munn et al., 2004). In general, the cross-education effect increases gradually over the training period (Cabric and Appell, 1987; Cabric et al., 1988; Carroll et al., 2006). In general the cross-education literature suggests that unilateral strength training over several weeks using isometric and concentric contractions with training loads of > 65%, increases strength on average by 5-25% in the contralateral muscle (Zhou, 2000). Furthermore, the magnitude of the cross-transfer of strength appears to be enhanced following training programs that employ eccentric contractions and electrically evoked contractions (Hortobágyi et al., 1997; Hortobágyi et al,. 1999).

2.5.3.2 Neural mechanism mediating the cross-education effect

With several studies demonstrating that cross-education occurs without a change in the parameter of the EMG signal (no change in motor unit activity) and without hypertrophy, it is unlikely that peripheral muscular adaptations are responsible for the

cross-transfer of strength (Hortobágyi, 2005; Lee and Carroll, 2007; Farthing, 2009). Possible neural mechanisms may include modifications in the organisation of neural activity associated with neural drive from the M1 along with adaptations within specific cortical and subcortical neural circuits that are involved in motor execution (Lee and Carroll, 2007; Carroll et al., 2006; Carson, 2005; Hortobágyi, 2005; Farthing, 2009).

There is robust evidence to support the prevalent network of neural circuits distributed throughout the cerebral cortex (Remy et al., 1994; Jancke et al., 2000; Colebatch et al., 1991; Carson, 2005) that are involved in the planning and execution of voluntary movement (Figure 2.6). There are crossed inter-hemispheric connections between the prefrontal cortices, basal ganglia, cerebellum, premotor areas (PMA), supplementary motor areas, M1 and brain stems (Carson, 2005; Barbas and Pandya, 1987; Boroojerdi et al., 2001b; Cauraugh and Summers, 2005; Carson et al., 2004). Therefore, it is possible that the cross-transfer of strength may occur within these connections, however, to date there is no single study that has investigated this, thus potential mechanisms for cross-education are speculative until research can support these hypotheses (Carroll et al., 2006).

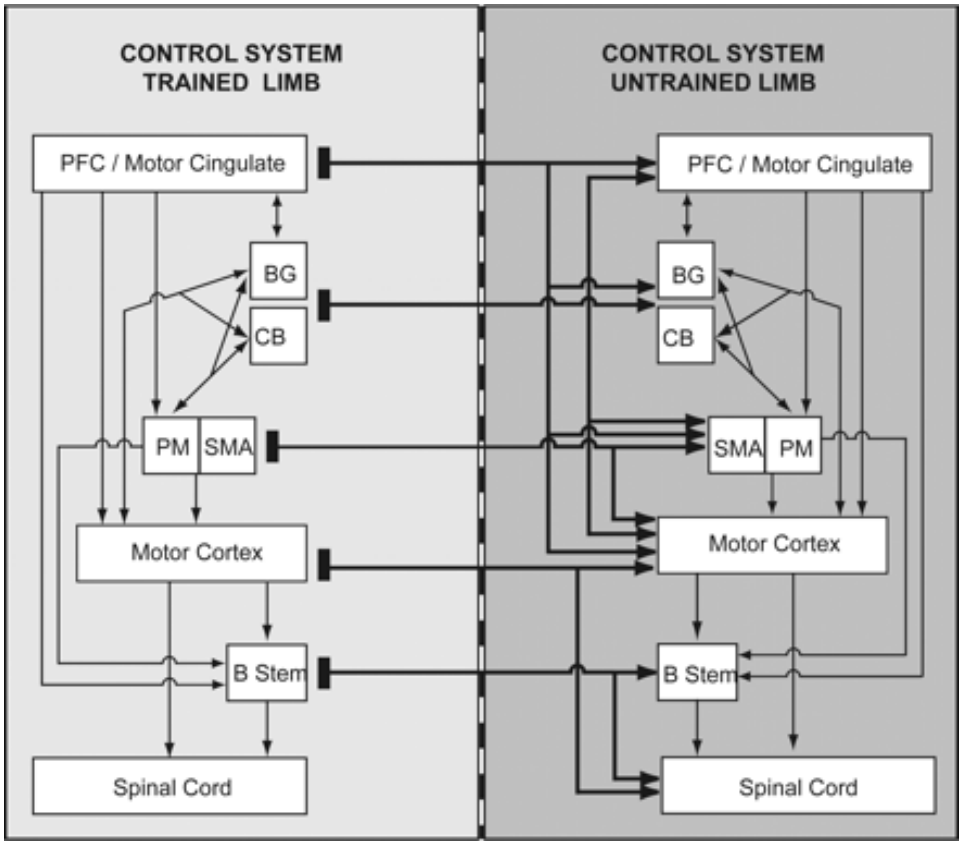

Figure 2.6. Representation of the supraspinal network involved in movement control in each limb, with cross-hemispheric connections depicted via bold lines. The bold lines highlight potential anatomical pathways that may mediate the cross-transfer of strength. PFC, prefrontal cortex; BG, basal ganglia; CB, cerebellum; PM, pre-motor cortex; SMA, supplementary motor area; B Stem, brain stem nuclei (Carroll et al., 2006).

Potential sites for adaptation could reside within the ipsilateral cortex itself. A small proportion of corticospinal fibres do not cross-over at the pyramidal decussation at the medulla, rather they project to ipsilateral spinal motoneurons, thus altering the excitability of ipsilateral pathways (Carson, 2005; Lee and Carroll, 2007; Hortobágyi, 2005; Phillips and Porter, 1964; Perez and Cohen, 2008; Hortobágyi et al., 2003). It has been reported that the size of the ipsilateral corticospinal projection is in the order of 10-30%; however there is some variation between individuals (Carpenter, 1985; Davidoff, 1990; Iwatsubo et al., 1990; Nyberg-Hansen and Rinvik, 1963). In the clinical neurophysiology literature, it has been suggested that increased utilisation of the ipsilateral pathways may provide a viable method for re-establishing motor control of upper limb muscles following lesions to the M1 (Rouiller et al., 1998). Recent data indicates that during unilateral contractions, the ipsilateral M1 may be involved in the planning and processing of motor information that improves the force output of the contralateral muscle (Strens et al., 2003). Strens et al. (2003) used TMS and repetitive (rTMS) to disrupt the function of M1 in order to determine the role of the ipsilateral M1 in force regulation. Following bilateral rTMS to both motor cortices, participants' were unable to match a target force, however when the contralateral M1 was stimulated repetitively, participants were able to match the target force, demonstrating that the ipsilateral M1 plays an important role in the modulation of force. Perez et al. (2008) also demonstrated, using paired-pulse TMS, bilateral M1 activity during unilateral wrist flexion and increased MEPs of the ipsilateral motor pathway with increasing force output. Further, Hortobágyi et al. (2003), showed increased MEPs, but depressed H-reflex excitability, in homologous right limb wrist flexors and extensors following moderate (50% MVC), to strong (75% MVC) acute voluntary contractions of the left hand. These authors suggested increased excitability in the M1 with little to no change

in the motoneuron pool. Although this cross-sectional datum did not use exercise as an intervention, the notion that the ipsilateral cortex can modulate force output directed to the ipsilateral limb suggests that repeated unilateral contractions, following cross-education strength training may lead to some form of adaptation within the M1 and corticospinal pathway contralateral to the trained arm (Carroll et al., 2006).

Although, the above studies support a contribution for ipsilateral corticospinal involvement in the cross-transfer of strength, there is still some uncertainty in describing these ipsilateral corticospinal projections, and it is possible that changes in the ipsilateral motor pathways may not be involved in the cross-education effect as there is evidence to suggest that these nondecussated pathways do not reach the muscles of the upper limbs on the ipsilateral side (Brinkman and Kuypers, 1973; Carroll et al., 2006; Hortobágyi, 2005).

An alternative mechanism may reside in the anatomical pathways that link the motor cortices together (Carson, 2005; Lee and Carroll, 2007). There are several studies that have used TMS to measure the functional connectivity within the cerebral cortex (Okabe et al., 2003; Mochizuki et al., 2004). Unilateral contractions that are greater than 40% of MVC have been shown to increase cortical excitability of the ipsilateral cortex, suggesting that repeated contractions performed within a unilateral training intervention may act as a mechanism for strength transfer (Hess et al., 1986; Hortobágyi et al., 2003; Farthing, 2009; Hortobágyi, 2005). Further, increases in ipsilateral corticospinal excitability may arise as a result of adaptive changes in interhemispheric pathway, most likely modulated by transcollasal pathways, thus providing a mechanism for the cross-transfer of strength (Carroll et al., 2006; Hortobágyi, 2005; Farthing, 2009; Wassermann et al., 1998; Foltys et al., 2003). Imaging studies have demonstrated that multiple areas of the cortex are activated during

unilateral contractions, such as the SMA, cingulate motor area and the prefrontal cortex (Civardi et al., 2001; Mochizuki et al., 2004; Farthing et al., 2007). Whilst these represent multiple potential sites for the cross-transfer of strength, objective studies using techniques such as TMS are required.

It is well documented that hemispheric asymmetries within the M1 are present due to limb dominance (Semmler and Nordstrom, 1998a; Macdonell et al., 1991; Triggs et al., 1994; Garry et al., 2004). Evidence suggests that the left hemisphere projecting and controlling the dominant right hand (in right-handed individuals) plays an important role in controlling the left limb, more so than the right hemisphere controlling the right limb (Verstynen et al., 2005; Farthing et al., 2005; Farthing, 2009; Kawashima et al., 1993). This interhemispheric difference is of interest, as recent cross-education strength training studies have reported increased transfer of strength when the right arm of right hand dominant individuals was trained compared to the left arm (Farthing et al., 2005; Farthing, 2009). Therefore, it could be suggested that the adaptations that occur within the M1 and corticospinal pathway following a period of strength training may enhance this relationship. For example, changes in corticospinal excitability of the left hemisphere projecting to the spinal motoneuron pool innervating the trained arm may improve strength of the contralateral untrained arm due to improved ipsilateral neural drive. Therefore, there is a need for studies to investigate the change in ipsilateral motor activity to test this hypothesis.

Although there are many potential sites of adaptation within the M1 and corticospinal pathway that may in part explain the cross-education phenomena, to date, only one study (Lee et al., 2009b) has used TMS to try and quantify the neural adaptations following unilateral strength training.

2.5.4 Vibration Training

The use of a commercially manufactured whole-body vibration (WBV) machine as a strength training intervention is relatively new (Jordan et al., 2005). There are a number of studies that have demonstrated increased muscle strength and power using this intervention, however the acute effects of WBV applied to the upper body on corticospinal excitability and inhibition is largely untested. Changes in the functional properties of the corticospinal pathway following acute WBV exposure may provide one of probably several mechanisms underlying the post vibratory performance improvements reported in the strength and conditioning literature (Dolny and Reyes 2008). The following will review the effects of local muscle and tendon vibration and WBV on corticospinal excitability and inhibition.

2.5.4.1 Vibration training, equipment and vibratory parameters

Vibration is a periodic mechanical stimulus that is characterised by an oscillatory motion that can be applied to an individual (Jordan et al., 2005; Cardinale and Bosco, 2003). Applying vibrations to the musculoskeletal system is not new and can be dated back four decades (Johnston et al., 1970; Bishop, 1974). The characteristics that affect the intensity of the vibration stimulus include the amplitude, frequency and magnitude (Luo et al., 2005; Carson et al., 2009). The magnitude of the oscillatory motion is determined by the amplitude (peak-to-peak displacement), the repetition rate determines the frequency, and the acceleration of the oscillation determines the magnitude of the vibration (Jordan et al., 2005; Rittweger, 2010).

There are different vibration waveforms that may be applied to the human body. These include sinusoidal, multi-sinusoidal, transient, shock and stationary random and non-stationary random (Figure 2.7).

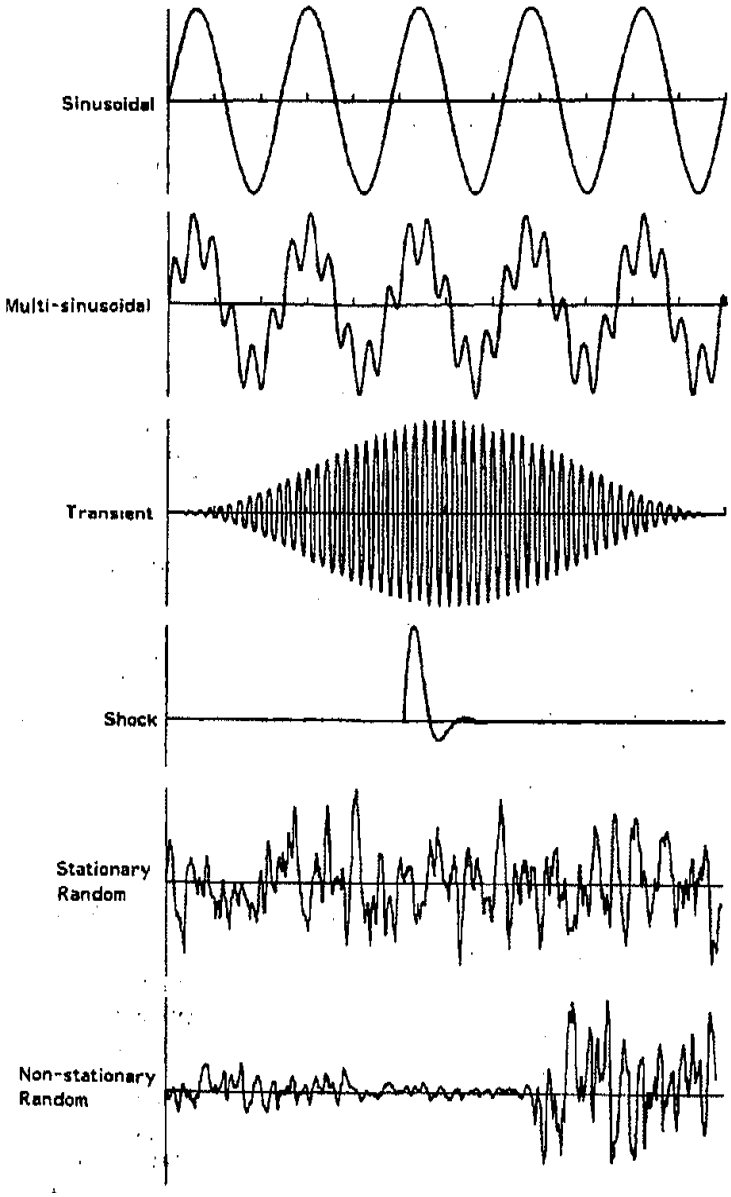

Figure 2.7. Different vibration waveforms (Jordan et al., 2005).

Two common methods of applying a vibration stimulus to the human body include high-frequency direct vibration (i.e. directly applying vibration to a tendon or muscle belly) and low-frequency WBV (Mileva et al., 2009). High-frequency direct vibration can be applied by attaching a vibration unit directly to a muscle of interest or by attaching it to an external support such as a cable or dumbbell (Issurin and Tenenbaum, 1999; Luo et al., 2005; Issurin, 2005). More recently, WBV plates have been developed (Bosco et al., 1998). In this instance, the oscillatory motion in a limb passes from distal to proximal structures, therefore the vibrations are transmitted from a vibrating source that is located away from the target (Luo et al., 2005). The fundamental difference in these methods is the magnitude and frequency of the original vibration as it reaches the target muscle (Luo et al., 2005). For example, with high-frequency direct vibration, the amplitude and frequency of the oscillatory motion does not differ from the values recorded from the vibration apparatus (Bongiovanni et al., 1990b; Jackson and Turner, 2003). However, with WBV, the parameters of vibration may be attenuated in a non-linear manner by soft tissues structures throughout transmission of the vibration to the muscle of interest (Mester et al., 1999).

High-frequency direct vibration and WBV have been used as a training intervention for strength and power athletes and in a clinical setting (Bruyere et al., 2005; Cochrane et al., 2008; Cochrane and Stannard, 2005; Issurin and Tenenbaum, 1999; Blottner et al., 2006; Cormie et al., 2006). Cormie et al. (2006) demonstrated a 3.9% increase in vertical jump height (VJ), which is in agreement to the findings of Cochrane et al. (2008) who also demonstrated a 4.7% increase in peak power output of the shoulder. In addition, Cochrane and Stannard (2005) demonstrated an 8.1 % increase in VJ height and an 8.2% increase in flexibility following a single bout of WBV exercise. Increases in neural drive, motor unit synchronisation and motor unit

recruitment have been suggested to account for the increase in muscle force observed during WBV (Issurin, 2005; Nordlund and Thorstensson, 2007; Rittweger et al., 2003; Bishop, 1974; Johnston et al., 1970; Bongiovanni et al., 1990b; Shinohara et al., 2005). The above observations provide the possibility of a new training methodology that may be employed by athletes to improve strength and power. However, the neural mechanisms behind the benefits of low-frequency WBV are poorly understood and comparisons between studies are difficult, due to the different exercise and WBV protocols, along with the outcome measures used (Carson et al., 2009).

2.5.4.2 Physiological effect of vibration

It is accepted that the primary endings of Ia afferent fibres (muscle spindles) are sensitive to small imposed changes in muscle length (Bongiovanni and Hagbarth, 1990a; Burke et al., 1976; Rosenkranz and Rothwell, 2003). During WBV, the mechanical action of the oscillatory motion produces a rapid change in the length of the muscle-tendon complex, which stimulates the primary endings of the Ia afferents, leading to excitation of α–motoneurons of the homonymous motor units, resulting in a tonic vibration reflex (TVR, Figure 2.8) (Martin and Park, 1997b). A number of studies have used TVR as the mechanism demonstrating acute changes in neuromuscular excitability (measured by changes in dynamic muscle function) following WBV exercise (Rittweger et al., 2003; Roelants et al., 2006; McBride et al., 2010).

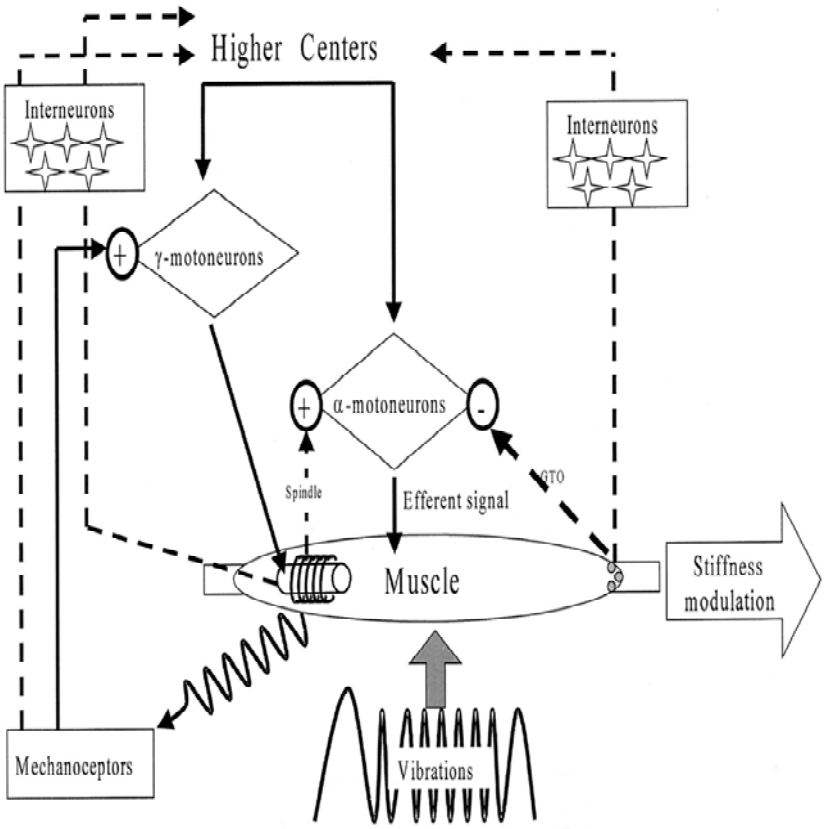

Figure 2.8. Diagram illustrating the physiological affect of vibration (Cardinale and Bosco, 2003).

Whilst discharge of the muscle spindle modulates monosynaptic and polysynaptic reflex pathways (Desmedt and Godaux, 1978; Martin and Park, 1997b; Matthews, 1966; Romaiguere et al., 1991), causing the muscle to contract, there is evidence to suggest that the TVR is more complicated than a segmental reflex (Bishop, 1974). Transection of the spinal cord abolishes the TVR, whilst the strength of the TVR is dependent upon support from higher neural centres (Gillies et al., 1971; Munte et al., 1996). Although the WBV literature have suggested the TVR as a potential mechanism for improved muscle activation, it is unlikely that during exposure to WBV, that the TVR is actually elicited. Several studies suggest that the stretch reflex and H-reflex are suppressed during vibration (Arcangel et al., 1971; De Gail et al., 1966) consequent to increased presynaptic inhibition modulated by GABAergic interneurons (Gillies et al., 1969) and reduced sensitivity of primary spindle endings (Ribot-Ciscar et al., 1998; Hayward et al., 1986). Further, the TVR is also disturbed during longer durations of vibration exposure (i.e. greater than 30 s), therefore linking the TVR as a potential mechanism following WBV seems unjustified at present (Ribot-Ciscar et al., 1998; Bongiovanni et al., 1990b). Given the previous data supporting the decreases in TVR and considering the protocols often used in low-frequency WBV (i.e. moderate levels of muscle activity and long exposure times), it is unlikely that facilitation of the TVR occurs during WBV exercise (Rittweger, 2010; McBride et al., 2010).

In determining the physiological effect of vibration (high-frequency direct and WBV) on corticospinal excitability, a distinction needs to be made as to the effects that occur during the vibration exposure ***versus*** the period immediately following cessation of the vibration stimulus. In support of vibration affecting higher neural control centres, Kossev et al. (1999) and Munte et al. (1996) demonstrated facilitated MEPs during high-frequency direct vibration. Specifically, Kossev et al. (1999) demonstrated that

trains of 4 s vibration (80 Hz, 0.5 mm amplitude), resulted in significant modulation in corticospinal activity in the form of increased MEPs following TMS compared to no changes preceding TES. Munte et al. (1996) also demonstrated increased cortical excitability during vibration at 80 Hz whilst using the electroencephalography technique. Similarly, Rosenkranz & Rothwell (2003) also observed an increase in the amplitude of the TMS evoked MEP during high-frequency direct vibration. Further, low amplitude (0.2-0.5 mm amplitude) local vibration (58 Hz) of the BB muscle, leads to an increase in the excitatory discharge of motor cortical cells during vibration (Fourment et al., 1996). Steyvers et al. (2003) demonstrated 49% increase in MEP amplitude during 75 and 120 Hz (0.5mm amplitude) of vibration over the flexor carpi radialis (FCR) muscle. This increase is in agreement with several other investigations that have used a similar frequency and amplitude (Roll et al., 1989; Roll and Vedel, 1982). These observations suggest that direct high-frequency vibration modulates the excitability of populations of corticospinal neurons within the M1 (Floeter and Rothwell, 1999), possibly improving motor unit activation.

In order to determine the effect of WBV on corticospinal excitability, Mileva et al. (2009) recorded MEPs during low-frequency WBV. In particular, they assessed corticospinal excitability through single pulse TMS and paired pulse TMS to assess SICI and short latency intracortical facilitation (SICF) (Mileva et al., 2009). Seven participants underwent a static squat hold for 330 s. During the first 110 s, no vibration was applied however, 5 single and 5 paired pulse TMS stimuli were applied. During the second period (next 110 s), participants were exposed to WBV (30 Hz, 1.5 mm amplitude) and 5 single and 5 paired pulse TMS was applied. The remaining 110 s was termed post vibration (i.e. no vibration) and TMS was applied again. The key findings to this study were increased corticospinal excitability of the tibialis anterior (TA) during

WBV, increased SICI, and reduced intracortical facilitation. These data intimate that WBV may alter corticospinal and intracortical process within the M1 and are consistent with the corticospinal responses that occur with high-frequency direct vibration.

Only a limited number of studies have actually examined the possible after-effects of high-frequency direct vibration on corticospinal excitability (Forner-Cordero et al., 2008; Steyvers et al., 2003). Steyvers et al. (2003) measured the amplitude of MEPs immediately following a bout of high-frequency direct vibration over the FCR and demonstrated no difference in corticospinal excitability. This finding is in agreement with Forner-Cordero et al (2008), who also found no significant difference in corticospinal excitability following low-frequency vibration of the FCR. In the only study to date on corticospinal responses to low-frequency WBV, Mileva et al. (2009) also reported no significant difference in corticospinal excitability immediately following acute WBV of TA and soleus muscles. Thus, it remains unclear what mechanisms contribute to the increases in muscle function following acute WBV exposure. There are no studies to demonstrate the effect of a single bout of low-frequency WBV applied to the upper body on corticospinal excitability and inhibition. Although the WBV literature supports the view that acute exposure to WBV may lead to facilitated reflex responses, the mechanisms of this enhancement are not yet understood.

2.6 Conclusion

There are many potential sites of adaptation within the nervous system following a period of strength training. However, there are currently no systematic studies that have examined the effect of different methods of strength training on corticospinal excitability and inhibition. One of the most reported neural adaptations to strength training is the adjustment in the strength of common corticospinal inputs onto pairs of concurrently active motor units. Although changes in motor unit synchronisation have been demonstrated in participants who engage in strength training on a regular basis, the data fails to provide information on the short-term adjustments in correlated motor unit activity that may occur as a direct consequence of strength training. Further, no studies have assessed the effect of different types of strength training on corticospinal excitability and inhibition systematically. The studies in this dissertation will therefore examine the corticospinal responses following isometric, isotonic, cross-education and WBV strength exercise. In particular, it will examine the effect of isometric strength training on the strength of motor unit synchronisation and corticospinal control of the FDI, and corticospinal excitability and inhibition following controlled isotonic strength training and cross-education strength training of the BB. This thesis will also investigate the acute effect of WBV applied to the upper body on BB corticospinal excitability and inhibition.

CHAPTER THREE

Motor Unit Synchronisation Following Short-Term Strength Training of an Intrinsic Hand Muscle

(This work was completed under the supervision of Dr John Semmler).

3.1 Introduction

Over the last three decades, discussions on the neural adaptations to strength training have inevitably included a role for motor unit synchronisation in the rapid gains in strength during the first few weeks of a strength training program. The rationale for this is based on the seminal study by Milner-Brown et al. (1975), who provided indirect evidence from the sEMG showing that strength training of a hand muscle enhances motor unit synchronisation. However, it has been shown that the indirect method of estimating synchronisation from the sEMG has several limitations, which restricts its usefulness as an index of synchronisation during voluntary contractions in humans (Yue et al., 1995; Keenan et al., 2007; Semmler and Nordstrom, 1999). Although a change in motor unit synchronisation is regarded as one of the most significant adaptations that occur in the nervous system in response to strength training, the use of the sEMG index by Milner-Brown et al. (1975) casts some doubt on the conclusions drawn from their data.

The most direct method to quantify motor unit synchronisation in humans is by the cross correlation of individual discharge times from pairs of concurrently active motor units, where the discharge times of one motor unit are used as a reference, and a histogram is constructed of the peri-event discharge times of the other motor unit. Using this procedure, several studies have shown that motor unit synchronisation varies with the details of the task performed. For example, when measuring from the same pairs of motor units in the FDI muscle, the strength of motor unit synchronisation was 15% less during isometric index finger flexion compared with abduction (Bremner et al., 1991b), whereas synchronisation strength was 35% greater during lengthening contractions compared with isometric and shortening contractions (Semmler et al., 2002). Furthermore, the strength of motor unit synchronisation may be altered by

habitual physical activity (Fling et al., 2009; Semmler and Nordstrom, 1998b). Using cross-correlation analysis, Semmler and Nordstrom (1998b) demonstrated that the strength of motor unit synchronisation was largest for the dominant and non-dominant hands in weightlifters, and was lowest in both hands of a group of highly skilled musicians. This data has recently been supported by Fling et al. (2009) who also demonstrated increased motor unit synchronisation in a group of strength-trained participants. However, because no training intervention was performed, it is not known if these synchronisation differences were related to some aspect of muscle strength, or more closely associated with skilled motor performance.

Additional information can be gained about the common input to motoneurons by examining the correlated activity from pairs of motor units in the frequency domain. This procedure, known as motor unit coherence analysis, is a measure of the strength of common oscillatory input to the motoneurons that is thought to originate in various cortical structures that includes the M1 (Farmer et al., 1993a; Baker and Baker, 2003). Similar to synchronisation, motor unit coherence is also modulated based on the requirements of the task, which includes reduced coherence during shortening contractions (Kakuda et al., 1999; Semmler et al., 2002) and alterations in coherence based on the compliance of a manipulated object during a precision grip (Kilner et al., 2002). Several studies have shown a strong association between motor unit synchronisation and high frequency (15-30 Hz) coherence, suggesting that these two measures of common input share similar mechanisms (Farmer et al., 1993a; Halliday et al., 1999; Kilner et al., 2002; Semmler et al., 2002; Semmler, 2002). Accordingly, Semmler and Nordstrom (1998b) used their original motor unit samples and found that motor unit coherence was greatest in the weightlifters and least in the musicians, with a strong correlation between motor unit synchronisation and high-frequency (15-30 Hz)

coherence, particularly for broad synchronisation peaks in the strength-trained participants (Semmler et al., 2004). However, this cross-sectional data again fails to provide information on the short-term adjustments in correlated motor unit activity that may occur as a direct consequence of training.

The purpose of this study was to quantify the strength of motor unit synchronisation and coherence from pairs of concurrently active motor units obtained before and after four-weeks of strength training a hand muscle. Based on previous data in strength-trained participants (Semmler and Nordstrom, 1998b, Milner-Brown et al., 1975; Fling et al., 2009), and the mechanistic link between motor unit synchronisation and coherence (Semmler et al., 2004; Farmer et al., 1993a), it was hypothesised that motor unit synchronisation and coherence in the FDI muscle would increase following short-term isometric strength training.

3.2 Methods

Eight participants (age 25.8 ± 5.0, range 20-33 yrs) volunteered to take part in the study, and gave informed consent to the procedures that were approved by the university human research ethics committee. Participants had no known history of peripheral or neurological impairment. Five participants completed the four-week training program, whereas the remaining three participants completed the experimental sessions that were separated by four-weeks with no training intervention. Four experimental sessions were performed on each participant, with two undertaken before training and two after training.

3.2.1 Experimental arrangement

Participants were seated comfortably in an experimental chair with their right arm and hand placed in a manipulandum as described previously (Sale and Semmler, 2005). Briefly, the shoulder was abducted 45°; the elbow joint was flexed to 90° and the palm of the hand facing downwards. The third to fifth digits were flexed around a handle located on the manipulandum and the thumb was kept extended by a support. This position acted to isolate index finger abduction force by restraining the other digits. Voluntary force was measured using a force transducer (MLP-25, Transducer Techniques, CA) that was located on the lateral side of the proximal interphalangeal joint. Participants were provided with visual feedback of force via an oscilloscope that was located approximately 1 m in front of them at eye level. Single motor unit recordings were obtained from the right FDI using 50 μm stainless steel wires that were insulated with formvar (California Fine Wire, Grover Beach, CA, USA) and inserted into the muscle with a 27 G hypodermic needle. A hook of 2 mm was created at the recording end of the electrodes so that the wires remained fixed within the muscle once the needle was removed. The motor unit signals were amplified (1000x) and filtered (90 Hz-8 kHz), and together with force were recorded on a digital recorder (Sony PC 116 DAT) then digitised (20 kHz for motor units, 2 kHz for force) and analysed off-line using the Spike2 data analysis system (Cambridge Electronic Design. Ltd., Cambridge, UK).

3.2.2 Organisation of the study

The training program involved maximum isometric abduction of the right index finger that was performed 3 times/week in the laboratory. The task consisted of rapid index finger abduction contractions that were held for 3 s, with a 3 s rest between

contractions. This was performed ten times (one set), and each participant performed 6 sets (separated by approximately two minutes) for a total of 60 contractions which lasted 18 minutes. Each participant underwent training for at least four-weeks (12 sessions), and training was continued until all post-training motor unit recordings were obtained. Before and after training, measurements of maximum strength and single motor unit activity were acquired on two occasions. For maximum strength, participants were asked to produce a gradual increase in index finger abduction force to maximum over a 3 s period, and verbal encouragement was provided while a maximal effort was maintained for a further 3 s. This task was performed three to four times, and the maximum voluntary contraction (MVC) force was obtained provided that a consistent (force within 5%) effort was performed in at least two contractions. Following this, 3-4 intramuscular electrodes were inserted into the FDI muscle to record single motor unit activity. The protocol involved identifying a feedback motor unit in one of the electrodes, and participants were provided with the discharge times of this motor unit via an audio signal. The trial commenced when a second motor unit was identified in a separate electrode, and the participant was asked to maintain the discharge rate in the feedback motor unit for 1-4 min while the activity of the second motor unit was continually monitored by one of the investigators. Sampling from motor units that were active at relatively low forces (i.e. 5% of MVC) minimised the effects of fatigue, and the participants were allowed to rest for several minutes at the end of each trial. After the rest period, a different motor unit from the second channel was selected, by either displacing the electrode at least 0.5 cm to obtain a completely different motor unit waveform, or by recording from a new electrode. No more than two recordings were obtained from each electrode to reduce the likelihood of recording from the same motor unit on separate occasions. Using this procedure, the goal was to match the same

feedback motor unit with at least 5 other different motor units within the muscle, as it has previously been shown that this method provides a reasonably good estimate of the strength of motor unit synchronisation within the FDI muscle (Semmler and Nordstrom, 1999). Due to the difficulty in maintaining the same feedback motor unit during multiple trials, it was not possible to follow this procedure during one recording session in one participant after training. On this occasion, 5 motor unit pairs were recorded from 9 unique motor units.

3.2.3 Data and statistical analyses

Single motor unit discharges were discriminated using a computerised waveform-matching template (Spike 2, Cambridge Electronic Design, UK), which identified action potentials based on waveform shape. To ensure discrimination accuracy, the interspike intervals of identified motor units were examined for every trial. Trials that contained abnormally short or long interspike intervals due to discrimination error were manually edited based on waveform shape and expected discharge times on a spike-by-spike basis. Mean motor unit discharge rate and the coefficient of variation of discharge rate were calculated from the individual discharge times. Motor unit synchronisation was assessed by cross-correlation of the discharge times from pairs of motor units obtained from separate electrodes using the synchrony index CIS (common input strength), which indicates the number of discharges in excess of chance divided by the duration of the trial when both motor units were tonically active. This index represents the *frequency* of extra synchronous discharges, and is not influenced by discharge rate of the contributing motor units (Nordstrom et al., 1992). As an alternative measure, the strength of synchronisation was also quantified using the index *E*, which corresponds to the total number of extra counts within the peak relative

to the number of discharges by the motor unit with the lowest mean discharge rate (Datta and Stephens, 1990). This index represents the *probability* of extra synchronous discharges for every discharge by the reference motor unit. The geometric mean discharge rate and coefficient of variation of discharge rate were calculated for each pair of motor units used for cross-correlation analysis. Coherence analysis was performed between the same pairs of motor units using a procedure that has been described previously (Rosenberg et al., 1989; Semmler et al., 2004; Amjad et al., 1997) and was implemented in MATLAB (v14, Math Works, Inc.; Natick, MA, USA). Briefly, the discriminated motor unit data were divided into contiguous, non-overlapping epochs of 1.28 s that comprised 256 bins. Each 5 ms bin was assigned a value of 1 when it contained a discriminated action potential and a value of 0 when no action potential was present, and these data were transformed into the frequency domain with a resolution of 0.8 Hz. Auto- and cross-spectra were averaged over the disjoint sections to obtain the coherence datum for each motor unit pair, which resulted in a measure of linear association with values between 0 (completely independent) and 1 (completely dependent). The pooled coherence was then calculated for each condition using the method described by Amjad et al. (1997). For comparison between participants, the coherence estimates for each pair of motor units were normalised into *z* scores (Rosenberg et al., 1989).

For statistical analysis, a three way repeated measures ANOVA was used to examine MVC force, with one between-participant factor of Training group (training, control) and two within-participant factors of Session (first, second) and Time (before, after). For the motor unit discharge properties (geometric mean discharge rate and variability, synchronisation, coherence), a three-way ANOVA was used to compare Training group, Session, and Time. Data were pooled between Sessions as no

significant effect in the ANOVA was observed between the first and second session for any dependent variable. Fishers post-hoc test was performed when significant effects were observed in the ANOVA. For all the comparisons, $p < 0.05$ was regarded as statistically significant. Data are shown as means ± SD.

3.3 Results

Maximum index finger abduction force for the training and control group are shown in Figure 3.1. The strength training program resulted in a mean increase in strength for index finger abduction of 54% (24 N, $p = 0.001$), with an increase that ranged from 36 to 79% in individual participants. In contrast, there was no significant change in strength for the control group when the measurements were separated by four-weeks ($p = 0.48$, range – 4 to + 25%).

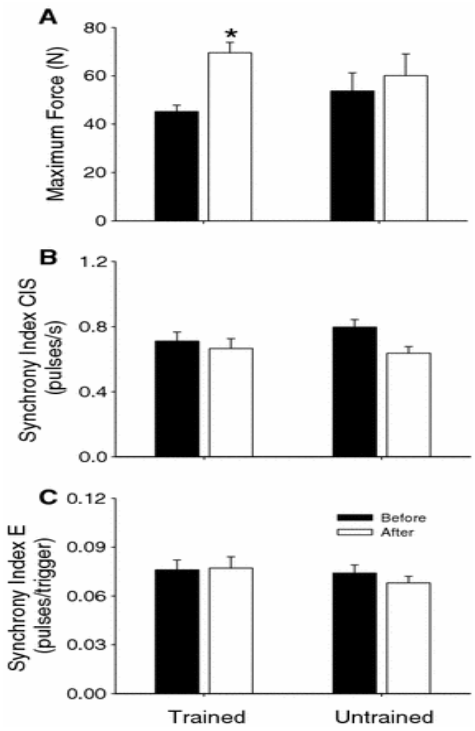

Figure 3.1. Maximal voluntary contraction force (A) and strength of motor unit synchronisation (B, C) measured before and after training in 4 participants. Data show a 54% increase in index finger abduction force and a 20% reduction in mean strength of motor unit synchronisation following four-weeks of strength training. * Statistical significance, $p < 0.05$.

A total of 163 motor unit pairs (198 individual motor units) were examined in eight participants, with each participant contributing an equivalent number (10) of motor unit pairs before and after the intervention. For the five participants in the training group, 52 motor unit pairs (62 motor units) were obtained on 10 occasions before and 51 motor unit pairs (64 motor units) were obtained on 10 occasions after strength training. For the three control participants, 29 motor unit pairs (35 motor units) were obtained on 6 occasions before and 31 motor unit pairs (37 motor units) were obtained on 6 occasions after four-weeks of normal daily activities.

There were no significant differences in the geometric mean discharge rate after the training intervention between the training and control groups ($p > 0.05$). In the training group, the geometric mean discharge rate was 10.4 ± 1.2 pulses/s (pps) before training and 9.5 ± 2.1 pps after training. For the control participants, the geometric mean discharge rate was 10.8 ± 1.9 pps before and 9.5 ± 2.1 pps four-weeks later (Figure 3.2). In contrast, the geometric mean discharge rate variability increased after the intervention in both participant groups ($p < 0.001$).

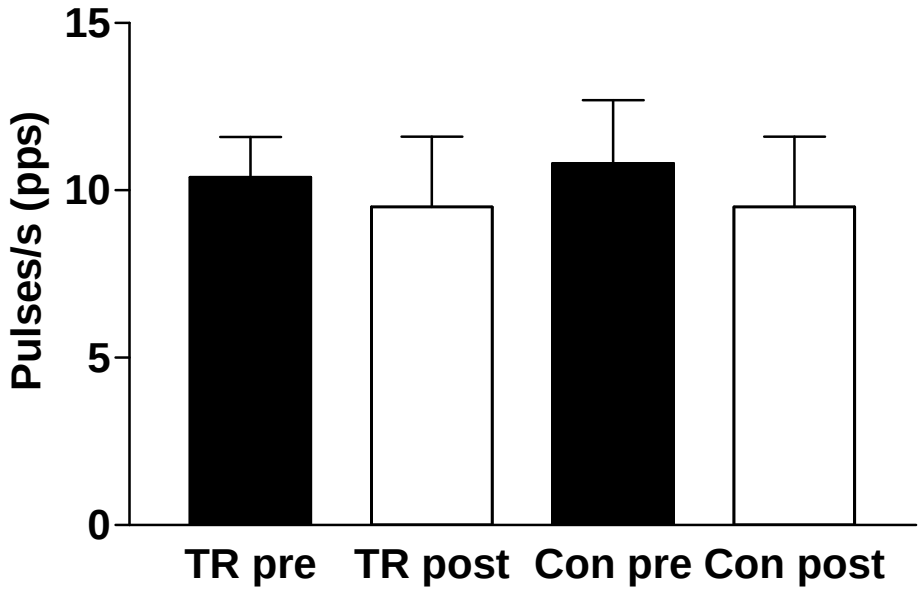

Figure 3.2. Mean geometric discharge rates prior to and following the strength training program for trained and untrained groups**.** Black bars represent pre training mean values, whilst the clear bars represent the post training values. There were no significant differences in geometric discharge rate pre vs. post strength training for both groups.

In the training group, the geometric mean coefficient of variation was 17.8 ± 3.8% before training and 18.7 ± 3.7% after training. For the control participants, the geometric mean coefficient of variation was 16.3 ± 2.7% before and 18.2 ± 3.4% after four-weeks. Again, no significant difference was observed for the geometric mean coefficient of variation between training and control groups ($p > 0.05$). These motor unit discharge properties were maintained with mean contraction intensities of 8.5 ± 8.8% MVC before training and 8.7 ± 9.7% MVC after training. The mean contraction intensities were significantly lower for the control participants ($p < 0.001$), which were 2.9 ± 2.7% MVC before and 2.7 ± 2.8% MVC after the four week period. However, there was no significant difference in mean contraction intensities before and after the intervention in both groups.

The significant increase in strength induced by the strength training program did not alter the mean strength of motor unit synchronisation in these participants (Figure 3.1 B and C). Using two different measures of the strength of synchronisation, there was no effect of Training, Group, or a Training × Group interaction in the ANOVA using the synchrony index CIS or index *E*. There was a slight tendency for reduced synchronisation after the intervention using the synchrony index CIS in both groups, although this comparison did not reach statistical significance ($p > 0.05$). Furthermore, training did not influence the width of the synchronous peak nor was it different between the training and control groups. The width of the central synchronous peak was 14.2 ± 6.1 ms in the training group and 15.8 ± 3.6 ms in the control group before the four week period, whereas it was 15.7 ± 4.8 ms in the training group and 16.0 ± 4.0 ms in the control group after the intervention (Figure 3.3).

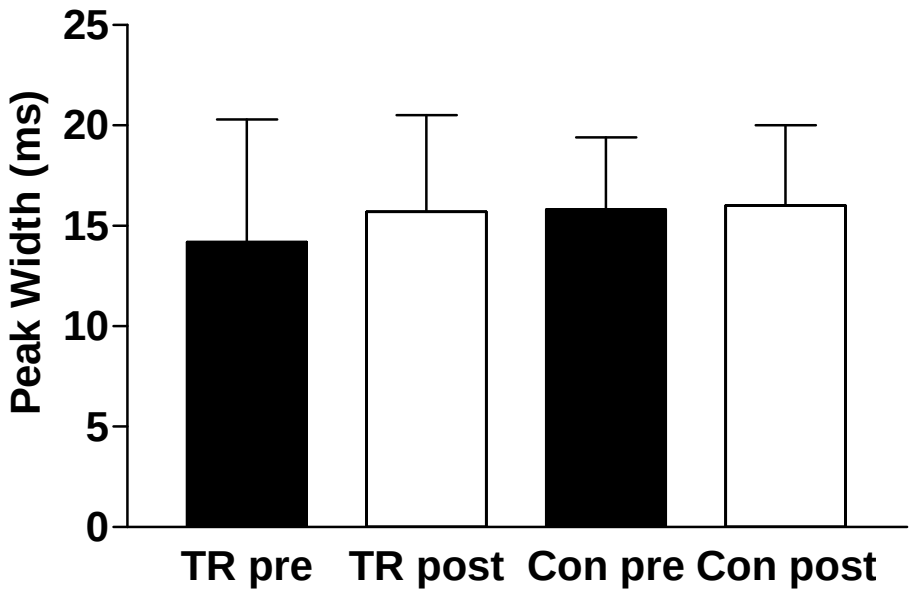

Figure 3.3. Mean width of the central synchronous peak obtained from the cross-correlation histogram for trained and untrained groups pre (black bars) and post (clear bars) the four-week strength training intervention. There were no significant differences in the central synchronous peak pre vs. post strength training for both groups.

The strength of motor unit coherence in the training and control groups obtained before and after the intervention is shown in Figure 3.4. The pooled coherence values are shown for descriptive purposes in A and B, whereas the mean coherence *z*-scores from 0 to 10 and 10 to 30 Hz are shown for use in statistical analysis in C and D. The number of 1.28 s data segments used in the coherence analysis did not vary between training groups or measurement sessions. The number of segments that contributed to the coherence analysis in the training group was 99 ± 6 before training and 111 ± 5 after training, whereas it was 108 ± 6 before and 104 ± 4 after 4 weeks in the control group. From these data, the typical pattern of motor unit coherence, consisting of a large amplitude low-frequency (0–10 Hz) peak, and a small amplitude high-frequency (10–30 Hz) peak, was observed in both participant groups, although a small peak was observed at 6 Hz in the trained group that was not present in either recording session in the control group. Statistical analysis of the mean coherence *z* scores (Figure 3.4) showed that there was no difference in coherence before and after strength training, or for the two recording sessions in the untrained participants at 0–10 or 10–30 Hz. Furthermore, there was no significant difference in mean coherence between the training and control groups at low (0–10 Hz) or high (10–30 Hz) frequencies.

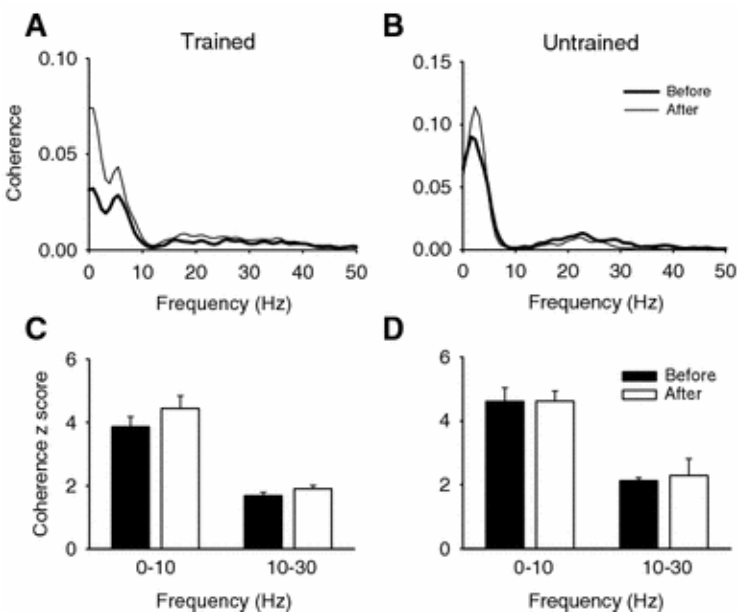

Figure 3.4. Motor unit coherence measured from pairs of motor units obtained before and after strength training (*Trained*) or no training (*Untrained*). **A**, **B,** the pooled coherence values; **C**, **D** the mean coherence *z* scores obtained from 0 to 10 Hz and 10 to 30 Hz. Short-term strength training did not influence motor unit coherence at low or high frequencies ($p > 0.05$).

3.4 Discussion

It is a commonly held view that the strength of motor unit synchronisation in a hand muscle increases as a result of a short period of strength training. Using cross-correlation of pairs of motor units, which represents the gold standard to quantify motor unit synchronisation during voluntary contractions in humans, this study found no change in the strength of motor unit synchronisation following training, despite significant strength gains that were obtained in all participants. Furthermore, strength training did not influence motor unit coherence at any frequency in these participants. These data suggest that increases in strength following four-weeks of training a hand muscle are not accompanied by increases in the correlated activity of motor units.

Because substantial variability exists in the measure of synchronisation obtained from cross-correlation (Nordstrom et al., 1992), the comparison of motor unit activity before and after training requires a sufficient sample size and an adequate number of measurements to adequately characterize the behaviour. The current study employed a sampling procedure that required the matching of one reference motor unit to at least five other unique units within the same muscle, rather than the typical approach of sampling from as many motor units in the muscle as possible. Although it was technically difficult to maintain the activity of the same motor unit throughout the 2 h recording session, this technique allowed sampling from a smaller number of motor units, whilst providing equivalent information from that obtained from a larger random sample of motor units. This rationale is based on a previous observation indicating that the mean strength of synchronisation obtained from cross-correlating the discharge of one reference motor unit to at least five other units in the muscle is strongly correlated ($r = 0.86$; $p < 0.001$) with the mean strength of motor unit synchronisation obtained when sampling from an average of 14 (range 9–23) randomly selected motor unit pairs

in the same muscle, with no significant differences in synchronisation between the two procedures in 85% of cases (Semmler and Nordstrom, 1999). To increase the sample size, the estimate of motor unit synchronisation for each participant was performed twice before and twice after training. However, this technique still only quantifies synchronisation in the selected population of motor units in the muscle on that day, and is not a measure of whole muscle synchronisation. For this reason, the motor units from all participants have been pooled, as opposed to examining the strength of synchronisation within participants. Furthermore, because up to four electrodes were used in each recording session, each new motor unit sampled was unique, and not simply a recording from other muscle fibers of the same motor unit, which is likely to occur when manipulating the electrode to sample from as many motor units in the muscle as possible, or when performing multiple measurements on separate days.

The most influential study on the role of motor unit synchronisation in strength training was performed by Milner-Brown et al. (Milner-Brown et al., 1975), who used an indirect measure of synchronisation derived from the sEMG. They found that EMG-based synchronisation was higher in the FDI muscle of a group of weightlifters, and that synchronisation measured in control participants could be enhanced by a six-week period of strength training. However, recent studies have indicated that the indirect method of estimating synchronisation from the sEMG used by Milner-Brown et al. (1975) has several limitations. For example, sEMG synchronisation is influenced by an artifact associated with the signal rectification process which varies with the signal-to-noise ratio, is positively correlated with background EMG levels due to recruitment of new synchronised motor units (Yue et al., 1995), and is influenced by neuromuscular factors that affect signal cancellation in the spike-triggered averages derived from the EMG (Keenan et al., 2006). Furthermore, there is a poor correlation between estimates

of motor unit synchronisation using the sEMG and the more robust cross-correlation method (Semmler and Nordstrom, 1999; Keenan et al., 2007), with the most likely explanation for this discrepancy related to the technical limitations with measuring synchronisation from the sEMG.

To further explore the role of synchronisation in muscle strength, Semmler and Nordstrom (1998b) used cross-correlation of motor unit discharge to compare the strength of motor unit synchronisation in groups of individuals with contrasting habitual use of their hand muscles. They found that the strength of motor unit synchronisation was largest in weightlifters, intermediate in untrained participants, and least for highly skilled musicians, suggesting that motor unit synchronisation is related to some aspect of strength in weightlifters, or to skilled hand function in musicians. These findings are in agreement to Fling et al. (2009) who also demonstrated; that motor unit synchronisation was greatest in a group of strength-trained participants compared to a group of controls. The current study, which used cross-correlation of motor units to examine synchronisation after a short-term strength training protocol, is a logical extension of this work. However, this study found that increases in strength of a hand muscle following several weeks of training were not accompanied by increases in motor unit synchronisation. In support of a recent computer simulation study (Yao et al., 2000), these data suggest that motor unit synchronisation is not important in the expression of muscle strength. It is possible that the divergent levels of motor unit synchronisation in chronic weightlifters and musicians obtained in the previous study by Semmler and Nordstrom (1998b), may reflect an inherent level of synchronisation that has been reduced by the long-term skilled muscle use that is necessary to play a musical instrument, rather than an increase in motor unit synchrony that is caused by strength training. Therefore, the findings from the present study suggest that the neural

adaptations that occur to induce changes in motor unit synchronisation are related to fine motor performance, with adjustments in the common inputs to motoneurons that generate synchronisation operating as an appropriate neural strategy to promote the accurate performance of skilled motor tasks, such as when playing a musical instrument (Semmler and Nordstrom, 1998b). Given the increase in motor unit synchrony in Semmler and Nordstrom (1998b) original motor unit study, it's most likely that the findings of the present study, suggest that motor synchrony may change as a consequence of long-term training and not short-term training.

In contrast to changes in motor unit synchronisation, there is less information on the training-related plasticity of common oscillatory inputs to motoneurons that is quantified as corticomuscular (cortex to muscle), EMG (muscle to muscle), or motor unit coherence. This common modulation by rhythmic inputs in the descending command to muscles is believed to represent an "echo" of multiple neural oscillators from different cortical and sub-cortical areas, and may provide a mechanism for the integration of sensory and motor system information during co-ordinated movement (Farmer, 1998). Much of the available evidence indicates that coherent oscillations in the motor system are influenced by the task performed, but only during skilled muscle use. For example, motor unit coherence at 15–30 Hz is increased with the compliance of the gripped object (Kilner et al., 2002) and during slow lengthening compared with shortening muscle contractions (Semmler et al., 2002). In addition to these acute neural adjustments, it has previously been shown that long-term habitual physical activity over many years involving skill and strength training are associated with divergent adaptations in motor unit coherence, with the least coherence in the hand muscles of musicians compared with weightlifters (Semmler et al., 2004). The current study demonstrates that a short period of strength training has no effect on motor unit

coherence during a simple index finger abduction task. Although the relevance of these coherent oscillations to the neural control of movement is not yet clear, the current study suggests that oscillatory inputs to motoneurons are not associated with the development of muscle strength. Therefore, it seems more likely that these coherent oscillations represent a more efficient strategy to maintain precise coordinated control of a large number of synergist muscles during skilled motor tasks, as has been suggested previously (Semmler et al., 2004; Kilner et al., 2002).

Motor unit synchronisation and coherence represent different statistical procedures that provide complimentary information on the common input to motoneurons during voluntary contractions. Both of these features of correlated motor unit activity are believed to be modulated by cortical input to the motoneurons. For example, motor unit synchronisation is altered in conditions that affect the corticospinal pathway such as in stroke (Farmer et al., 1993b) and amyotrophic lateral sclerosis (Schmied et al., 1999), but is not affected by vigorous vibration of a hand muscle that is known to excite muscle spindles (Farmer et al., 1997). Using a similar rationale, several studies have indicated that motor unit coherence is also mediated, at least for high frequencies (10–30 Hz), by the corticospinal pathway (Farmer et al., 1993a; Baker and Baker, 2003; Salenius et al., 1997). As such, variations in the strength of correlated motor unit activity in the time and frequency domains are interpreted as a change in the common inputs to motoneurons from supraspinal sources. This study found no change in motor unit synchronisation or coherence following short-term strength training of a hand muscle, indicating that this intervention is unlikely to involve adaptations of common descending inputs from the M1. In support of this view, Carroll et al. (2002) found that four-weeks of strength training a hand muscle did not alter corticospinal excitability measured by TMS when obtained at rest, and was reduced at contraction

levels of 50% MVC. Because the reduction in MEP amplitude during the contraction was also observed following transcranial electrical stimulation (which activates corticospinal axons directly), they concluded that strength training altered the functional properties of the spinal cord circuitry, but not the output from the M1. Despite numerous reports describing functional changes in the M1 control of movement following short-term skill training (Karni et al., 1995; Pascual-Leone et al., 1995; Classen et al., 1998; Ziemann et al., 2001; Jensen et al., 2005; Katiuscia et al., 2009), these data from TMS (Jensen et al., 2005; Carroll et al., 2002) and correlated motor unit activity (present study) suggest that strength training does not influence the features of M1 control that are quantified by these techniques.

3.5 Conclusion

In conclusion, increases in strength following several weeks of strength training a hand muscle are not accompanied by alterations in motor unit synchronisation or coherence, suggesting that correlated motor unit activity is not important for the expression of muscle strength (Yao et al., 2000). Although strength training undoubtedly involves adaptations within the nervous system during the first few weeks of a training program (Semmler and Enoka, 2000; Duchateau et al., 2006), the datum from the present study suggest that strength training does not influence the features of M1 control that are revealed by measures of correlated motor unit activity. The changes in correlated motor unit activity are likely to be most important for the coordinated activity of multiple muscles during the learning and performance of skilled motor tasks. This proposition remains to be tested.

CHAPTER 4

Corticospinal Responses Following Isometric Strength Training of an Intrinsic Hand Muscle

4.1 Introduction

The contributions of the CNS to improvements in strength are well documented (Duchateau and Enoka, 2002; Folland and Williams, 2007; Duchateau et al., 2006). However, the mechanisms underlying these improvements are less understood, particularly in the M1 and corticospinal pathway. Whilst evidence for the muscle morphological changes that occur with strength training are clearly demonstrated through hypertrophy (Folland and Williams, 2007), the neural adaptations induced by strength training may be comprised of more subtle changes (Datta and Stephens, 1990) in many areas including supraspinal centres (Carroll et al., 2002; Farmer et al., 1993b), descending neural tracts (Aagaard et al., 2002a; Fimland et al., 2009a), spinal circuitry (Cannon and Cafarelli, 1987; Garry et al., 2004; Del Balso and Cafarelli, 2007), and the motor end plate connections between motoneurons and muscle fibers (Staron et al., 1994). Several investigations have reported maximal force increases of up to 15% within days following an exercise session (Berg, 1997; Vandenborne et al., 1998; Schneck and Forward, 1965; Rogers and Evans, 1993), and up to 200% increase after eight weeks, with no changes in the cross-sectional area of muscle (Folland and Williams, 2007). These results imply that the early stages of strength development may be due to some form of neural adaptation. Although there is a general consensus that the CNS mediates this increase in strength following a period of strength training, there is considerable debate concerning the extent and nature of involvement of specific sites within the CNS. Recently, a number of studies have used TMS to determine whether the M1 and corticospinal pathway contributes to strength development, providing a potential site for neural adaptations to strength training (Carroll et al., 2002; Griffin and Cafarelli, 2007; Jensen et al., 2005; Hortobágyi et al., 2009). Given that the M1 is heavily populated with corticospinal cells that descend onto motoneurons located within

the spinal cord (Porter, 1985), the use of TMS enables the assessment of corticospinal excitability and inhibition following specific training interventions. For example, Carroll et al. (2002) examined the effect of moderate to heavy load (70 to 85% of MVC) isometric strength training on corticospinal excitability following four-weeks of strength training the FDI muscle. Although strength training resulted in a 33% increase in strength, the strength training program did not modify the size of the TMS produced MEPs. Carroll et al. (2002) also used TES to stimulate subcortical structures and concluded that strength training does not affect the organisation of the M1, suggesting that adaptations are confined to the spinal cord. Similarly, Jensen et al. (2005) had participants perform heavy load (80% of MVC) dynamic strength training (five sets of six to ten repetitions) of the BB three times per week for four-weeks. MEP amplitude at 5% of MVC and stimulus-response curves were constructed prior to and after the four-week training intervention. Following training, muscle strength increased by 31%, however maximal MEP amplitude produced by TMS at rest was reduced, suggesting a minimal role for the M1 and corticospinal pathway in strength development. In contrast to these findings, Beck et al. (2007) demonstrated increased MEP amplitude produced by TMS following four-weeks of ballistic strength training in the soleus muscle, whilst Griffen and Cafarelli (2007) found a 32% increase in MEP amplitude with no change in peripheral nerve excitability, suggesting that strength training leads to a task specific adaptation within the corticospinal pathway. Therefore, strength training studies using TMS show either increased (Griffin and Cafarelli, 2007; Beck et al., 2007), reduced (Jensen et al., 2005), unchanged (Carroll et al., 2002) or task specific modulation of corticospinal excitability (Beck et al., 2007).

Although the above mentioned TMS studies have tried to determine the effects of strength training on corticospinal excitability (by measuring MEP amplitude

produced by TMS), changes in cortical inhibition may also be an important neural adaptation that contributes to strength development. Cortical inhibition refers to the neural mechanisms by which output from M1 is attenuated by inhibitory γ-aminobutryic acid (GABA) receptor mediated interneuron transmission (McCormick, 1989). Inhibitory neurons located in the M1 use GABA as their neurotransmitter and the activity of these neurons can be investigated with paired pulse or single pulse TMS (Kujirai et al., 1993; Jones, 1993; Inghilleri et al., 1993). The paired pulse technique measures SICI that is mediated by $GABA_A$ receptors (Kujirai et al., 1993), whereas the single pulse technique measures inhibition mediated by $GABA_B$ (Siebner et al., 1998). Using the paired pulse technique, SICI can be measured and may be important for shaping the output from the M1 (Chen, 2004). For example, SICI is reduced during voluntary muscle contractions and has been proposed to improve corticospinal drive during intended movement by releasing corticospinal cells from inhibition, therefore improving subsequent excitatory drive to produce the desired movement (Floeter and Rothwell, 1999). Using single pulse TMS, it has been demonstrated that there is a reduction in the duration of the silent period (SP) during both slow and fast finger movements, illustrating a task dependant change in corticospinal inhibition mediated by $GABA_B$ interneuronal transmission (Pearce and Kidgell, 2009; Pearce and Kidgell, 2010). Currently, no studies have examined the effect of strength training on corticospinal inhibition, although adjustments in inhibition may be important in force production. Studies have demonstrated in M1 that prior to and during movement, there is not only an increase in corticospinal excitability, but there is also a reduction in corticospinal inhibition (Reynolds and Ashby, 1999; Chen et al., 1998; Ridding et al., 1995b). Furthermore, the change in inhibition is specific to the intended agonist muscle, as MEPs in antagonist muscle remain unchanged (Reynolds and Ashby, 1999;

Ridding et al., 1995a). Therefore, changes in inhibition seem to be selective and act to focus the output from the MI by improving excitatory drive onto corticospinal cells that produce the intended movement (Ridding et al., 1995a). In light of this, previous strength training studies that have used TMS have not included the analysis of SP duration, despite several investigations demonstrating changes in inhibition prior to and during movement (Reynolds and Ashby, 1999; Ridding et al., 1995b). The novel aspect of the present study was the investigation of whether strength training of the FDI induces changes in corticospinal inhibition (SP duration) as previous TMS strength training studies have not addressed this issue.

The purpose of the present investigation was to extend upon previous work (Jensen et al., 2005; Carroll et al., 2002) by investigating the corticospinal responses following isometric strength training of an intrinsic hand muscle. The specific aim of the investigation was to determine whether isometric strength training of the FDI altered corticospinal excitability and inhibition during moderate muscle activation. In order to investigate whether strength training causes adaptations along the corticospinal pathway, this study determined the effect of isometric strength training on the magnitude of MEPs and the duration of the cortical SP produced by TMS. It was hypothesised that strength training would alter the amplitude of the MEP, reflecting changes in corticospinal excitability and the duration of the SP, reflecting a change in corticospinal inhibition and this would result in an increase in MVC force following training.

4.2 Methods

4.2.1 Participants

Sixteen healthy (24.12 ± 5.21 years, 13 males, and 3 females), right-handed university students were randomly allocated into either a strength training (7 males, 1 female) or a control group (6 males, 2 females). All participants were right-handed, as assessed by the Edinburgh handedness inventory (Oldfield, 1971) and had not participated in any kind of strength training in the past two years. All participants gave written, informed consent to the experimental procedures, and were approved by the human research ethics committee.

4.2.2 Organisation of the study

Participants assigned to the strength training group were required to undertake 12 supervised strength training sessions over a four-week training period. Participants assigned to the control group completed no training, but participated in all testing procedures and were instructed to continue their current activities for the four-week period. TMS was applied prior to and following the four-week strength training intervention at 10% above active motor threshold (AMT) during a constant isometric contraction of 5% and 20% MVC of the right FDI.

4.2.3 Electromyography and transcranial magnetic stimulation

Surface electromyography (sEMG) activity was recorded from the FDI muscle of the right hand using bipolar Ag-AgCl electrodes**.** Two electrodes were placed 1-2 cm apart over the FDI muscle, with the reference electrode (ground electrode) placed over the bony prominence of the III, IV, or V metacarpal. EMG signals were amplified

(1000×) with bandpass filtering between 10 Hz and 1 kHz and digitized at 1.5 kHz for 500 ms, recorded and analysed off-line using LabVIEW (National Instruments V4.0) software. TMS was applied using a Magstim 200^2 stimulator, with a standard 90 mm circular coil. The coil was held manually and placed over the vertex of the head and held tangential to the skull in an antero-posterior orientation, so that the current flowed in a counter-clockwise direction for activating the left M1 (right-side muscles). For reliability of coil placement, participants wore a snugly fitting cap (Figure 4.1), positioned with reference to the nasion-inion and interaural lines. The cap was marked with sites at 1 cm spacing in a latitude-longitude matrix to ensure reliable coil position throughout the testing protocol and for repeated testing sessions over the period of the study. The cap and coil position were checked consistently to ensure that no changes in position occurred. Sites near the estimated centre of the FDI area were explored to determine the site at which the largest MEP amplitude was evoked during a low level contraction at 5% of MVC. This site was defined as the "optimal" site. Active motor threshold (AMT) was established as the stimulus intensity at which an MEP could be obtained with at least five of the 10 stimuli with a peak-peak amplitude greater than 200 μV during 5% of MVC (Rothwell et al., 1999). Once AMT was obtained, five TMS stimuli were then delivered at 10% above each participant's AMT during a controlled isometric contraction of the FDI at 5% and 20% of each participant's pre-determined MVC force.

Figure 4.1. Participants wearing the fitted cap with markings of 1 cm distance in both antero-posterior (A-P) and medio-lateral (M-L) directions. A circular coil (90 mm) was held tangential to the skull in an antero-posterior orientation, so that the current flowed in a counter-clockwise direction for activating the left M1.

4.2.4 Maximum strength testing

Participants were seated in a comfortable chair with a headrest to support the head and neck. The right arm was abducted at the shoulder to allow the elbow, forearm and right hand to be supported by a specially designed board that acted to isolate the right FDI (Figure 4.2) (Pearce and Kidgell, 2010). A low-sensitivity force transducer (MLP-25, Transducer Techniques, CA) was fitted to the board and was used to act as the resistance during the static abduction task of the first index finger. The transducer was fixed but adjustable to suit the individual variations of hand/finger size. The participants hand was restrained by Velcro straps at the wrist and on the remaining three fingers to isolate the FDI muscle. Participants were required to push against (abduction) the force transducer and produce a gradual rise in force to its maximum over a 3 s interval. Once the maximum force was obtained it was held for a subsequent 3 s. Verbal encouragement and visual feedback of the force exerted was provided via an oscilloscope which was located at eye level approximately 1.5 m away from the participant. The average of the three trials was used as the participants MVC.

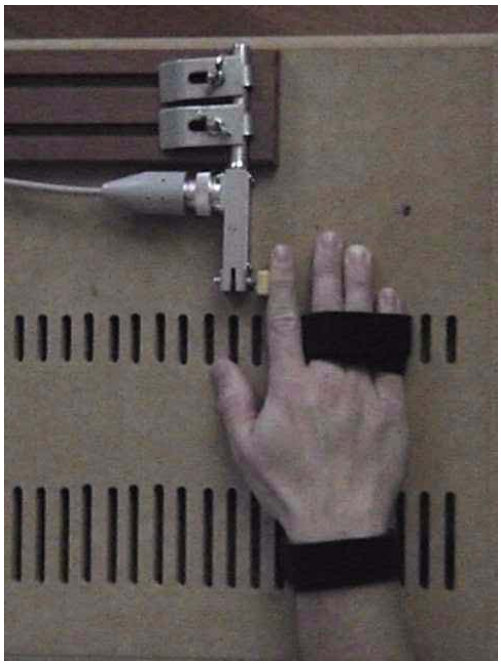

Figure 4.2. The force transducer used to measure finger force pre and post strength training. The force transducer was fitted to a specially designed board to isolate the right FDI muscle. The participants hand was fastened by Velcro straps allowing the first index finger to abduct and statically hold against the transducer.

4.2.5 M-waves

Direct muscle responses (M-waves) were obtained from the right FDI by supramaximal electrical stimulation of the ulnar nerve at the wrist under resting conditions. A Digitimer (Hertfordshire, UK) DS7A constant-current electrical stimulator (pulse duration 100 μs) was used to deliver each electrical pulse. An increase in current strength was applied to the ulnar nerve until there was no further increase in the amplitude of the EMG response. To ensure maximal responses, the current was increased an additional 20% and the average M-wave was obtained from five stimuli delivered at <0.5 Hz.

4.2.6 Strength training procedures

The training program involved maximum isometric abduction of the right index finger that was performed 3 times/week (Monday – Wednesday – Friday) in the laboratory. The task consisted of fast index finger abduction contractions that were held for 3 s, with a 3 s rest between contractions. This was performed ten times (one set), and each subject performed 6 sets (separated by approximately three minutes) for a total of 60 contractions.

4.2.7 Data and statistical analyses

All MEPs (500 ms epochs) were displayed and averaged online for visual inspection as well as stored off-line for further analysis. All corticospinal parameters (latency, amplitude and SP duration) were analysed off-line. MEP amplitude was normalised as a percentage of the M-wave. Latency was calculated from stimulus artifact to MEP onset and to measure SP duration (via visual inspection and cursored) its onset was defined as the commencement of the MEP and the endpoint coincided with the reoccurrence of EMG activity in individual trials (Mills, 1999; Pearce and Kidgell,

2010; Byrnes et al., 1999; Wilson et al., 1993a; Wilson et al., 1993b). Force signals were sampled at 200Hz and analysed off-line using custom designed software (National Instruments V4.0).

All data were first screened to ensure they were normally distributed. In order to have sufficient data to test for questions of normality, all MEP, SP and MVC data were used to establish the distributional properties. No variable's z-score of skew or kurtosis were excessive. Further, Shapiro-Wilk tests suggested MEP amplitude, SP duration and MVC variables were normally distributed (MEP, $p = 0.42$; SP duration, $p = 0.17$; MVC, $p = 0.09$). In order to determine the corticospinal responses to strength training, a two-way ANOVA was used to compare group (trained vs. control) by session (pre vs. post). Pearson product-moment correlation coefficients were used to determine correlations between significant criterion measures. Alpha was set at $p < 0.05$ and results are presented as means ± SD.

4.3 Results

All participants in the training group completed all training sessions, and all participants in both groups completed the pre and post testing sessions.

4.3.1 Voluntary muscle strength

Figure 4.3 presents absolute strength changes following the training intervention for the strength training and control groups. No significant differences were observed in strength between the groups prior to the training period ($p = 0.2$). Isometric strength training increased MVC force during index finger abduction by 33.8% ($p = 0.01$) in the strength-trained group, compared to a 13% increase for the control group. The average MVC forces exerted during index finger abduction were 44.4 ± 5.9 N (before training)

and 59.5 ± 15.7 N (after training) for the strength-trained group, and 49.3 ± 24.5 N (before training) and 55.4 ± 22.7 N (after training) for the control group.

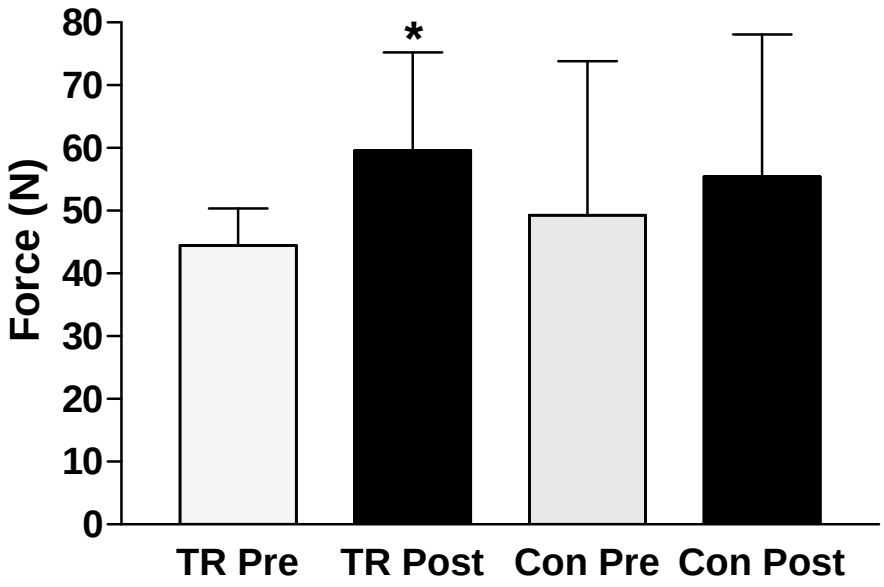

Figure 4.3. Mean (±SD) isometric force recorded from the right FDI during a MVC for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. Four-weeks of isometric strength training resulted in a 33.8% increase in MVC strength. Asterisk denotes significant increase in isometric force from before to after training between groups ($p = 0.01$).

4.3.2 Corticospinal excitability

There were no significant differences in latency (all participants, mean 21.3 ± .1 ms) and normalised MEP amplitude/M-wave at 5% (p = 0.3) and 20% (p = 0.3) of MVC between groups at pre training (Figures 4.4 and 4.5).

Following the strength training intervention there were no significant differences in MEP/ M-wave between groups at 5% of MVC (trained; pre 40.3 ± 10.4 to post 48.9 ± 7.2%, versus control; pre 46.1 ± 28.6 to post 43.4 ± 18.1%, p = 0.4; Figure 4.4). Similarly, there were no significant differences in MEP/ M-wave at 20% of MVC between groups (trained; pre 49.2 ± 15.6 to post 58.9 ± 12.6% versus control; pre 49.4 ± 20.2 to post 49.1 ± 16.7%, p = 0.2; Figure 4.5) following the strength training intervention.

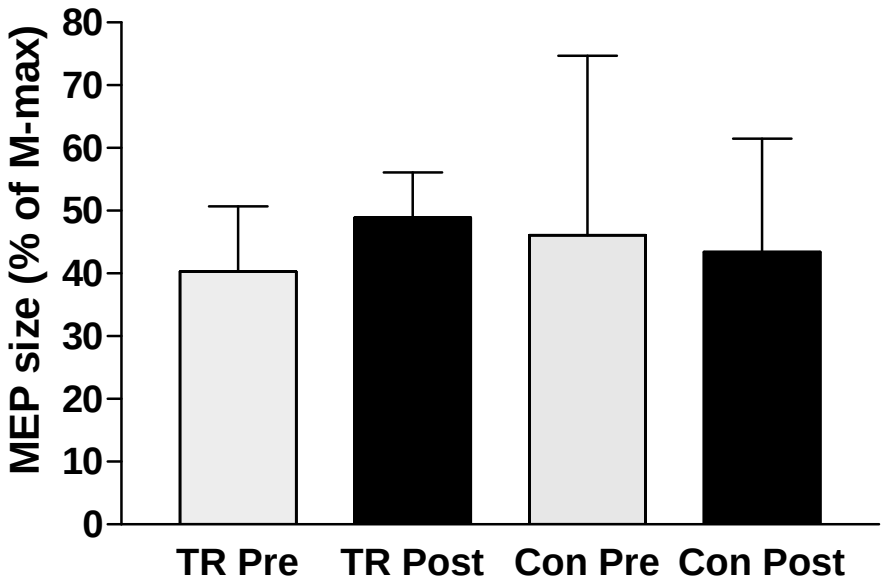

Figure 4.4. Mean (±SD) data for right FDI MEPs at 5% of MVC for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. MEP amplitudes are displayed as a percentage of the right FDI M-wave. There were no significant differences in MEPs pre vs. post strength training for both groups.

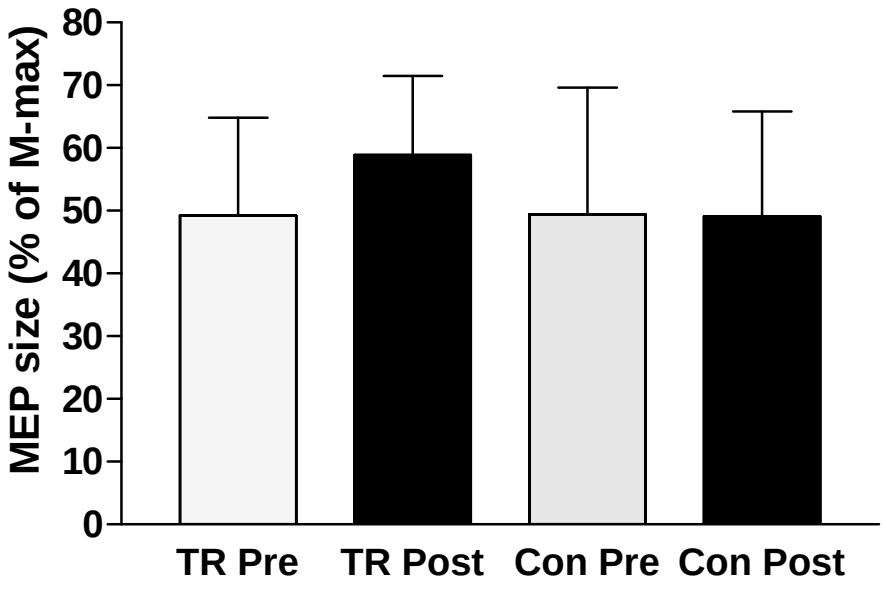

Figure 4.5. Mean (±SD) data for right FDI MEPs at 20% of MVC for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. MEP amplitudes are displayed as a percentage of the right FDI M-wave. There were no significant differences in MEPs pre and post strength training for both groups.

4.3.3 Corticospinal inhibition

No significant differences in SP duration were observed between groups at 5% (p = 0.1) and 20% (p = 0.8) of MVC pre-training. However, the duration of the SP following strength training was 16 ms (p = 0.01, Figure 4.6) shorter in the trained group compared to the control group at 5% of MVC. Furthermore, the duration of the SP following strength training was 25 ms (p = 0.03, Figure 4.7) shorter in the trained compared to the control group at 20% MVC. Following the strength training intervention, there was a significant, but moderate correlation between the change in strength and the pooled change in SP duration (r = -0.51, p = 0.05, Figure 4.8 and Figure 4.9) for the strength training group.

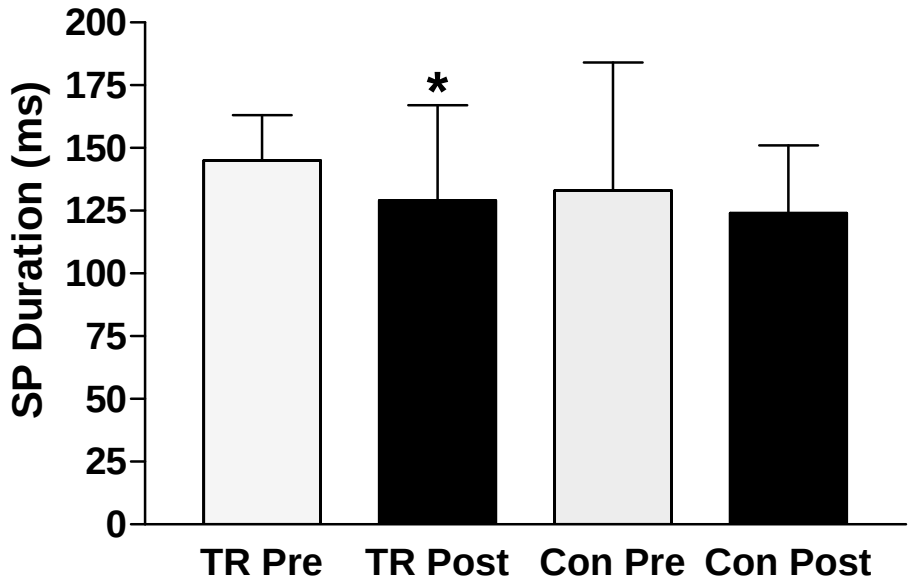

Figure 4.6. Mean (±SD) data showing right FDI SP duration at 5% of MVC for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. Asterisk denotes significant reduction in SP duration from before to after training between groups ($p = 0.04$).

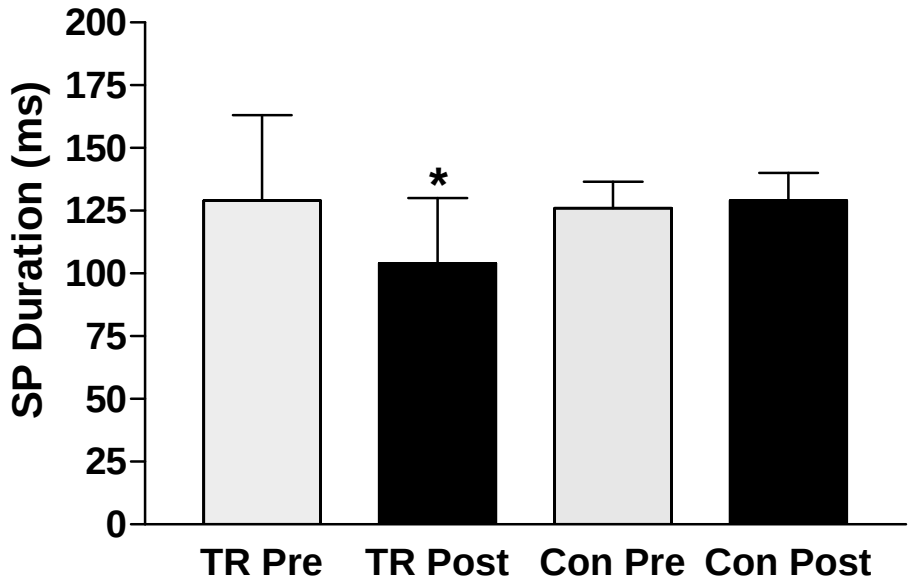

Figure 4.7. Mean (±SD) data showing right FDI SP duration at 20% of MVC for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. Asterisk denotes significant reduction in SP duration from before to after training between groups ($p = 0.01$).

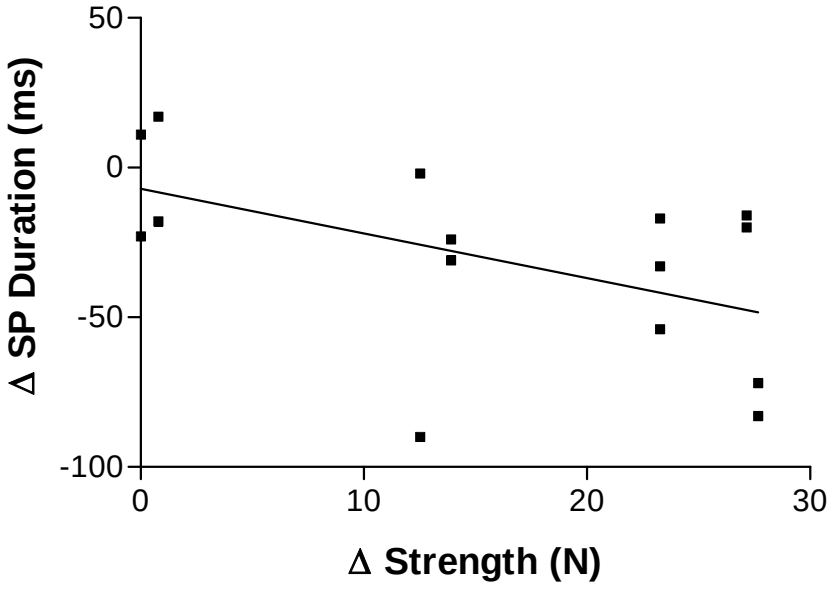

Figure 4.8. The realtionship between changes (as represented by delta [△]) in strength of the right FDI and pooled SP duration of the strength-trained group (r = -0.51, p = 0.05).

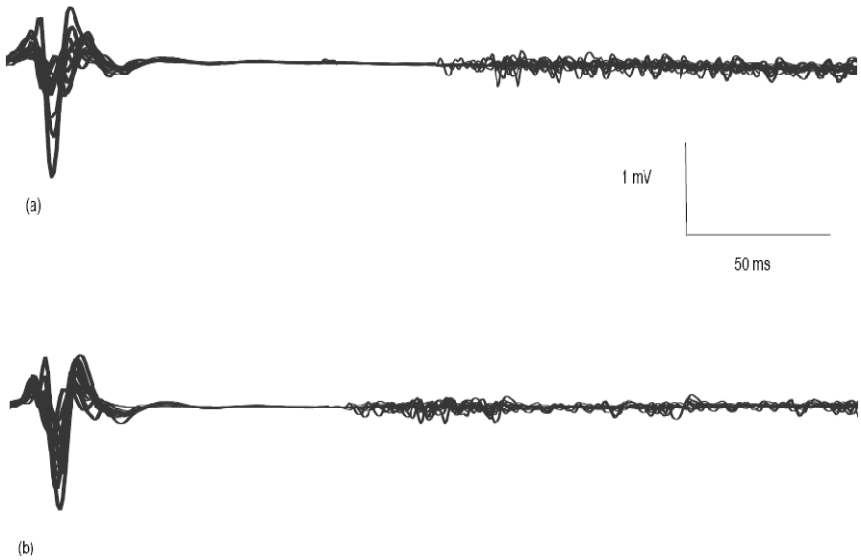

Figure 4.9. Overlay of raw MEP sweeps in one participant (at 20% MVC) illustrating the reduction in SP duration pre (a) and post (b) training period.

4.4 Discussion

In the present study, the aim was to investigate the neural mechanisms contributing to strength development following short-term strength training of the FDI using TMS, observing a significant increase in MVC force in the training group and a reduction in cortical inhibition.

There was a 33.8% increase in MVC force in the trained participants and this increase was comparable to other short-term strength training studies that have exercised intrinsic muscles of the hand (Olafsdottir et al., 2008; Carroll et al., 2002; Kidgell et al., 2006; Patten et al., 2001). Increases in the expression of muscular force following short-term strength training are thought to be as a result of adaptive changes within neural control circuits projecting to the trained musculature (Folland and Williams, 2007; Carroll et al., 2002).

Although it has long been reported that adaptations in the CNS may account for increases in strength following short-term strength training (Sale et al., 1983; Sale, 1988), the present study did not observe any difference in the size of the descending corticospinal volley during isometric contractions of 5 and 20% of MVC. These findings concur with other studies, who following strength training of the hand and arm, found either no difference or small decreases in corticospinal excitability (Jensen et al., 2005; Carroll et al., 2002; Lee et al., 2009a). These authors reported that the number of motoneurons activated; the size of the descending corticospinal volley and the excitability of corticospinal cells for a particular level of muscle activity remained unaffected by short-term strength training. However, this result is in contrast to the recent findings of Griffin and Cafarelli (2007) and Beck et al. (2007) who reported increases in corticospinal excitability in lower leg muscles following short-term strength training. It was put forward that the increase in MEP amplitude was as a result of an

increase in the size of the descending corticospinal volley and this consequently lead to an increase in motor unit recruitment (Beck et al., 2007; Griffin and Cafarelli, 2007). The differences between the results of the present study and that of other studies (Jensen et al., 2005; Carroll et al., 2002; Lee et al., 2009a) may partly reside in the divergent distribution of corticospinal cell projections onto spinal motoneurons being different between upper and lower limb muscles (Devanne et al., 1997) and as a result of the different strength training paradigm employed. Individual muscles respond differently to TMS and display differences in the input-output properties of the corticospinal pathway (Schieppati et al., 1996).

A novel finding to the present study was the significant reduction in SP duration following the strength training program. Although changes in SP duration have been reported during different functional skilled tasks of the hands (Sale and Semmler, 2005; Tinazzi et al., 2003; Pearce and Kidgell, 2009; Pearce and Kidgell, 2010) this is the first study to report associated changes in corticospinal inhibition (using single pulse TMS) following a period of strength training. From this datum and due to limitations in the technique of single-pulse TMS, one can only speculate about the underlying mechanism responsible for this reduction. Several studies have established that the initial portion (50-75 ms) of the TMS evoked SP is primarily due to spinal inhibitory mechanism such as after-hyperpolarisation and recurrent inhibition of α-motoneurons (Schnitzler and Benecke, 1994; Fuhr et al., 1991; Chen et al., 1999). The later component (> 75 ms) represents intracortical inhibitory mechanism that is mediated by $GABA_B$ receptors generated within the M1 that leads to a failure in corticospinal drive (Kimiskidis et al., 2005; Chen, 2004; Schnitzler and Benecke, 1994; Fuhr et al., 1991). While the single pulse technique can be used to assess changes in SP duration (Sale and Semmler, 2005; Tinazzi et al., 2003), the technique of paired-pulse TMS is a more appropriate method

to measure changes in cortical inhibition. Therefore, this study was not able to determine whether the changes in SP were predominantly of a cortical origin as only the single-pulse technique was used and the peripheral SP was not measured. Despite these limitations, the associated reduction in SP duration observed following the strength training program, provides indirect support for a reduction in corticospinal inhibition probably confined to the M1 and spinal cord circuitry.

There is a general consensus in the literature that strength training is a form of motor skill acquisition as it requires the participants to produce muscle recruitment patterns that are associated with optimal performance of the task (Carroll et al., 2002; Zhou, 2000; Farthing, 2009). Given that previous studies have demonstrated task dependant changes in corticospinal inhibition of the FDI during skilled tasks (Tinazzi et al., 2003; Sale and Semmler, 2005; Pearce and Kidgell, 2009; Pearce and Kidgell, 2010), the changes in SP duration observed in the present study may also be as a result of task dependant changes that are similar to those observed with motor skill acquisition (Tinazzi et al., 2003). It appears that the strength training program has altered the balance between excitation and inhibition, and improved voluntary motor drive due to the reduction in SP duration. Ridding et al. (1995b) demonstrated reduced corticospinal inhibition during 5% of MVC (right FDI) when compared to rest and suggested that voluntary contraction may be important in reducing the effect of inhibitory neurons which project onto corticospinal neurons involved in the intended movement, thus facilitating corticospinal drive.

Despite the limitations of the present study, alterations in corticospinal inhibition have been associated with mechanisms that induce cortical plasticity and given that inhibition is reduced during voluntary contractions (Ridding et al., 1995b), it is possible that the repeated contraction of the FDI throughout the strength training intervention

lead to some form of long-term inhibition (LTI) (Butefisch et al., 2000) and this would support the finding of task dependant adaptations in corticospinal output that occur with repetitive skill training (Perez and Cohen, 2008; Pascual-Leone et al., 1995). Changes in cortical inhibition have been suggested to "release" corticospinal neurons from inhibition, thus enhancing the net excitatory drive during movement (Floeter and Rothwell, 1999; Reynolds and Ashby, 1999). Although there was a reduction in SP duration, this was not as a result of a reduction in the size of the descending corticospinal volley; therefore it appears that the strength training intervention may have resulted in a shift in the balance between inhibitory and excitatory inputs onto corticospinal cells demonstrating that inhibition is physiologically separate from excitation.

4.5 Conclusion

In conclusion, in accordance with previous studies, the results of this chapter have demonstrated that following four-weeks of strength training an intrinsic hand muscle, there was a rapid increase in strength; however there were no significant differences in corticospinal excitability as determined by MEP amplitude. The novel finding of a reduced SP duration suggests that strength training has resulted in a task specific neural adaptation, which is most likely due to both reduced inhibition within spinal cord circuitry and in $GABA_B$ mediated cortical inhibition confined to the M1. Based upon this novel finding, future strength training studies should assess changes in both corticospinal excitability and inhibition. The interpretation of a reduced SP duration being a possible mechanism for improved strength seems unjustified at present, and should be taken with caution, as it is still unclear what the functional properties of inhibitory circuits are during voluntary force production. Although contributions from

segmental sources cannot be excluded, these findings suggest that isometric strength training has resulted in some form of neural adaptation within the corticospinal pathway that maybe important in mediating strength development.

CHAPTER FIVE

Neurophysiological Adaptations following Short-Term Heavy Load Strength Training

5.1 Introduction

Changes in MVC force following a period of strength training have been attributed to adaptive modifications in the neuromuscular system (see review by Folland and Williams 2007). Neural adaptations have been suggested to account for the rapid increase in strength within the first four weeks of a strength training program (Sale, 1988), however, the specific mechanism contributing to this adaptation are not well understood. Proposed neural mechanisms may range from an increase in efferent neural drive to subtle changes in motor unit behaviour, suggesting that there is no single mechanism responsible for the increase in strength and that adaptations probably extend to both supraspinal and spinal regions (Folland and Williams, 2007).

Adaptations in neural function following strength training have usually been investigated and quantified via changes in the amplitude of the muscle sEMG signal (Aagaard, 2003; Aagaard et al., 2000; Hakkinen et al., 2000) and more recently following single motor unit recordings (Griffin et al., 2009; Kamen and Knight, 2004; Patten et al., 2001; Kidgell et al., 2006). An increase in the amplitude of the sEMG signal has, by default, been interpreted as an increase in efferent neural drive, therefore contributing to the increase in force (Davies et al., 1985; Narici et al., 1989). Changes in efferent neural drive can be investigated by recording evoked spinal cord responses such as the H-reflex, used to determine the level of motoneuron excitability and the magnitude of presynaptic inhibition of muscle spindle Ia afferents (Palmieri et al., 2004). Alternatively, the V-wave which is a variant of the H-reflex can be used to quantify the training induced modifications in efferent motoneuronal output (Aagaard et al., 2002b; Fimland et al., 2009a). Elevated H-reflexes and V-wave amplitudes have been reported following maximal dynamic and isometric strength training (Aagaard et al., 2002a; Del Balso and Cafarelli, 2007; Duclay et al., 2008; Fimland et al., 2009a),

suggesting enhanced neural excitability in descending corticospinal pathways. However, adjustments in H-reflex and V-wave amplitude following strength training may arise as a result of changes in the intrinsic properties of Ia afferents, such as presynaptic inhibition, intrinsic motoneuron properties, and changes in motoneuron firing rate (Hortobágyi et al., 2009).

Changes in corticospinal excitability can be measured using TMS. TMS enables the assessment of corticospinal responses during voluntary contractions in humans and has recently been used in strength training research (Carroll et al., 2002; Lee et al., 2009a; Griffin and Cafarelli, 2007; Taube et al., 2007a; Hortobágyi et al., 2009; Jensen et al., 2005). TMS applied over the M1 can induce a series of descending volleys in the corticospinal pathway, which in turn, causes a muscle response referred to as a MEP. Changes in MEP amplitude are thought to reflect adjustments in the physiological strength of corticospinal cell projection onto the spinal motoneuron pool innervating the target muscle. The excitability of corticospinal projections can also be assessed by a stimulus-responses curve, which is produced by stimulating the M1 at a range of stimulus intensities, and plotting the size of the MEP against TMS intensity. The slope of the curve reflects a balance between inhibitory and excitatory inputs onto the M1 and spinal motoneuron pool (Devanne et al., 1997).

Although MEP amplitude and the slope of the stimulus-response curve reflects the excitability of corticospinal cell projection, changes in corticospinal inhibition may also be important for voluntary muscular activity and therefore a potential mechanism contributing to changes in strength. Corticospinal inhibition can be measured during single pulse TMS and is determined by the duration of the SP. Corticospinal inhibition refers to the neural mechanisms by which output from the M1 is attenuated by

inhibitory GABA receptor mediated interneuron transmission (McCormick, 1989). Therefore, TMS can been used to measure changes in corticospinal excitability (quantified by MEP amplitude and area) and corticospinal inhibition (SP) under a variety of conditions including, but not limited to, motor practice (Pearce et al., 2000), neuromuscular fatigue (Taylor and Gandevia, 2001); and clinical conditions such as limb immobilisation (Liepert et al., 1995) and recovery from stroke (Byrnes et al., 1999).

Motor skill practice studies have provided convincing evidence for a task dependant adaptation in corticospinal control with suggested mechanisms including; increased excitability of populations of corticospinal neurons projecting to spinal motoneurons innervating the muscles involved in the skilled task (Pearce et al., 2000; Pascual-Leone et al., 1995; Katiuscia et al., 2009), unmasking of latent synapses (Adkins et al., 2008; Adkins et al., 2006) and functional reorganisation of the M1 (Pearce et al., 2000). It has been hypothesised that strength training may also result in a similar adaptation, due to the skilled element of strength training exercises (Zhou, 2000; Farthing, 2009). TMS has been used to investigate the corticospinal responses following a period of strength training. However, results have been inconsistent and may be attributed to the different training paradigms used, muscles trained and/or the different methods used to assess corticospinal excitability. For example, four-weeks of moderate to heavy-load strength training of the FDI decreased corticospinal excitability at rest and during voluntary contraction, despite a 33% increase in strength (Carroll et al. 2002). Similarly, four-weeks strength training of the BB increased strength by 31% however, this was associated with a decrease in corticospinal excitability (Jensen et al., 2005). In contrast to these findings, Beck et al. (2007) demonstrated increased MEP amplitude following four-weeks of ballistic strength training of the TA. In support of

this, Griffen and Cafarelli (2007) following four-weeks of strength training of the TA muscle, found a 32% increase in MEP amplitude, suggesting that strength training resulted in a task specific adaptation within the corticospinal pathway. However, it is difficult to compare the data across studies as different muscles and TMS protocols have been used.

Although repetitive execution of a simple movement against light and heavy loads may not induce task-specific modulation of corticospinal excitability (Plautz et al., 2000), strength training (where the goal is to increase maximal force output) of muscles primarily used in fine motor tasks on a daily basis may account for some of the inconsistent findings relating to task-specific corticospinal excitability. In other words, exercising intrinsic muscles with relatively low task complexity (such as abduction of the index finger which does not require a high degree of precision) that are used during fine movement activities on a regular basis (such as the FDI) may have already undergone some form of adaptive plasticity as a result of habitual use (Semmler and Nordstrom, 1998a), thus contributing to the reduction in corticospinal excitability. It has recently been demonstrated that completing the same movement under different levels of precision, leads to significant adjustments (increase MEPs) in corticospinal control (Pearce and Kidgell, 2009; Pearce and Kidgell, 2010). Therefore, employing a strength training program that has some degree of task complexity, such as a heavy resistance with controlled repetition timing or ballistic contractions (which increases task complexity) may be an important factor in the corticospinal responses to strength training (Taube et al., 2007a).

The purpose of the present study was to investigate whether short-term controlled strength training stimulated changes in human corticospinal excitability and

inhibition following four-weeks strength training of the biceps brachii (BB) muscle. This chapter compared the effects of heavy load controlled strength training on corticospinal conduction, excitability and inhibition at active motor threshold (AMT), 20% above AMT and at MEP_{max} during 10% of MVC background muscle activation. It was hypothesised that four-weeks of heavy-load controlled strength training would increase muscle strength and this would be reflected by an increase in corticospinal excitability, a reduction in corticospinal inhibition providing evidence for a corticospinal mechanism for strength development.

5.2 Methods

The methods and procedures used in this chapter form the basis for all methods and procedures of data collection for subsequent chapters in this thesis. Therefore, the methods in each experimental chapter are an abridged version of the current chapter, with only the most appropriate sections reproduced.

5.2.1 Organisation of the study

Twenty three healthy participants (10 males, and 13 females, 26.8 ± 7.3 years) were randomly allocated into either a strength training (6 male and 7 females) or a control group (5 males and 5 females). All participants were right-handed, as assessed by the Edinburgh handedness inventory (Oldfield, 1971), and none of the participant's had involvement in any kind of strength training in the previous two years. Each participant gave written informed consent and all procedures were approved by the university human research ethics committee. Participants assigned to the strength training group were required to undertake 12 supervised strength training sessions over

a four-week training period. Participants assigned to the control group completed no training. At the beginning and at the end of the training period each subject participated in a testing session that involved: (1) strength testing to evaluate maximal voluntary dynamic elbow flexor muscle strength (1-RM) and maximal root mean square electromyography (rmsEMG) during an isometric MVC; and (2) single pulse TMS applied over the left M1 to evoke MEPs in contralateral right BB. All testing post-training was conducted within 48 hours of the final supervised strength training session. Participants assigned to the control group completed no training but undertook all tests at similar time intervals.

5.2.2 Maximum strength testing

Participants in both groups performed a standard unilateral one-repetition maximum (1-RM) test and an isometric MVC for the right arm. Each participant completed a 1-RM test following the protocol of Munn et al. (2005b). Participants were asked what they believed their 1-RM elbow flexion strength was and this load served as their initial starting weight. Participants performed the 1-RM test standing, holding a weighted dumbbell with one hand, with their elbow in full extension, forearm supinated, and the opposite arm placed behind their back whilst standing against a wall to prevent excessive body movement. Participants were then asked to flex their arm and lift the dumbbell as if doing a standard "biceps curl". If the trial was successful, the weight of the dumbbell was increased accordingly (0.5 kg increments) on each trial after a three-minute recovery to minimise the development of muscular fatigue (Munn et al., 2005b). This procedure continued until the subject could no longer complete one repetition and their prior trial served as their 1-RM elbow flexion strength (Munn et al., 2005b).

In order to obtain the isometric MVC, participants were seated in a chair with the elbow flexed to 90º, as measured by an electronic goniometer (Biometrics, USA) and with their hand in a supinated position. A portable dynamometer (Microfet^2, USA) was positioned on a modifiable bench so the dynamometer was inside the participant's forearm at the level of the wrist. The participant was then instructed to flex the elbow against the dynamometer as forcefully as possible for 3 s. Three attempts, with a two-minute rest between each attempt were performed. The trial with the highest MVC and rmsEMG level was recorded and subsequently used to determine background muscle activity during the TMS protocol. The standard criteria for measurement of MVCs were fulfilled and included a period of familiarisation (prior to data collection) and verbal encouragement, feedback of rmsEMG displayed on a computer monitor at eye level, standardised verbal encouragement provided by the investigators and the rejection of a trial in the case the participant felt it was not a maximal effort (Gandevia, 2001).

5.2.3 Arm circumference

In order to determine whether there was any change in muscle hypertrophy as a result of the strength training program, arm circumference of the right upper arm was measured with a tape measure. Specifically, arm circumference was determined at the largest circumference of the upper arm whilst participants attempted a strong contraction of the elbow flexors in a shortened position, with the shoulder at 90^0 flexion and the forearm 45^0 to the upper arm (Munn et al., 2005a).

5.2.4 Strength training procedures

The strength training group performed heavy load strength training (80% of their 1-RM) of the right elbow flexors only, three times per week for four-weeks (12 sessions

in total). Biceps curls with a dumbbell were performed by undertaking flexion-extension movements of the elbow with the forearm supinated. The participants performed four sets of 6-8 repetitions at 80% 1-RM with a three-minute recovery period between sets (Munn et al., 2005b). Participants were required to perform each repetition with a repetition timing of 3 s concentric and 4 s eccentric, as data suggests that this repetition timing produces the greatest increase in strength (Munn et al., 2005a; Hortobágyi et al., 1997). The principle of progressive overload was employed throughout the training period to maximise the training response (Peterson et al., 2005). Specifically, when participants could complete four sets of 8 repetitions, at the beginning of the next training session, the training weight (kg) was increased by 5%.

5.2.5 Electromyography and transcranial magnetic stimulation

Surface EMG activity was recorded from the right BB muscle using bipolar Ag-AgCl electrodes**.** Two electrodes were placed 2 cm apart over the BB muscle, located by manual muscle testing and placed over the belly of the muscle, with the third reference electrode (ground electrode) placed over the bony prominence at the elbow (lateral epicondyle). The area of electrode placement was prepared by shaving and cleaned with 70% isopropyl alcohol. The site was marked with permanent marker and continually maintained by the investigator and participant, to ensure no differences in electrode placement occurred relative to the innervation zone before and after the four-week training period. EMG signals were amplified (1000×) with bandpass filtering between 10 Hz and 1 kHz and digitised at 1.5 kHz for 500 ms using custom-designed software (National Instruments V4.0). The surface rmsEMG was calculated from a 500 ms segment occurring during the asymptote of the MVC (Wilson et al., 1993b; Griffin and Cafarelli, 2007).

TMS testing followed the method employed in chapter 4, however, a 70 mm figure of 8 coil was used. AMT was defined as the stimulus intensity at which an MEP could be obtained with at least 5 of the 10 stimuli with peak-to-peak amplitude being greater than 200 μV during 10% rmsEMG MVC (del Olmo et al., 2006; Dartnall et al., 2009; Rothwell et al., 1999). MVC rmsEMG was determined from the participants MVC (section 5.2.2, page 134 and 135) and was used to control for background muscle activity during TMS trials. Each set of five stimuli were delivered during a controlled, low level voluntary contraction of the BB muscle at 10% (± 3%) of MVC rmsEMG (Pearce et al., 2000; Wilson et al., 1993a; Pearce and Kidgell, 2010). Feedback of the participant's rmsEMG level was displayed on a computer monitor positioned 1.5 m away at eye level using custom-built software (National Instruments V4.0). The computer displayed a static cursor that represented 10% (± 3%) of the participant's maximum rmsEMG and a response cursor that reflected the participants change in rmsEMG activity. The participants' were instructed to maintain the response cursor at the level of the stationary cursor during the TMS trials. Each stimulus was delivered in random intervals every 10 to 12 s to avoid stimulus anticipation and 30 s rest was provided between each set of stimuli to reduce the possibility of muscular fatigue.

5.2.6 Data and statistical analysis

All MEPs collected (n = 10, two sets of five 500 ms recordings, see Figure 5.1 for an example), at each stimulus intensity from below the participant's AMT until saturation of the MEP were displayed and averaged online for visual inspection, in determining the optimal site, and then stored off-line for further analysis.

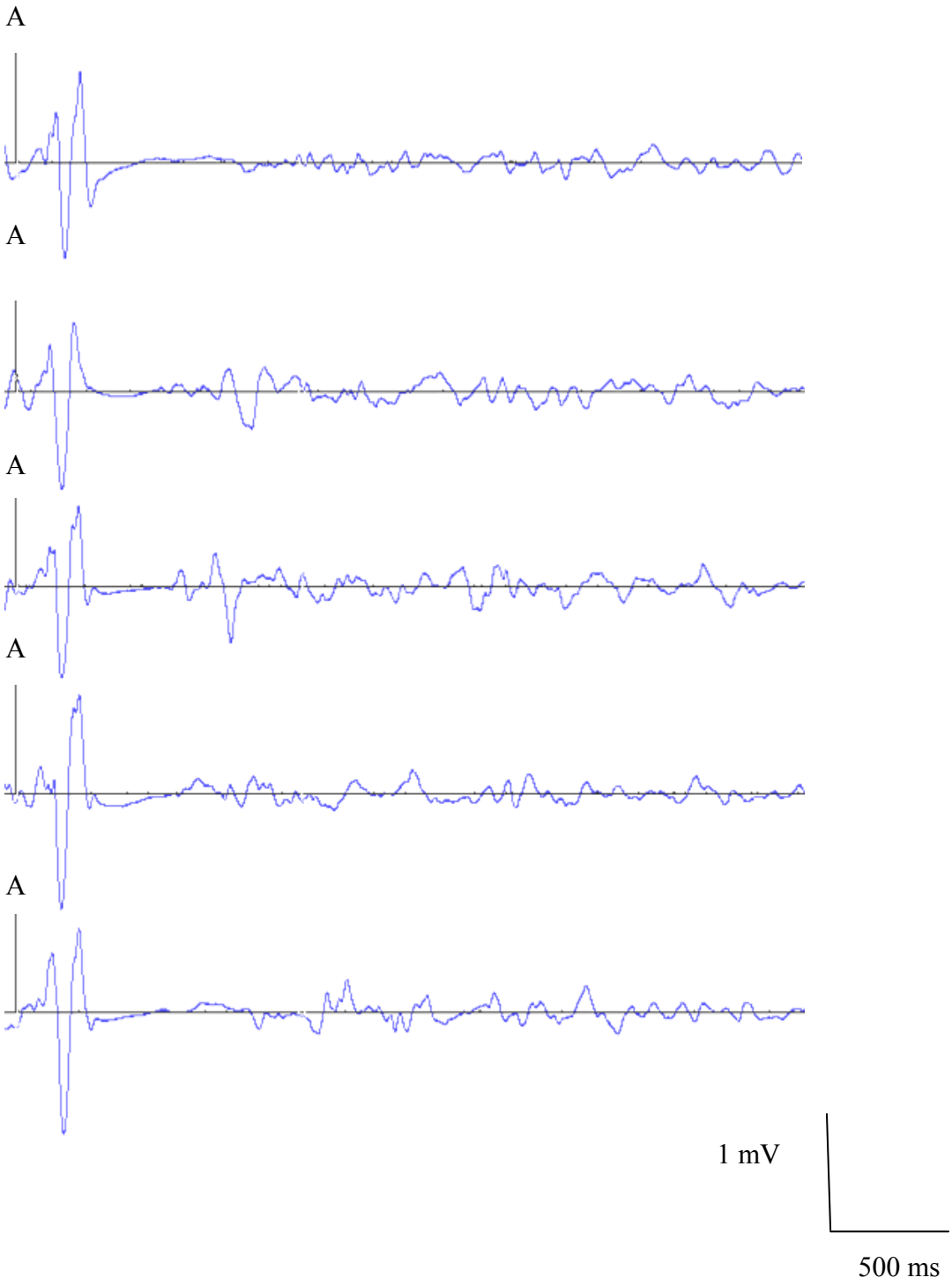

Figure 5.1. Example of five raw MEP sweeps (500 ms) from one participant during the TMS trials. The black spike (A) represents the stimulus artifact.

Stimulus-response curves were constructed according to the protocol of Carroll et al. (2002). Stimulus intensity was plotted against MEP amplitude, and the data was fitted with a three parameter sigmoid equation:

$$MEP(s) = \frac{MEP_{MAX}}{1 + e^{m(S50-s)}}$$

Where *s* is stimulus intensity, *m* is the estimated slope, *S50* is the estimated peak slope, and MEP_{max} is the measured maximum the participant's MEP amplitude reached in a given trial. A non-linear data fit iterative model to each participant's data using SPSS17.0 (SPSS Inc, Chicago, Ill) was applied. This procedure estimated the values for *m* and *S50* and provided a measure of the curves fit to the data. All iterative fits significantly fitted the data.

All data were first screened for normal distribution. In order to have sufficient data to test for questions of normality, all MEP parameters (AMT, 20% above AMT and MEP_{max}) and dynamic 1-RM strength data were used to establish the distributional properties. No variable's z-score of skew or kurtosis were excessive. Further, Shapiro-Wilk tests showed MEP amplitude at 20% above AMT, MEP_{max} and dynamic 1-RM strength variables were clearly normally distributed (20% above AMT, $SW = 0.9$, $p = 0.8$; MEP_{max}, $SW = 0.9$, $p = 0.2$; 1-RM strength, $SW = 0.8$, $p = 0.1$). Although MEP amplitude at AMT was apparently not normally distributed, ($SW = 0.7$, $p = 0.01$), this violation was only mild following examination of frequency histograms and detrended Q-Q plots, and was not considered sufficient to warrant a more conservative analytic strategy. Consequently, it was decided to treat the data as essentially normal in distribution. To identify changes in the functional properties of the corticospinal pathway, the slope and plateau values of the stimulus-response curve was used to characterise the physiological strength of corticospinal connections projecting to the spinal motoneuron pool innervating right BB. Latency was calculated from stimulus

artifact to MEP onset; MEP peak-to-peak amplitude and SP duration (onset of MEP to return of uninterrupted EMG) were cursored and measured (Williams et al., 1992; Pearce and Kidgell, 2010; Byrnes et al., 1999; Wilson et al., 1993a; Wilson et al., 1993b). To test the hypothesis that unilateral strength training increases strength and corticospinal excitability and inhibition, a two-way ANOVA was used to compare training group (trained vs. control) by session (pre vs. post). Data is presented as means (± SD) and a level of significance used for all tests was accepted at $p < 0$ .05.

5.3 Results

5.3.1 Voluntary muscle strength

Figure 5.2 represents absolute changes in strength following the training intervention for the training and control groups. There were no significant differences in 1-RM strength at pre-training between the control and trained groups $p = 0.87$; Figure 5.2). Following the four week training intervention, 1-RM BB strength increased by 28% (3.3 kg, $p = 0.0001$) in the trained group (11.5 ± 4.5 kg to 14.8 ± 5.2 kg; Figure 5.2). There were no differences in 1-RM strength for the control group (13.3 ± 4.2 kg to 13.2 ± 4.3 kg; $p = 0.34$).

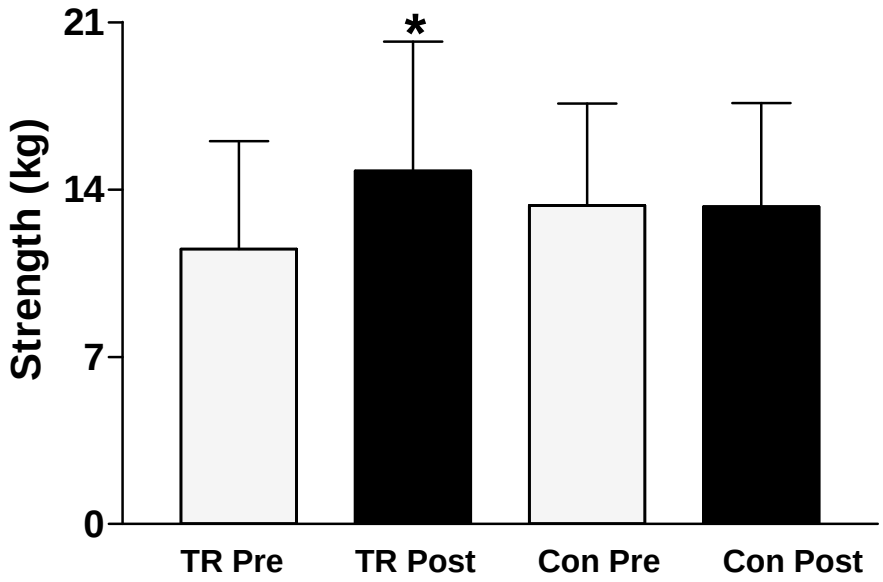

Figure 5.2. Mean (± SD) 1-RM right elbow flexion strength (expressed as kg) for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training of the right elbow flexors. There was a 28% increase in 1-RM elbow flexor strength. Asterisk denotes significant increase in elbow flexion strength from before to after training between groups ($p < 0.05$).

5.3.2 Arm circumference

There were no differences between groups prior to the training intervention (trained; pre 31.9 ± 5.6 cm versus control; pre 31.3 ± 5.2 cm; $p = 0.49$). No significant changes were observed in arm girths within and between groups following the training period (trained; post 32.2 ± 4.9 cm versus control; post 31.4 ± 3.3 cm; $p = 0.86$).

5.3.3 Muscle activation

There were no significant differences at pre-training for group mean right BB MVC rmsEMG activity between the groups (control, right arm: 0.41 ± 0.24 mV; trained, right arm: 0.50 mV ± 0.20 mV, $p = 0.50$). There were also no differences following training to pre-training values within or between the groups (control, right arm: 0.41 ± 0.21 mV; trained, right arm: 0.58 mV ± 0.17 mV, $p = 0.56$). Further, no interaction was found between groups by training ($p = 0.76$). Similarly, no differences were observed between rmsEMG at 10% of MVC contraction pre and post testing sessions (pre control, right arm: 0.04 ± 0.02 mV; pre trained, right arm: 0.05 ± 0.02 mV, $p = 0.40$; post control, right arm: 0.04 ± 0.02 mV; post trained, right arm: 0.05 mV ± 0.01 mV, $p = 0.50$).

5.3.4 Latency period

No significant differences in latency were seen between groups (trained: 13.3 ± 0.8 ms; control: 12.9 ± 0.5 ms; $p = 0.27$) at 20% AMT at baseline. Following the training intervention, there were also no differences in latency duration in both trained and control groups (trained: 13.1 ± 0.8 ms vs. 12.9 ± 0.3 ms; $p = 0.31$; control: 12.9 ± 0.5 ms vs. 12.8 ± 0.5 ms; $p = 0.40$).

5.3.5 Corticospinal excitability

There were no significant differences at pre-training for the percentage of stimulator output at AMT within and between the trained and control groups left M1 (p = 0.36). Following the training period, there were no significant differences for percentage of stimulator output at AMT between the trained and control groups (control left M1 vs. trained left M1; p = 0.83; Table 5.1).

Table 5.1 displays mean data for the control and trained groups for mean MEP amplitude at AMT, 20% above AMT and MEP_{max}.

Table 5.1. Mean data (± SD) for percentage of stimulator output at AMT (%), MEP amplitude at AMT, 20% above AMT, MEP_{max} (mV), SP duration at 20% above AMT and at MEP_{max} (ms), prior to and following the four-week strength training intervention for the control and trained groups left M1. There was a significant increase in MEP amplitude at AMT (53%), 20% above AMT (33%) and at MEP_{max} (38%) following the strength training program (shaded boxes). Asterisk indicates significant effect, $p < 0.05$.

Group		Stimulator Output at AMT (%)		AMT Amplitude (mV)		MEP Amplitude (mV) @ 20% above AMT		MEP_{max} (mV)		SP Duration (ms) at 20% above AMT		SP Duration (ms) at MEP_{max} (mV)	
		Pre	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
Control	Left M1	49.37 ± 6.7	45.62 ± 7.7	1.04 ± 0.72	0.93 ± 0.19	2.87 ± 1.42	2.76 ± 0.93	3.35 ± 1.81	3.39 ± 1.34	96.60 ± 18.2	99.65 ± 12.8	115.75 ± 12.94	114.23 ± 15.05
Trained	Left M1	50.0 ± 10.4	49.5 ± 9.6	0.82 ± 0.28	*1.26 ± 0.51	2.45 ± 0.92	*3.26 ± 1.19	2.81 ± 0.96	*3.89 ± 1.09	107.93 ± 23.9	104.91 ± 18.86	112.07 ± 17.36	107.86 ± 22.41

There were no significant differences in mean MEP amplitude at AMT pre-training between groups (p = 0.16). MEP amplitude at AMT increased by 53% (p = 0.01, Figure 5.3) in the left M1 in the trained group following the training intervention. There were no significant differences (p = 0.32) in the mean MEP amplitude at AMT in left M1 in the control group following the training intervention. Further, there were no interaction effects between the groups (p = 0.21).

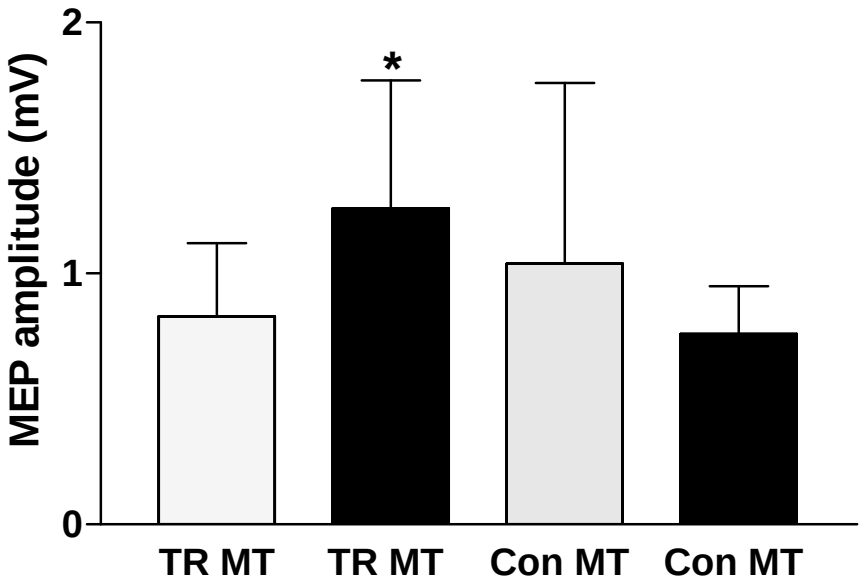

Figure 5.3. Mean (±SD) data for right BB MEPs evoked by single pulse TMS at AMT for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a 53% increase in MEP amplitude for right BB for the trained group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups ($p < 0.05$).

There were no significant differences in the estimated slope (m) of the stimulus-response curve following strength training in the trained group (pre: 0.16 AU ± 0.06 AU, post: 0.15 AU ± 0.05 AU, $p = 0.46$, Figure 5.4) for the left M1. Furthermore, no significant differences were identified for $S50$ following the training intervention for the left M1 (pre; 4.9 AU ± 3.7 AU, post; 5.6 AU ± 4.8 AU, $p = 0.66$).

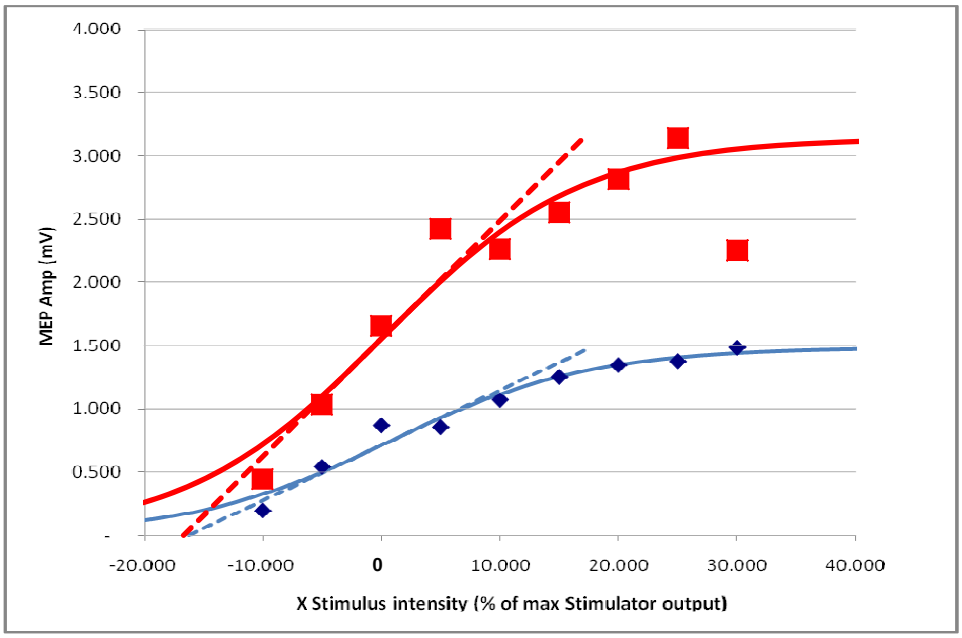

Figure 5.4. Average MEPs recorded from one participant right BB pre (diamonds) and post (squares) strength training. The smallest to largest MEPs are responses to stimulation at: −10, 0, 10, 20, 30 and 40% of the stimulator output above AMT. The two curves represent the calculated sigmoid curve based on mean MEP amplitude data pre and post training, whilst the broken straight lines represent the slope of the curve pre and post training.

There were no difference in mean MEP amplitude at 20% above AMT at pre-training between groups for left M1 (p = 0.43). There were also no significant differences (p = 0.61) in MEP amplitude for the left M1 at 20% above AMT in the control group, however, there was a 33% increase (p = 0.05, Figures 5.5 and 5.6) in the trained group following the intervention. No significant interaction effect was observed between the groups (p = 0.17).

5.3.6 Corticospinal inhibition

Table 5.1 (page 142) displays all SP data between groups' pre and post training intervention (see Figures 5.1 [page 136] and 5.6 [page 149], for illustration of SP duration). No significant differences in SP duration were observed between groups at 20% above AMT at pre-training (p = 0.27). Following the training intervention, there were no significant differences detected between the strength-trained and control group (p = 0.50). Further, there were no significant differences detected in the duration of the mean SP at MEP_{max} between groups pre-training (p = 0.42) or following the strength training intervention (p = 0.35).

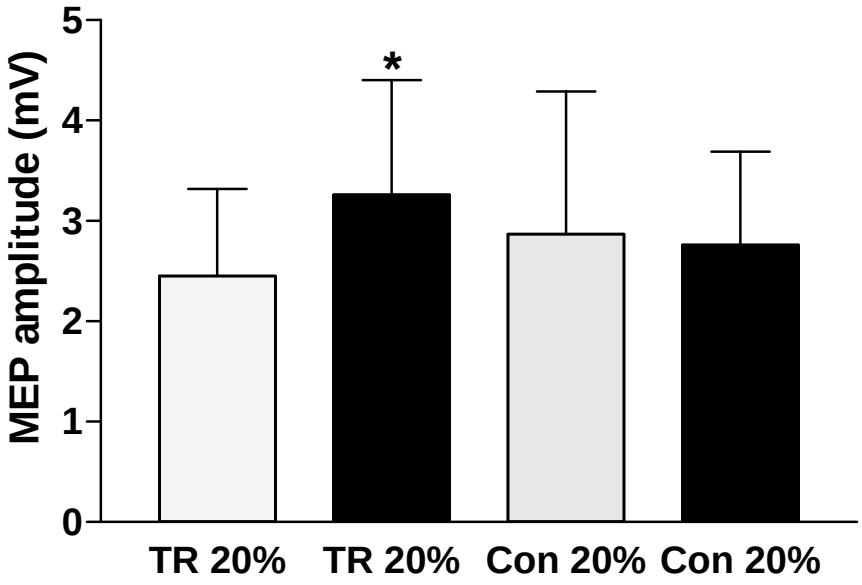

Figure 5.5. Mean (± SD) data for right BB MEPs evoked by single pulse TMS at 20% above AMT for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a 33% increase in MEP amplitude at 20% above AMT for the right BB in the trained group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups ($p < 0.05$).

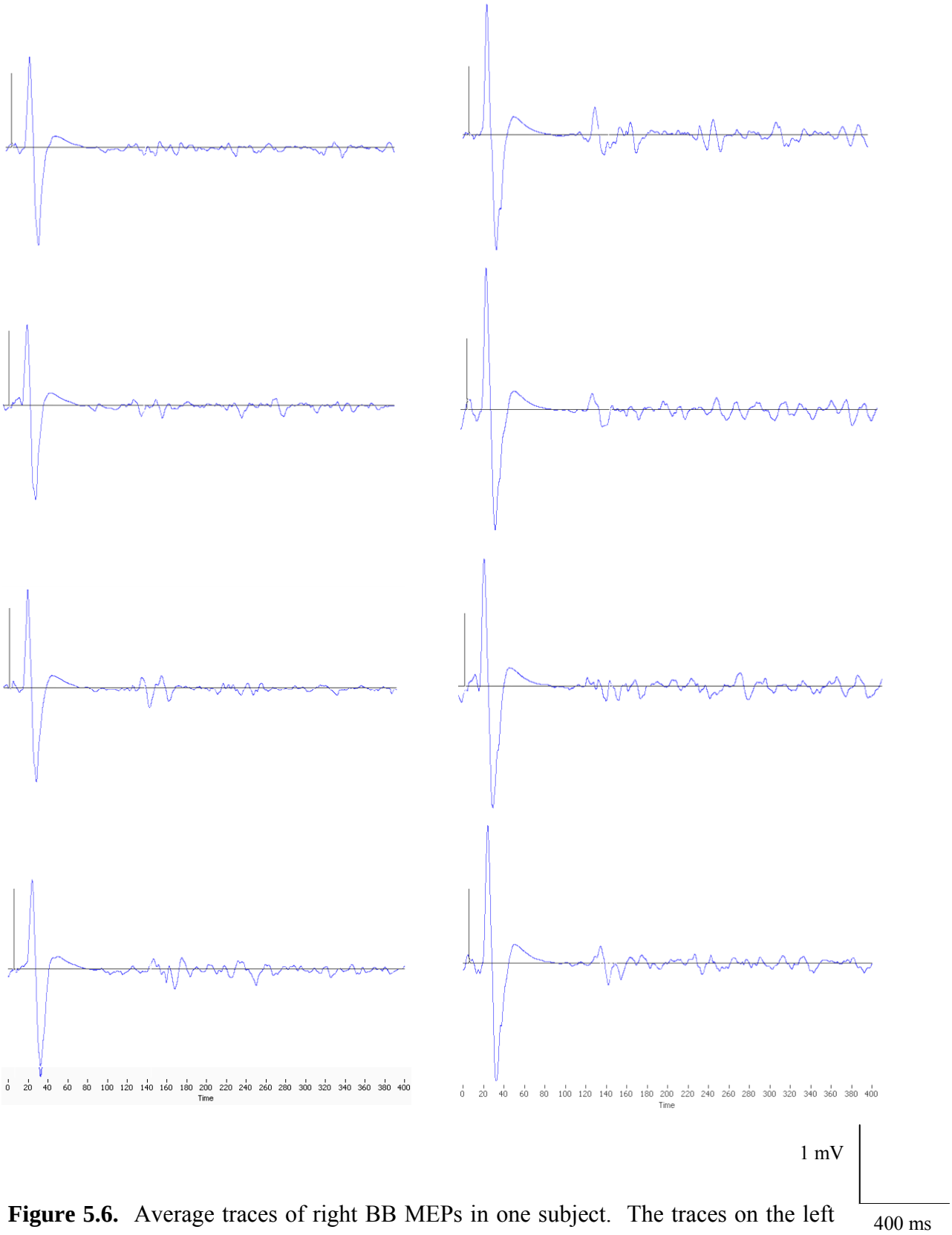

Figure 5.6. Average traces of right BB MEPs in one subject. The traces on the left are MEPs obtained at 20% above AMT prior to strength training and the traces on the right are MEPs obtained following the strength training intervention.

There were no significant differences in mean MEP_{max} amplitude pre-training between groups (p = 0.41). Following training, there was a 38% increase in the amplitude of MEP_{max} (p = 0.02, Figure 5.7) in the trained group, whilst there were no significant differences detected for the control group (p = 0.81). There were no significant interaction effects between groups (p = 0.31).

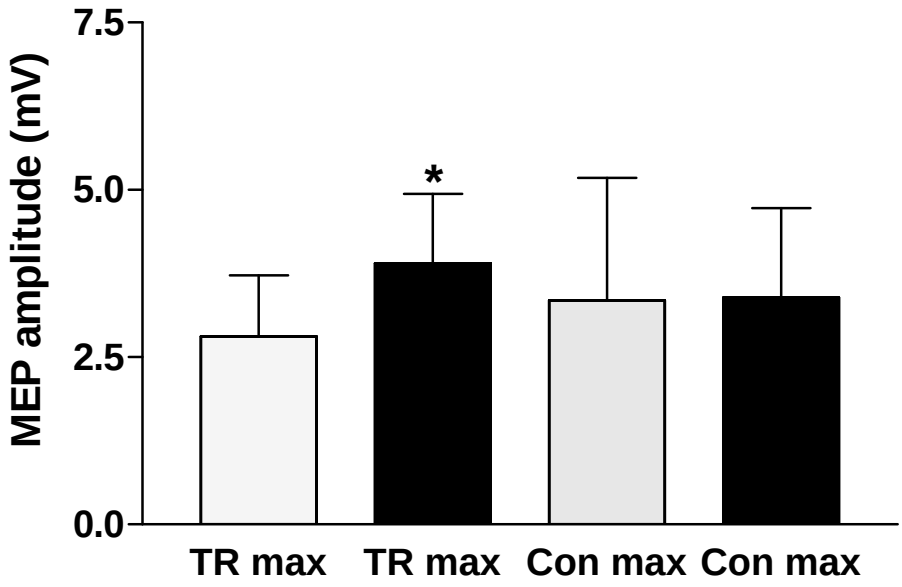

Figure 5.7. Mean (± SD) data for right BB MEPs evoked by single pulse TMS at MEP_{max} for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a 38% increase in MEP_{max} amplitude for the right BB in the trained group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups ($p < 0.05$).

5.4 Discussion

There have been limited studies that have attempted to determine the neural adaptations confined to the corticospinal tract projecting to the spinal motoneuron pool innervating the BB muscle following a period of strength training (Jensen et al., 2005). The aim of the present study was to investigate the corticospinal responses following heavy load controlled isotonic strength training of the elbow flexors. It was hypothesised that this method of strength training would increase corticospinal excitability due to the skilled element of performing each repetition in a controlled manner as it has recently been put forward that strength training and skill training may share similar characteristics that may result in changes in corticospinal control to the trained musculature (Farthing, 2009; Zhou, 2000). The main findings of the study were the significant increases in 1-RM elbow flexion strength, in the absence of muscle hypertrophy and increased MEP amplitude at and above AMT. The significant increase in strength (i.e. 28%) following the strength training program is in accordance to previous short-term strength training studies that have used both isotonic and isometric contractions across a range of upper and lower limb muscles (Fimland et al., 2009a; Jensen et al., 2005; Aagaard et al., 2002b; Griffin and Cafarelli, 2007; Carroll et al., 2002; Lee et al., 2009a; Kidgell et al., 2006; Olafsdottir et al., 2008; Del Balso and Cafarelli, 2007; Patten et al., 2001).

It has been proposed that increased excitability of populations of corticospinal cells projecting to spinal motoneurons innervating the trained muscles may account for some of the observed increases in strength (Hortobágyi et al., 2009; Gabriel et al., 2006). The finding in the present study of increased MEP amplitude at, and above AMT evoked by TMS demonstrates that heavy-load strength training altered the excitability of the corticospinal tract projecting to the spinal motoneurons innervating

the BB muscle. These findings are consistent with increases in corticospinal excitability following strength training that have previously been reported by Griffen and Cafarelli (2007) and Taube et al. (2007), however, inconsistent with the findings from Lee et al. (2009a), Carroll et al. (2002) and Jensen et al. (2005), who reported either a decrease or no change in corticospinal excitability. The factors that may contribute to the potential differences across studies, most likely reside in the different muscles subjected to strength training, the type of strength training employed, the conditions in which TMS was elicited and the strength of corticospinal projection to the spinal motoneurons innervating the trained muscles being different.

There is good evidence to suggest that corticospinal excitability is adjusted based upon the requirements of the task performed (Datta et al., 1989; Flament et al., 1993; Tinazzi et al., 2003), therefore the observed differences in corticospinal excitability observed in the present study are likely to reflect the specific demands of the strength training itself. The study by Carroll et al. (2002) involved strength training an intrinsic hand muscle, where the participants completed 4 sets of 6 repetitions at 70 - 85% 1-RM. Although each repetition was performed slowly, the exact repetition timing was not provided, even though repetition timing is an important component to exercise prescription and strength development (Munn et al., 2005a). Likewise, Jensen et al. (2005) had participants perform bicep curls for four-weeks. The exact load lifted by participants throughout the training period, the timing of each repetition and how progressive overload was applied were not reported. Therefore, it may be necessary that all parameters of a strength training program (i.e. exercise selection, training load, repetition timing and progressive overload) be accurately monitored. In the current study, the participants precisely controlled the timing of each repetition and increased their training load (kg) by 5% as soon as they could complete four sets of 8 repetitions.

A unique aspect to the present study was that the training load prescribed to novice participants commenced at 80% of their 1-RM, without any reported contra-indications, whilst other studies have started training participants at a lower intensity with a gradual increase up to 80% and this could explain the observed differences.

Given that repetitive skill training (both short-term and long-term) has been shown to increase neural excitability within populations of corticospinal cells (Buonomano and Merzenich, 1998; Pearce et al., 2000), it may be important that the type of strength training prescribed should focus on skilled movements that challenge the nervous system (Zhou, 2000; Jensen et al., 2005; Farthing, 2009). For example, increases in corticospinal excitability following ballistic strength training, which requires acceleration and deceleration forces has been shown to increase corticospinal excitability (Taube et al., 2007a; Taube et al., 2007b). Although it has recently been suggested that corticospinal excitability maybe unchanged following strength training due to low task complexity and limited peripheral feedback (Jensen et al., 2005; Hortobágyi et al., 2009), repetitive movements against resistive loads that require a certain level of task complexity and precision may underpin the corticospinal responses observed within the present study and that of others (Taube et al., 2007b). The repetition timing employed in the present strength training program (3 s concentric and 4 s eccentric) may have increased the difficulty of performing a standard bicep curl exercise and subsequently increased peripheral feedback, which has resulted in increased corticospinal excitability. Previous research has demonstrated that slow velocity strength training is associated with a greater level of neural adaptation compared to high velocity strength training alone and it is thought such adaptations may be mediated by peripheral feedback mechanisms (Hortobágyi et al., 1997; Hortobágyi et al., 1996). Therefore, purposefully controlling the time to perform each repetition

during both the concentric and eccentric phases in the present study has resulted in an increase in task complexity and peripheral feedback which has lead to an increase corticospinal excitability. The repetition timing used was based upon previous work that demonstrated increased corticospinal excitability when participants performed the same task, with the same force levels, under different levels of precision, being the timing of the movement (Pearce and Kidgell, 2009; Pearce and Kidgell, 2010). Therefore, a repetition timing protocol was prescribed (i.e. controlled timing) to increase the level of difficulty of a relatively simple movement in an attempt to increase corticospinal excitability.

The increase in the mean amplitude of the descending corticospinal volley at AMT, 20 % AMT and at MEP_{max} following strength training, lends support to the concept of activity-dependant changes in corticospinal excitability (Perez and Cohen, 2008) and demonstrates adaptive changes within the intrinsic properties of the corticospinal pathway following strength training. The changes in corticospinal excitability are likely to reflect changes in synaptic strength of existing corticospinal connections projecting to the spinal motoneuron pool (Nielsen and Cohen, 2007; Chen et al., 1998; Ridding and Rothwell, 1997; Adkins et al., 2006). It has been demonstrated that such connections are widespread and exhibit activity dependant modifications in synaptic strength following the acquisition of novel tasks (He et al., 1995; Jones, 1993; Katiuscia et al., 2009). Since AMT and MEP amplitude are two related, but independent measures of corticospinal excitability, the observed changes in MEP amplitude at and above AMT, demonstrates that the strength training program has resulted in a shift in the balance between inhibitory and excitatory inputs onto cortical and/or spinal motoneurons. Moreover, the change in MEP amplitude above AMT, demonstrates an increase in the number and size of the descending volleys generated by

the cortical stimulus or from an increase in the number of corticospinal cells activated. Overall, these changes suggest that, in the strength training group, there has been a change in the level of cortical and/or spinal excitability.

The present investigation did not support our hypothesis that strength training, increasing muscle strength, would reduce the duration of the SP, demonstrating reduced corticospinal inhibition. The duration of the SP can be used to assess the excitability of cortical inhibitory circuits within the M1 (Orth and Rothwell, 2004). Changes in corticospinal inhibition may be an important mechanism in the early phases of strength development as inhibition is reduced during voluntary muscle contractions and has been proposed to improve corticospinal drive during intended movement by releasing corticospinal cells from inhibition and improving subsequent excitatory drive to produce the desired movement (Floeter and Rothwell, 1999). To the authors' knowledge, there are currently no studies that have assessed the effect of strength training on changes in corticospinal inhibition, despite previous investigations that have used TMS. This study found no change in the duration of the SP following strength training at 20% above AMT and at MEP_{max}, which suggests that the strength of inhibitory elements within the corticospinal pathway remained unchanged following training. Nevertheless, the role of intracortical inhibitory circuits should not be ignored as output from the M1 is a balance between excitation and inhibition and changes in inhibition may represent an important mechanism in strength development (Werhahn et al., 2007).

Although this study has reported increased corticospinal excitability, given the divergent pattern of corticospinal cell projection onto spinal motoneurons and that MEPs evoked by TMS represent the entire corticospinal pathway (Devanne et al., 1997), it is likely that changes in strength may be related to adaptations in neural

circuits not confined to the corticospinal pathway. There may have been small adaptive changes at multiple sites within the CNS, which combined may have altered the way in which the BB was activated. Alterations in coactivation with strength training have been related to a change in the ability to focus the motor command to the appropriate muscles (Zoghi et al., 2003). Given that changes in antagonistic or synergistic muscle activity were not measured in this study and that changes in coactivation occur as early as the first week of a training program (Carolan and Cafarelli, 1992; Hortobágyi et al., 1997), the strength gains observed in this study may reflect mechanisms confined to the subcortical and/or spinal level (Fimland et al., 2009a). Changes in spinal motoneuron activity, such as changes in presynaptic inhibition could possible account for the changes in strength observed. Indeed, several recent studies have demonstrated increased motoneuron excitability following isometric and maximal strength training (Del Balso and Cafarelli, 2007; Fimland et al., 2009a). Since the corticospinal pathway as a whole includes cortical circuitry, the motoneuron pool and its intrinsic properties, as well as spinal interneuronal pathways (Porter, 1985), increased excitability of the motoneuron pool and changes in presynaptic inhibition may have occurred and could explain the increases in strength observed. However, Griffen and Cafarelli (2007) suggested that the larger MEP following training resulted from an increase in motor unit recruitment, indicating multiple potential sites of adaptation within the CNS following strength training. Since single motor unit behaviour and spinal cord reflexes were not performed in the present study, it cannot therefore, be excluded that modifications in the efficacy of neural transmission across synaptic connections between corticospinal fibres and spinal motoneurons may have occurred.

5.5 Conclusion

The present investigation demonstrated, using TMS, an increase in MEP amplitude during a 10% rmsEMG MVC background contraction at stimulus intensities at and above AMT following four-weeks of strength training the BB muscle. The increase in corticospinal excitability demonstrates changes in synaptic strength of existing corticospinal connections that project onto the spinal motoneuron pool innervating the trained BB. It cannot be ruled out that changes in excitability or inhibition within other neural circuits in the nervous system not confined to the corticospinal pathway were also involved. Despite this, the present findings demonstrate that heavy-load controlled isotonic strength training altered neural transmission via the corticospinal pathway projecting to the motoneuron pool innervating the trained muscle and provides one of probably multiple mechanisms that contribute to the observed changes in strength in the current study.

CHAPTER SIX

Corticospinal Adaptations Following Cross-Education Strength Training: A TMS Study.

6.1 Introduction

A common observation that underscores the complexity of neuromuscular interactions between homologous limbs is the phenomenon of cross-education. Initially described by Scripture et al. (1894) whereby unilateral motor training of one limb improves motor task performance of the contralateral limb, there is good evidence to support cross-education in strength training of upper and lower limbs using various muscular contraction and movement types (Hortobágyi et al., 1997; Shaver, 1975; Brown et al., 1990; Cannon and Cafarelli, 1987; Scripture et al., 1894; Farthing and Chilibeck, 2003; Hortobágyi et al., 1999; Lee et al., 2009b; Farthing et al., 2007; Fimland et al., 2009b; Yue and Cole, 1992; Adamson et al., 2008).

A recent meta analysis of randomised, controlled cross-education studies focussing on strength, found a mean increase of 7.8% in muscle strength of the contralateral homologous muscle (Munn et al., 2004). However, Munn et al. (2004) presented data from studies ranging from a reduction of 2.7% (Meyers, 1966) to an increase of 21.7% (Carolan and Cafarelli, 1992), and suggested that the exclusion of an adequate control measure, not only underpowers most studies but may also explain the inconsistent findings. Typical control measures have included the comparison of within-subjects' strength between the trained and untrained limbs. Carroll et al. (2006) suggested that with such a design, the changes in contralateral strength may be due to familiarisation. Using this procedure, it has been demonstrated that repeated exposure to muscle testing can improve performance through learning (Gleeson and Mercer, 1996). Given that these studies have not included a separate control group (Garfinkel and Cafarelli, 1992; Meyers, 1966; Adamson et al., 2008)

it is possible that as the participants are strength training a single arm, they are becoming familiar with the movement pattern, thus biasing the post-testing period. A potential approach to overcome this problem and obtain more objective data concerning the cross-education effect would be to randomise participants into two groups (experimental and control) and then compare the increases in strength of the contralateral untrained limbs between groups (Carroll et al., 2006; Munn et al., 2004). Despite these methodological differences (Munn et al., 2004), considerable evidence illustrates that the cross-education effect exists; however the exact mechanisms underlying the cross-transfer of strength remains unclear, although neural adaptations have been implicated (Carroll et al., 2006; Lee et al., 2009b).

In an attempt to explain the neural contribution to cross-transfer of strength (Fimland et al., 2009b), it has been suggested that 10% (Nyberg-Hansen and Rinvik, 1963; Carpenter, 1985) to 30% (Nathan et al., 1990) of pyramidal tract neurons do not decussate providing ipsilateral corticospinal projections. Recently, it has been demonstrated using the combined techniques of fractional anisotropy and paired-pulse TMS, functional connectivity between M1 hand areas in both hemispheres (Wahl et al., 2007). Taken together, neuro-anatomical studies have provided a structural explanation for ipsilateral projection and interhemispheric integration underpinning physiological mechanisms for the cross-education effect.

In determining neurophysiological mechanisms for cross-education, studies have employed TMS to investigate corticospinal excitability. Hortobágyi et al. (2003), showed increased MEPs, but depressed H-reflex excitability, in homologous right limb wrist flexors

and extensors following moderate, 50% MVC, to strong (75% MVC) acute voluntary contractions of the left limb. These authors suggested an increased excitability in the M1 with little to no change in the motoneuron pool. More recently, Lee et al. (2009b) demonstrated an increase in voluntary activation of the opposite untrained limb following four-weeks of isometric strength training of the right wrist extensor muscles. Twitch interpolation, using TMS, was used to assess the changes in cortical voluntary activation of the untrained wrist extensors. Following training there was a significant increase in strength of the trained (31.5%) and untrained wrist extensors (8.2%) which was accompanied by a significant decrease in twitch amplitude (35%) contributing to a significant increase in voluntary activation (2.9%). The finding of a reduced amplitude of the superimposed twitch following the strength training period was interpreted as increased motor cortical output to the untrained wrist extensors (Lee et al., 2009b).

There is evidence to suggest that during a unilateral contraction, there is bilateral activation of the M1, termed motor irradiation (Muellbacher et al., 2000; Hortobágyi, 2005; Carson, 2005; Stedman et al., 1998; Hortobágyi et al., 2003; Todor and Lazarus, 1986; Perez and Cohen, 2008). Todor and Lazarus (1986) suggest that the degree of motor irradiation to the contralateral limb is conditional to the level of neural drive directed to the muscles undergoing the movement. More recently, Perez et al. (2008) demonstrated, using paired-pulse TMS, bilateral motor cortical activity during unilateral wrist flexion and increased MEPs of the ipsilateral motor pathway with increasing force output. Therefore, with interhemispheric connections between the cortices via the corpus callosum, along with ipsilateral and contralateral corticospinal projections, there are many potential sites within

the nervous system that could contribute to the cross-transfer of strength (Carroll et al., 2006).

A further question raised within cross-education research is attributing the effects of cross-education to strength training or practice of a motor skill. Zhou (2000) and Farthing (2009) suggested that cross-education is consequential to the specificity to the prescribed training, and indeed has been shown to occur during both motor skill training (Schulze et al., 2002) and following strength training (Teixeira and Caminha, 2003). Evidence for cross-education being related to motor skill acquisition come from studies that have shown maximal contralateral strength gains when the movement tested is the same as the training movements (Hortobágyi et al. 1997). Similarly, studies that have employed unfamiliar movements as part of the strength training regime have also shown cross-education effects. Farthing et al. (2007) using fMRI demonstrated an enlarged region of activation in the contralateral sensorimotor cortex and activation of the ipsilateral temporal lobe of the untrained limb, proposing that the temporal lobe may be important for the cross-transfer of strength; however, the effect of incremental learning, particularly in light of using an unfamiliar movement exercise, could not be discounted.

Despite current evidence supporting the cross-education phenomenon coming from strength training and motor skill acquisition literature, it remains unknown whether heavy load (80% of 1-RM) unilateral strength training has the capacity to increase corticospinal excitability projecting to the spinal motoneuron pool of the untrained limb. Therefore, this study was designed to extend on previous work by investigating the neural mechanisms underpinning the cross-education effect with heavy load (80% 1-RM), controlled (timing of

each repetition**,** 3 s concentric/4 s eccentric) unilateral strength training using a between groups design (Munn et al., 2004). The primary objective was to determine whether cross-education strength training induces changes in corticospinal excitability and inhibition projecting to the spinal motoneuron pool innervating the untrained limb. The general aims of the investigation were to compare the changes in the input-output properties of the corticospinal pathway following unilateral strength training (ULS). The specific aims of the study were to compare the changes in TMS AMT, MEP latency, MEP amplitude, MEP_{max}, and SP duration, at and 20% above AMT, to assess the influence of heavy load ULS on the contralateral transfer of strength. It was anticipated that the present study would allow us to determine the responses that occur within the contralateral corticospinal pathway projecting to the spinal motoneuron pool of the untrained limb.

6.2 Methods

The methods and procedures employed in the current study are comprehensively outlined in Chapters 4 and 5. The following is an abridged version of the sections applicable to this chapter.

6.2.1 Organisation of the study

Twenty six healthy participants (26.8 ± 7.3 years, 12 males, and 14 females) were systematically (by gender) and randomly assigned into either a strength training (6 males, 20.3 ± 3.4 years and 7 females, 24.5 ± 3.0 years) or a control group (6 males, 27.6 ± 7.9 years and 7 females, 29 ± 6.2 years).

6.2.2 Maximum strength testing

Participants in both groups performed a standard unilateral 1-RM test for the right and left arm, refer to section 5.2.2 (page 134) for a detailed description of the method employed.

6.2.3 Arm circumference

In order to determine whether there was any change in muscle hypertrophy as a result of the strength training program, arm circumference of the right and left upper arm was measured with a tape measure. Refer to section 5.2.3 (page 135) for a detailed description.

6.2.4 Strength training procedures

For a more detailed description of the strength training procedures employed, refer to chapter 5, and section 5.2.4 (page 135-36).

6.2.5 Contralateral strength transfer

The contralateral transfer of strength was quantified according to the procedure of Carroll et al. (2006). The transfer was determined by the difference in change in mean strength of the untrained left arm in the control group and the experimental group post training. The calculation was performed as follows:

$$\left(\frac{EPost - EPre}{EPre} - \frac{CPost - CPre}{CPre} \right) 100$$

Where *EPost* refers to mean post training 1-RM strength for the experimental group's untrained arm, *E*Pre refers to mean pre training 1-RM strength for the experimental group's untrained arm, *CPost* refers to mean post training 1-RM strength for the control group's untrained arm, and *CPre* refers to mean pre training 1-RM strength for the control group's untrained arm.

6.2.6 Electromyography and transcranial magnetic stimulation

Surface EMG activity and TMS evoked MEPs (stimulus-response curves) were recorded from both the left and right M1 projecting to the spinal motoneuron pool innervating the left and right BB pre and post training. Refer to sections 4.2.3 (page 106) and 5.2.5 (page 136) for a more detailed description of the methods employed.

6.2.7 Data and statistical analyses

All MEPs collected (n = 10, two sets of five 500 ms recordings, at each stimulus intensity from below participant's AMT until saturation of the MEP) were displayed and averaged online for visual inspection, in determining the optimal site, and then stored off-line for further analysis. Stimulus-response curves were constructed according to the procedures described in section 5.2.6 (page 135).

All data were first screened to ensure they were normally distributed. In order to have sufficient data to test for questions of normality, all data from 68 trials were used to establish the distributional properties. No variable's z-score of skew or kurtosis was excessive. Further, Kolmogorov-Smirnov tests suggested the variables *S50* (KS = 0.07, p = 0.2) and MEP_{max} (KS = 0.1, p = 0.08) were clearly normally distributed, while m was

apparently non-normal, (KS = 0.1, p = 0.01) however; this violation appeared to be only mild from examination of frequency histograms and detrended Q-Q plots, and was not considered sufficient to warrant a more conservative analytic strategy than used herein. Consequently, it was decided to treat the data as essentially normal in distribution. To identify changes in the input-output properties of the corticospinal pathway, the slope and plateau values of the stimulus-response curve was used to characterise the physiological strength of the corticospinal connections projecting to the left and right BB (Carroll et al., 2002; Boroojerdi et al., 2001a). Latency was calculated from stimulus artefact to MEP onset; MEP peak-to-peak amplitude and SP duration (onset of MEP to return of uninterrupted EMG) were cursored and measured for both motor cortices (Williams et al., 1992; Pearce and Kidgell, 2010; Byrnes et al., 1999; Wilson et al., 1993a; Wilson et al., 1993b). Furthermore, MEP sweeps (n = 10) obtained at AMT, 20% above AMT and MEP_{max} were analysed to quantify changes in membrane excitability and corticospinal cell recruitment following the strength training intervention (Hallett, 2007).

To test the hypothesis that unilateral strength training increases contralateral strength and corticospinal excitability, a two-way ANOVA, and Fisher's least significant difference (LSD) procedure for post hoc testing, for each arm was used to compare group interaction (trained vs. control) by testing session (pre vs. post) for each dependant variable (elbow flexion strength, rmsEMG, MEP latency and amplitude, and SP duration). Pearson's correlation coefficient was used to determine correlations between changes in corticospinal excitability and changes in contralateral strength. Data is presented as means (± SD) and the level of significance used for all tests was set at $p < 0.05$.

6.3 Results

All participants in the training group completed all training sessions, however three participants (1 male and 2 females) in the control group were not able to complete the post-testing session and subsequently their data was not used. No significant differences were observed in muscle girths between groups pre training (right arm trained group pre 31.9 ± 5.6 cm versus control group pre 31.3 ± 5.2 cm, $p = 0.49$; left arm trained group pre 31.3 ± 4.9 cm versus control group pre 30.9 ± 6.2 cm, $p = 0.56$). No significant differences in arm girths were observed within and between groups following the training period (right arm trained group post 32.2 ± 4.9 cm versus control group post 31.4 ± 3.3 cm, $p = 0.86$; left arm trained group post 31.2 ± 4.7 cm versus control group post 31.5 ± 3.1 cm, $p = 0.39$).

6.3.1 Voluntary muscle strength

There were no significant differences in dynamic elbow flexion strength (1-RM) at baseline between the control and trained groups in both right and left arms (right arm: $p = 0.86$; left arm: $p = 0.37$). Dynamic elbow flexion mean strength increased by 28% ($p = .0001$) in the trained (right) arm (11.5 ± 4.5 kg to 14.8 ± 5.2 kg) and a 19.2% ($p = 0.0001$) increase in strength to the untrained (left) arm (11.3 ± 4.9 kg to 13.7 ± 5.4 kg; Figure 6.1). There were no significant differences in voluntary strength for the control group (right arm: 13.3 ± 4.2 kg to 13.2 ± 4.3 kg, $p = 0.34$; left arm: 11.8 ± 3.9 kg to 12.0 ± 3.8 kg, $p = 0.17$).

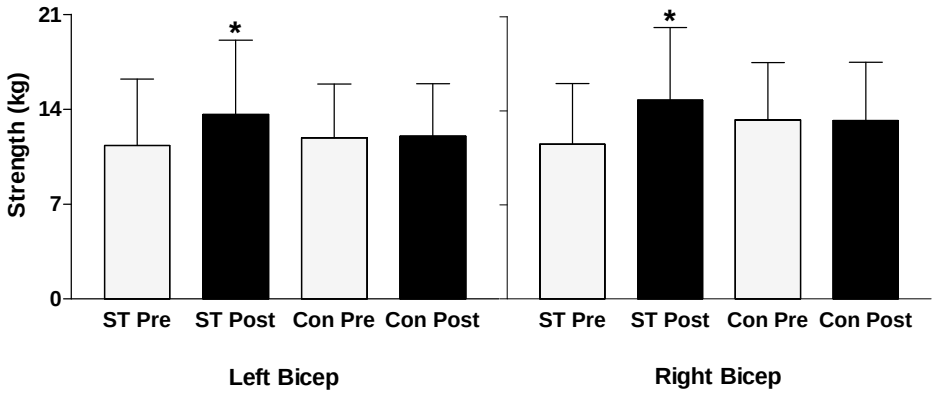

Figure 6.1. Mean (± SD) 1-RM left and right elbow flexion strength (expressed as kg) for the strength training (ST) and control (CON) groups before (light bars) and after (black bars) strength training of the right elbow flexors only. There was a 19.2% increase in left elbow flexion strength and a 28% increase in right elbow flexion strength for the trained group. Asterisk denotes significant increase in elbow flexion strength from before to after training between groups ($p < 0.05$).

There was a significant correlation between the percentage of strength gained in the trained right limb and the percentage of the contralateral transfer of strength to the untrained left limb ($r = 0.67$, $p = 0.01$; Figure 6.2).

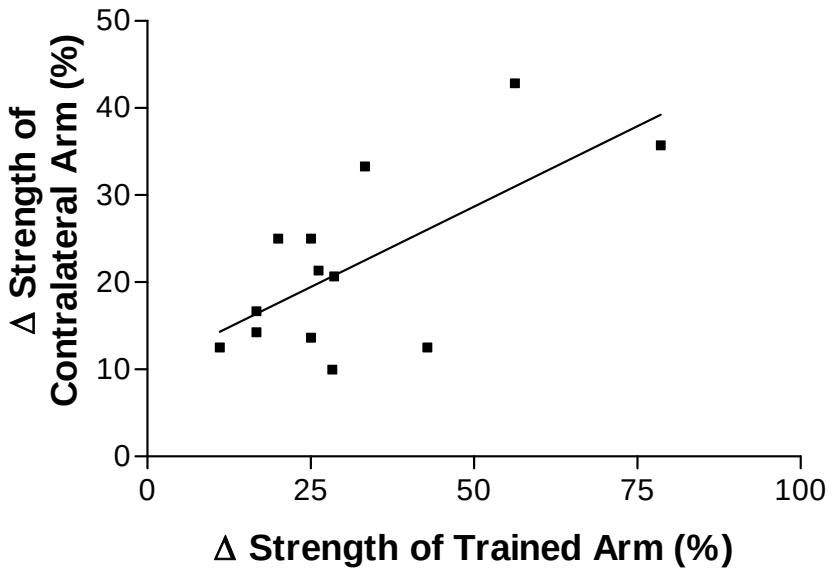

Figure 6.2. Strength changes (as represented by delta [△]) for the elbow flexors of the trained and contralateral limb in trained participants after four-weeks of heavy load controlled unilateral strength training, expressed as a percentage of pre-training strength ($r = 0.67$; $p < 0.05$).

6.3.2 Muscle activation

Table 6.1 displays the mean data for trained and control groups' rmsEMG max and 10% rmsEMG max. There were no significant differences at baseline for group mean left and right BB MVC rmsEMG activity between the groups (control, left arm: 0.39 ± 0.12 mV; trained, left arm: 0.52 mV ± 0.22 mV, $p = 0.17$; control, right arm: 0.41 ± 0.24 mV; trained, right arm: 0.50 mV ± 0.20 mV, $p = 0.56$). There were also no differences following training to pre-training values within or between the groups (control, left arm: 0.37 ± 0.12 mV; trained, left arm: 0.60 mV ± 0.22 mV, $p = 0.17$; control, right arm: 0.41 ± 0.21 mV; trained, right arm: 0.58 mV ± 0.17 mV, $p = 0.57$). Further, no interaction was found between groups by training ($p = 0.71$). Similarly, no differences were observed between rmsEMG at 10% of MVC contraction pre and post testing sessions (pre control, left arm: 0.04 ± 0.01 mV; pre trained, left arm: 0.05 mV ± 0.02 mV, $p = 0.24$); post control, left arm: 0.04 ± 0.01 mV; post trained, left arm: 0.06 ± 0.02 mV; pre control, right arm: 0.04 ± 0.02 mV; pre trained, right arm: 0.05 ± 0.02 mV, $p = 0.40$; post control, right arm: 0.04 ± 0.02 mV; post trained, right arm: 0.05 mV ± 0.01 mV, $p = 0.50$).

Table 6.1. Group mean data for rmsEMG values pre vs. post training. Values are expressed as mV (± SD) for both maximum rmsEMG and 10% maximum rmsEMG.

Group	Limb	rmsEMG Max (mV)		10% rmsEMG (mV)	
		Pre	Post	Pre	Post
Control	Right	0.41 ± 0.24	0.41 ± 0.21	0.84 ± 0.43	0.04 ± 0.02
	Left	0.39 ± 0.12	0.37 ± 0.12	0.04 ± 0.1	0.04 ± 0.01
Trained	Right	0.50 ± 0.20	0.58 ± 0.17	0.05 ± 0.02	0.05 ± 0.02
	Left	0.52 ± 0.22	0.60 ± 0.22	0.05 ± 0.02	0.06 ± 0.02

6.3.3 Latency period

No significant differences in latency duration were seen between groups at 20% above AMT at pre-training (right M1, $p = 0.86$; left M1, $p = 0.27$). Following the training intervention, there was no significant difference in latency duration pre vs. post training in both trained (right M1: 13 ± 0.8 ms vs. 12.8 ± 0.5 ms, $p = 0.86$, left M1: 13 ± 0.8 ms vs. 12.9 ± 0.3 ms, $p = 0.31$) and control groups (right M1: 12.9 ± 0.5 ms vs. 12.8 ± 0.5 ms, $p = 0.86$; left M1: 12.9 ± 0.5 ms vs. 12.8 ± 0.5 ms, $p = 0.40$).

6.3.4 Corticospinal excitability

Mean group data for the control and the trained groups for percentage of stimulator output at AMT are shown in Table 6.2. There were no significant differences at pre-training for the percentage of stimulator output at AMT within and between the trained and control groups left ($p = 0.36$) and right M1 ($p = 0.76$). Following the training period, there were no significant differences for percentage of stimulator output at AMT between the trained and control groups (control left M1 vs. trained left M1; $p = 0.83$; control right M1vs. trained right M1; $p = 0.93$, Table 6.2).

Table 6.2 displays the mean data for both the control and the trained group for mean MEP amplitude at AMT, 20% above AMT and MEP_{max}. There was no significant difference in mean MEP amplitude at AMT at baseline between groups (right M1: $p = 0.97$; left M1: $p = 0.16$). MEP amplitude at AMT increased by 53% ($p = 0.01$) in the left M1 and increased by 30.3% ($p = 0.03$) in the right M1 in the trained group following the training intervention (Figures 6.3 and 6.4 respectively). There were no significant differences ($p = 0.34$) in the mean MEP amplitude at AMT in the right M1 and left M1 ($p = 0.32$) in the

control group following the training intervention. Further, there were no interaction effects between the groups ($p = 0.27$).

Table 6.2. Mean data (± SD) for percentage of stimulator output at AMT (%), MEP amplitude at AMT, 20% above AMT, MEP_{max} (mV), SP duration at 20% above AMT and at MEP_{max} (ms), prior to and following the four-week strength training intervention for the control and trained groups. The shaded boxes denote a significant increase in MEP amplitude for both the right and left M1 following strength training. Asterisk indicates statistical significance ($p < 0.05$).

Group		Stimulator Output at AMT (%)		AMT Amplitude (mV)		MEP Amplitude (mV) @ 20% above AMT		MEP_{max} (mV)		SP Duration (ms) at 20% above AMT		SP Duration (ms) at MEP_{max}	
		Pre	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
Control	Right M1	48.57 ± 5.5	48.42 ± 7.4	0.84 ± 0.43	0.75 ± 0.16	1.70 ± 1.12	1.73 ± 1.12	2.57 ± 2.05	2.51 ± 1.9	99.91 ± 18.5	99.86 ± 17.3	112.56 ± 14.59	111.99 ± 14.54
	Left M1	49.37 ± 6.7	45.62 ± 7.7	1.04 ± 0.72	0.93 ± 0.19	2.87 ± 1.42	2.76 ± 0.93	3.35 ± 1.81	3.39 ± 1.34	96.60 ± 18.2	99.65 ± 12.8	115.75 ± 12.94	114.23 ± 15.05
Trained	Right M1	48.4 ± 8.9	46.5 ± 6.8	0.89 ± 0.54	*1.16 ± 0.55	2.77 ± 2.05	*3.06 ± 1.56	3.02 ± 1.94	*3.82 ± 2.08	101.04 ± 19.05	97.13 ± 22.5	111.07 ± 15.94	113.54 ± 18.86
	Left M1	50.0 ± 10.4	49.5 ± 9.6	0.82 ± 0.28	*1.26 ± 0.51	2.45 ± 0.92	*3.26 ± 1.19	2.81 ± 0.96	*3.89 ± 1.09	107.93 ± 23.9	104.91 ± 18.86	112.07 ± 17.36	107.86 ± 22.41

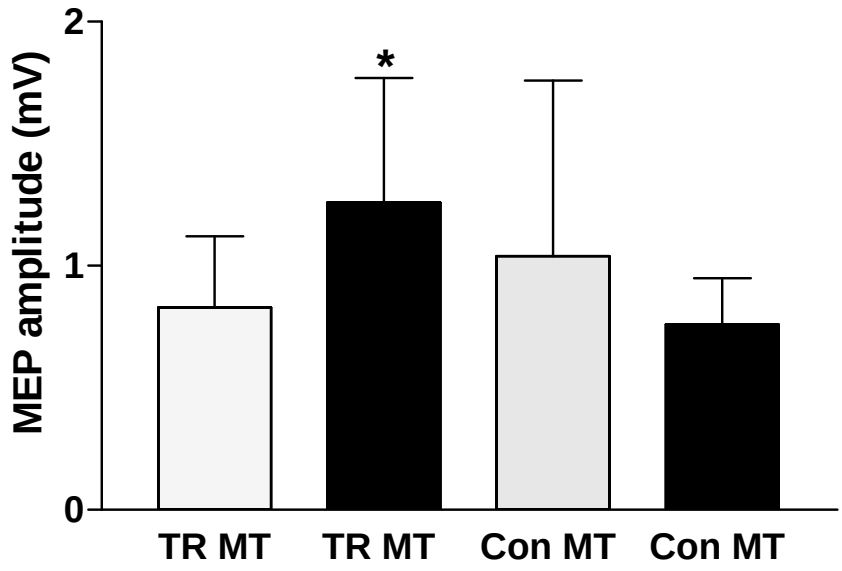

Figure 6.3. Mean (±SD) data for right BB MEPs evoked by single pulse TMS at AMT for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a significant increase (p = 0.01) in MEP amplitude at AMT following the strength training intervention for the trained group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups (p < 0.05).

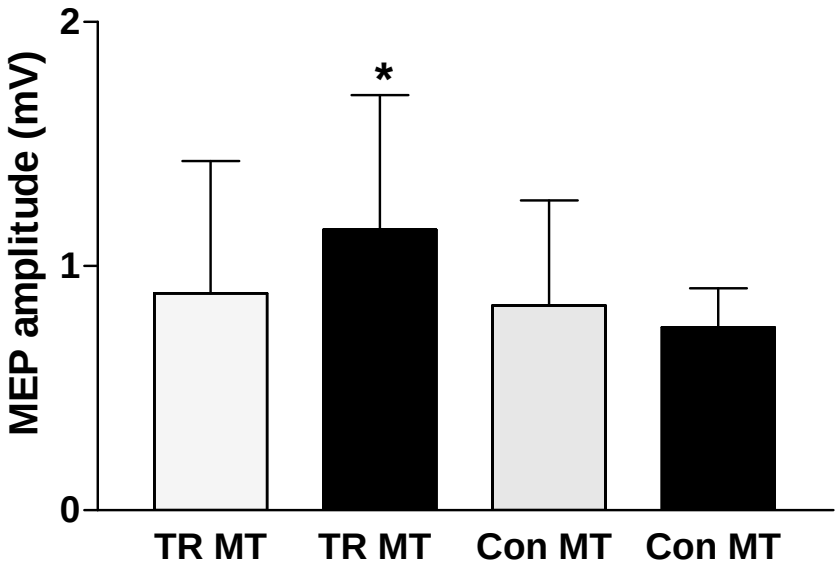

Figure 6.4. Mean (±SD) data for left BB MEPs evoked by single pulse TMS at AMT for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a significant increase (p = 0.03) in MEP amplitude at AMT following the strength training intervention for the trained group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups (p < 0.05).

There were no significant differences in the estimated slope (m) of the stimulus-response curve following strength training in the trained group (pre: 0.15 AU ± 0.05 AU; post: 0.14 AU ± 0.03 AU; p = 0.35) for the right M1. There were also no significant differences in m for the left M1 (pre: 0.16 AU ± 0.06 AU, post: 0.15 AU ± 0.05 AU, p = 0.46). Furthermore, no significant differences were identified for $S50$ following the training intervention for the right or left M1 (right M1: pre; 4.3 AU ± 3.4 AU, post; 4.5 AU ± 3.3 AU, p = 0.86; left M1: 4.9 AU ± 3.7 AU, post; 5.6 AU ± 4.8 AU, p = 0.66), Figure 6.5).

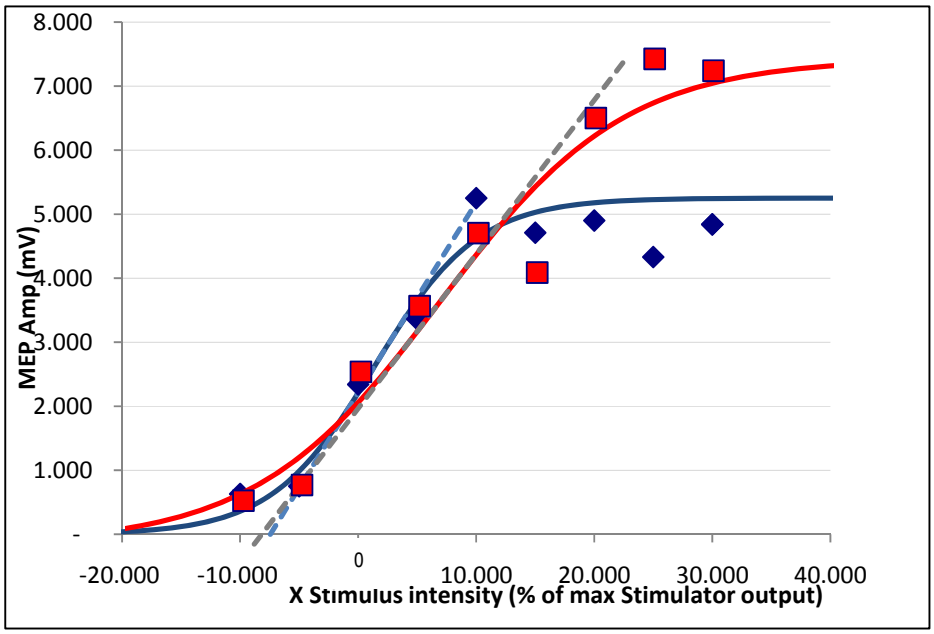

Figure 6.5. Average MEPs recorded from one participant's left BB pre (diamonds) and post (squares) strength training of the right BB only. The smallest to largest MEPs are responses to stimulation at: −10, 0, 10, 20, 30 and 40% of the stimulator output above AMT. The curves represent the calculated sigmoid curve based on mean MEP amplitude data pre (diamonds) and post (squares) training, whilst the broken straight lines represent the slope of the curve pre and post training.

There was a moderate, but non-significant, correlation between the amplitude of MEPs at AMT in the right M1 and changes in strength of the untrained left limb ($r = 0.42$, $p = 0.06$). Following strength training, there was a significant correlation between the amplitude of MEPs at 20% above AMT in the right M1 and the change in strength of the untrained left limb ($r = 0.57$, $p = 0.04$, Figure 6.6). In addition, there was also a significant correlation between the amplitude of MEPs at 20% above AMT in the left M1 and the change in strength of the untrained left limb ($r = 0.62$, $p = 0.02$, Figure 6.7).

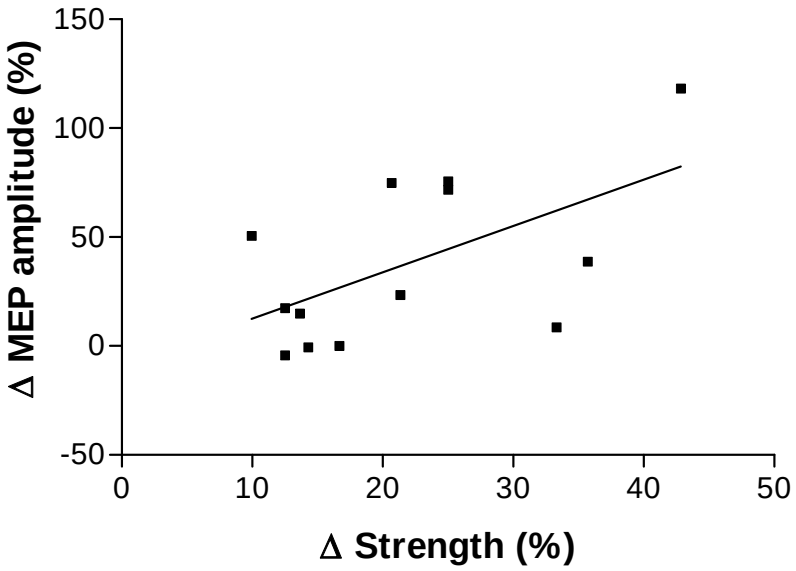

Figure 6.6. The relationship between changes (as represented by delta [△]) in strength of the untrained arm and MEP amplitude at 20% above AMT for the right motor cortex of the trained group ($r = 0.57$; $p < 0.05$).

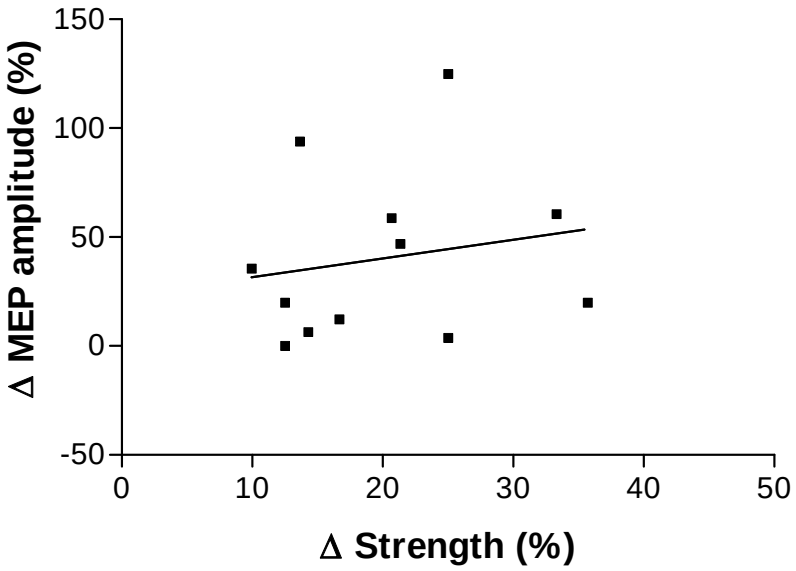

Figure 6.7. The realtionship between changes (as represented by delta [△]) in strength of the untrained arm and MEP amplitude at 20% above AMT for the left motor cortex of the trained group ($r = 0.62$, $p < 0.05$).

There were no difference in mean MEP amplitude at 20% above AMT at pre-training between groups (right M1: $p = 0.20$; left M1: $p = 0.43$). There were no significant differences ($p = 0.41$) in MEP amplitude of the right M1 in the control group at 20% above AMT, however, there was a 33% increase in MEP amplitude in the right M1 for the trained group ($p = 0.05$, Figures 6.8 and 6.9). There were also no significant differences ($p = 0.61$) in MEP amplitude of the left M1 at 20% above AMT in the control group, however, there was a 33% increase ($p = 0.05$) in the trained group following the intervention (Figure 6.10). No significant interaction effect was observed between the groups (right M1: $p = 0.93$; left M1: $p = 0.12$).

There were no significant differences in mean MEP_{max} amplitude at pre-training between groups (right M1: $p = 0.61$; left M1: $p = 0.41$, see Table 6.2 page 175). Following the training intervention, there was a 26.5% increase in the amplitude of the MEP_{max} in the right M1 ($p = 0.01$; Figure 6.11) and a 38% increase in the left M1 ($p = 0.02$; Figure 6.12) in the trained group. There were no significant ($p = 0.81$) differences detected for the control group or any significant interaction effects (right M1: $p = 0.9$; left M1: $p = 0.31$).

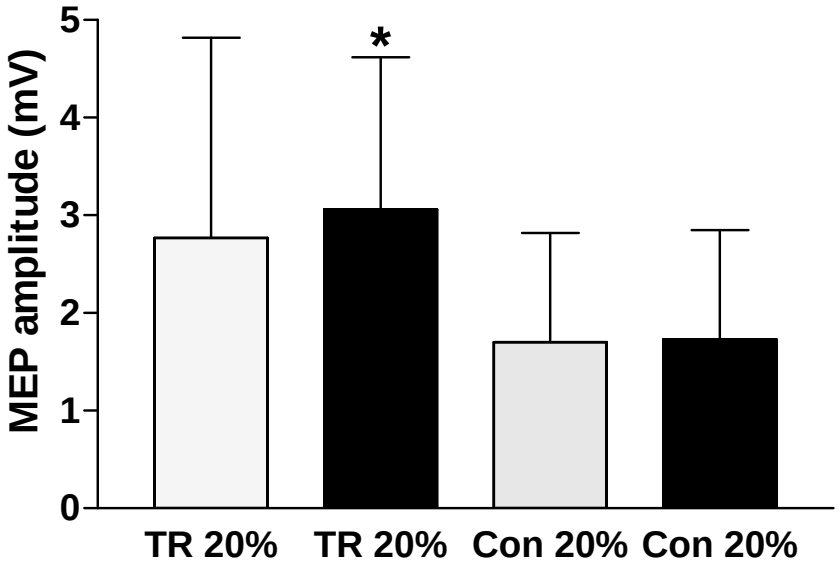

Figure 6.8. Mean (±SD) data for left BB MEPs evoked by single pulse TMS at 20% above AMT for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a significant increase ($p = 0.05$) in MEP amplitude following the strength training intervention for the trained group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups ($p < 0.05$).

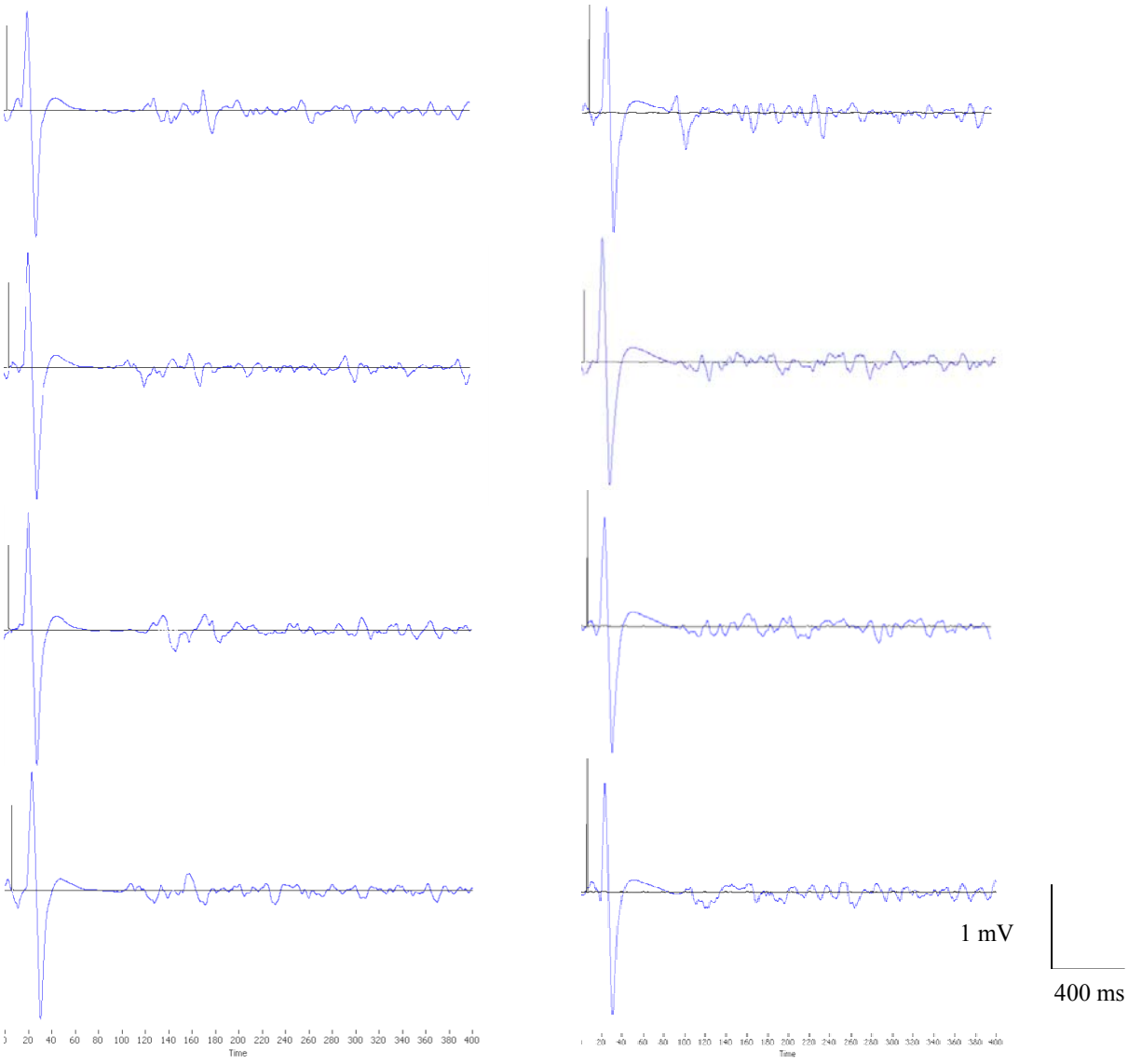

Figure 6.9. Raw MEPS from left BB from one participant. The traces on the left are pre-training MEPs obtained at 20% above AMT and the traces on the right are post-training.

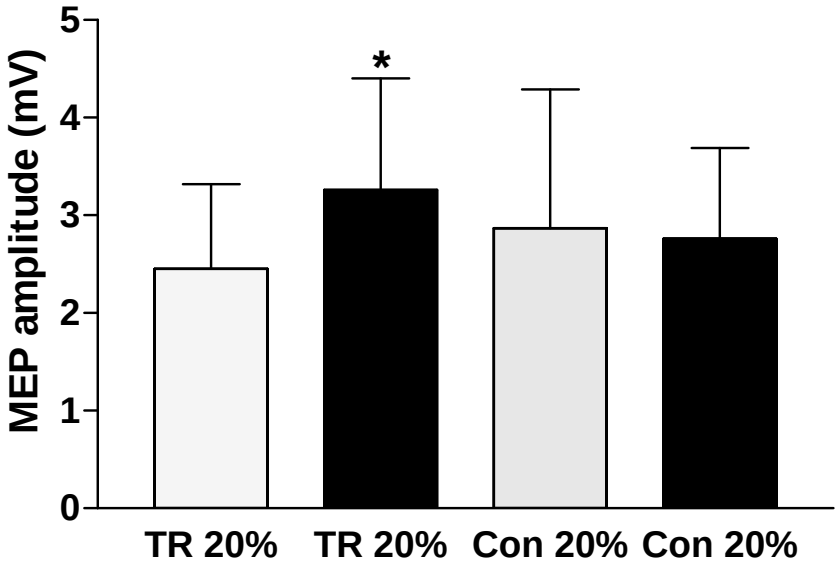

Figure 6.10. Mean (±SD) data for right BB MEPs evoked by single pulse TMS at 20% above AMT for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a significant increase (p = 0.05) in MEP amplitude following the strength training intervention for the trained group. There were no significant differences detected for the control group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups (p <0.05).

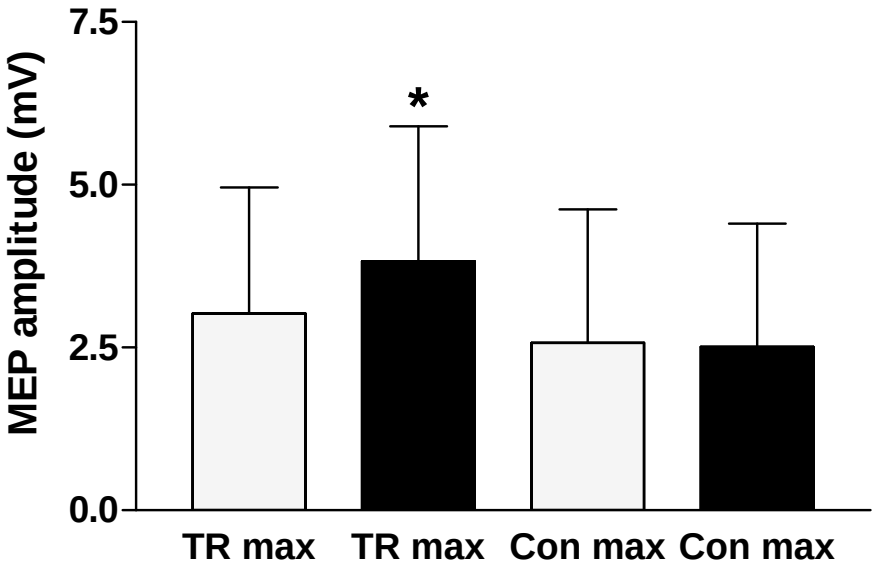

Figure 6.11. Mean (±SD) data for left BB MEPs evoked by single pulse TMS at at MEP_{max} for the strength training (TR) and control (CON) groups before (light grey bars) and after (black bars) strength training. There was a significant increase ($p = 0.01$) in MEP amplitude following the strength training intervention for the trained group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups ($p < 0.05$).

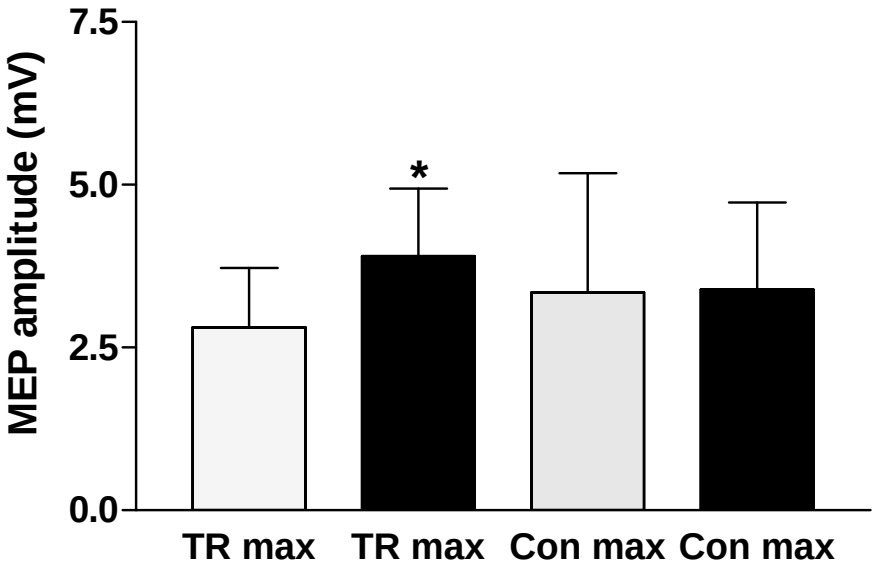

Figure 6.12. Mean (±SD) data for right BB MEPs evoked by single pulse TMS at at MEP_{max} for the strength training (TR) and control (CON) groups before (light bars) and after (black bars) strength training. There was a significant increase (p = 0.02) in MEP amplitude following the strength training intervention for the trained group. There were no significant differences detected for the control group. Asterisk denotes significant increase in MEP amplitude from before to after training between groups ($p < 0.05$).

6.3.5 Corticospinal inhibition

Table 6.2 (page 175) displays all SP data of the two groups' pre and post training intervention. No significant differences in SP duration were observed between groups at 20% above AMT at pre-training (right M1: p = 0.86; left M1: p = 0.27, table 6.2). Following the training intervention, there was no significant differences in mean SP duration in the trained group (right M1: p = 0.72, left M1: p = 0.50) or the control group (right M1: p = 0.73; left M1: p = 0.50) at 20% above AMT. No significant differences were seen in the mean duration of the SP at MEP_{max} between groups at baseline (right M1: p = 0.92; left M1: p = 0.42). Following training, there was no significant difference in mean SP duration at MEP_{max} in the trained group (right M1: p = 0.71; left M1: p = 0.35) or the control group (right M1: p = 0.76; left M1: p = 0.35).

6.4 Discussion

This study extends on existing evidence supporting contralateral strength and corticomotor changes following a period of unilateral strength training. The major findings from the present study are that four-weeks of heavy load dynamic strength training for the right elbow flexors, in participants with no strength training experience, increased dynamic 1-RM strength for both the right trained (28% increase) and left untrained (19.2% increase) upper limbs. In the absence of muscle hypertrophy, this chapter has demonstrated an increase in corticospinal excitability (MEPs) projecting to the spinal motoneuron pool of the untrained left arm, with no significant differences observed in latency duration or corticospinal inhibition (SP).

The contralateral transfer of strength observed in this study is greater than recent investigations that have used a similar between subjects design, reporting a contralateral

strength transfer of 7% (Lee et al., 2009b) and 9% (Munn et al., 2005b). The large difference in the cross-transfer of strength between this study and that of Munn et al. (2005b) may be due, in part, to using the preferential direction of transfer, being right to left in right handed participants (Farthing et al., 2005; Farthing, 2009), as well as the methodology of the strength training employed. For example, Munn et al. (2005b) used an identical protocol in terms of volume and intensity of training; however, they employed a faster repetition scheme of 1 s concentric and 1 s eccentric whereas the present study employed a repetition cycle of 3 s concentric and 4 s eccentric. The rationale for using a slow controlled repetition timing for training was chosen following recent studies demonstrating increased corticospinal excitability during motor tasks when the level of precision required to complete the task has been altered by slowing and purposefully controlling the movement (Pearce and Kidgell, 2010; Pearce and Kidgell, 2009). Farthing and Chilibeck (2003) investigated cross-transfer of strength in the untrained limb following isokinetic strength training, also focusing on the eccentric component of the movement. However, these investigators demonstrated increased cross-transfer following high velocity training, which contradicts the findings in this study. Methodological differences may also explain the contrary findings as the present study trained participants using free weights whereas Farthing and Chilibeck (2003) employed an isokinetic training regime. In light of these differences, both the present study and Farthing and Chilibeck (2003) still employed muscle actions that were high intensity and this may be an important factor in the cross-transfer of strength. The change in contralateral strength observed in the preset study is larger compared to the recent study by Lee et al (2009b). The differences may largely be related to the strength training paradigm employed. Lee et al. (2009b) employed isometric contractions of the extensor carpi radialis brevis, whilst the present study adopted a

dynamic strength training protocol, whereby the timing of each repetition was controlled and as such may have resulted in the observed differences. Furthermore, dynamic strength training that involves both concentric and eccentric contractions has been shown to increase strength when compared to isometric strength training alone and this may also account for the observed differences in contralateral strength (Higbie et al., 1996; Brown et al., 1988).

The observation of increased MEP amplitude projecting to the spinal motoneuron pool of the untrained left arm suggests increased excitability of neurons in the M1 as well as by the excitability of the spinal motoneuron pool (Rothwell et al., 1991); supporting the findings and the suggestion by Hortobágyi et al. (2003) that a general increase in motor cortical excitability occurs following strong voluntary contractions. It has been suggested that excitatory motor cortical activity during strong unilateral contractions diffuse from the active M1 to the "inactive" M1 through interhemispheric pathways (Zhou, 2000; Farthing, 2009). Neuro-imaging and TMS studies have shown mechanisms whereby unilateral motor activity is associated with bilateral activation of both the left and right M1 (Cramer et al., 1999; Muellbacher et al., 2000; Carson, 2005) via increased excitability of existing intrinsic horizontal pathways within the M1. Corticospinal cells within layer II and III of the M1 form a broad, intrinsic horizontal projection system (Mountcastle, 1997). Rioult-Pedotti et al. (1998) provided the first line of evidence that motor activity leads to an increase in strength of horizontal cortical connections within the M1 as demonstrated by an increase in amplitude of field potentials via micro stimulation of corticospinal cells. Given that high force unilateral voluntary contractions have been shown to affect the efficacy of neural circuits controlling the untrained limb (Hortobágyi et al., 2003; Carson et al., 2004; Sohn et al., 2003) the results illustrate that the strength training program employed in the present study increased the neural excitability of the contralateral homologous muscle due to

chronic changes in synaptic strength and connectivity within specific neural circuits between hemispheres that contribute to the ability to generate force. The adaptations observed within the right M1 may have contributed in some capacity to the contralateral transfer of strength to the left arm, as the results demonstrated a moderate to strong correlation between the change in MEP amplitude and change in strength of the untrained arm.

In this study, repeated strong and controlled voluntary contractions may have also induced a motor learning (improved motor coordination of the prescribed exercise) effect contributing to increased corticospinal excitability at stimulus intensities at and above AMT. A general consensus exists in the literature that cross-education of strength might be similar to cross-education of motor skill acquisition (i.e. learning and retention of specialised movement tasks) (Carroll et al., 2002; Farthing, 2009; Lee and Carroll, 2007; Zhou, 2000). Carroll et al. (2002) has put forward that strength training is a form of motor learning, in the sense that participants are required to learn to produce muscle recruitment patterns associated with optimal performance of the task. Other authors concur that short-term increases in strength stem from improved coordination between opposing muscles (Olafsdottir et al., 2008; Enoka, 1997). Moreover, Farthing et al. (2007) have affirmed that skill learning does not induce muscle hypertrophy but still contributes to strength gains. As first proposed by Parlow and Kinsbourne (1989), the cross-activation model suggests that motor task or skill memory engrams are stored in both hemispheres following unilateral skill acquisition. It has also been suggested that adaptations associated with skill learning involve changes in synapse number and/or synaptic strength (Muellbacher et al., 2001; Jones, 1999a; Jones et al., 1999b). Whilst it is not possible from the present study to determine the precise underlying mechanism responsible for the changes in corticospinal

excitability, the novel aspect of the strength training program employed (i.e. high intensity strength training, with controlled timing of each repetition) in untrained participants, lead to some form of neural adaptation, as a result of both strength and skill training influences.

Limitations in the present study include quantifying cross sectional area of the muscle by objective means, i.e. ultrasonography, quantification of muscle activity in the contralateral limb during the training period and the technique of magnetic stimulation. It has been suggested that contralateral increases in strength may arise as a result of contraction of muscles in the untrained limb during unilateral training (Carolan and Cafarelli, 1992; Hortobágyi et al., 1997). As this study did not collect EMG datum in the untrained limb whilst participants undertook strength training, it is possible that participants were coactivating limb musculature, despite instructing the participants to keep their arm behind their back. However, more recent studies (Fimland et al., 2009b; Evetovich et al., 2001; Lee et al., 2009b) have published similar findings of strength increases of the contralateral limb without within-training EMG data. Furthermore, the observation of no change in maximum rmsEMG pre and post training is consistent with the findings of Evetovich et al. (2001) and Lee et al. (2009b). A second limitation of this study was that only single-pulse TMS and contralateral MEP responses were recorded, limiting the conclusions that can be drawn from the data, particularly in relation to the questions of adaptation occurring at the cortical or spinal level and the influence of ipsilateral projection changes. However, previous research has shown that the mechanisms underpinning increases in cross-education of strength are unlikely to occur at subcortical and spinal levels. For example, Hortobágyi and colleagues (2003) following acute high intensity contractions (80 – 100% of MVC) showed increases in MEPs, but not in cervicomedullary MEPs (CMEPs) which remained unaffected, or H-reflex which showed depression.

Similarly, Lagerquist et al. (2006) demonstrated a 17.6% increase in strength of the contralateral untrained limb in the absence of modifications in spinal cord excitability.

Alterations in ipsilateral inhibition have been previously documented in unimanual motor tasks and alter depending on the involvement of distal or proximal muscles (Harris-Love et al., 2007), movement complexity (Avanzino et al., 2008) and motor learning acquisition (Perez et al., 2007). Recently, Perez and Cohen (2008) demonstrated unilateral activity-dependant changes in M1 ipsilateral projection using paired and triple-pulse TMS technique which can access intracortical inhibitory circuits that use the neurotransmitter GABA. The single pulse TMS method can also be used to assess $GABA_B$ receptors (Chen, 2004; Siebner et al., 1998) reflected as the SP duration on the EMG. The present investigation, found no change in the duration of the SP in either hemisphere at 20% above AMT and at MEP_{max}, suggesting that there were no changes in cortical inhibition. However, this may not mean that the level of inhibition has not altered, but rather a failure of the single-pulse technique to show changes in intracortical inhibition. It has been suggested (Foltys et al., 2003; Hortobágyi, 2005) that an association exists between the intensity of M1 activation and the amount of inhibition in the contralateral M1. With the present study employing high intensity training of a repetitive nature, the left M1 may have influenced and altered the right M1 excitability via a reduction in the level of inhibition. Although SP duration did not alter, changes were observed in corticospinal excitability in the M1 projecting to the untrained arm above AMT which may be due to decreases in inhibition reflecting greater excitation (i.e. MEP amplitude increases) in the contralteral corticopspinal pathway (Hortobágyi, 2005; Foltys et al., 2003). It is intended that further research will investigate ipsilateral projection in elbow flexors following a period of high-intensity strength training using a between groups design.

6.5 Conclusion

In conclusion, the results of the present study demonstrate that high intensity unilateral strength training increases strength, in the absence of muscle hypertrophy, and alters the functional properties of the corticospinal pathway projecting to the untrained arm in healthy humans. The present data suggests that adaptation of the corticospinal pathway is reflective of the specific nature of the strength training employed, but is also likely to be due to motor learning adaptations. Although this study has demonstrated increased corticospinal excitability, the results do not discount that additional adaptations may have also occurred within neural structures not confined to the M1 and corticospinal pathway. Further research should investigate ipsilateral corticospinal excitability and inhibition, using a similar training intervention.

CHAPTER SEVEN

Acute Upper-Body Vibration Does Not Alter the Functional Properties of the Corticospinal Pathway in Healthy Humans

7.1 Introduction

The application of low-frequency (i.e. 10-50 Hz) vibration stimuli to the body through WBV platforms or parts of the body (direct vibration) via high-frequency (i.e. > 65 Hz) vibration has been shown to enhance muscular performance in response to sensory receptor stimulation (Cochrane and Stannard, 2005; Rosenkranz and Rothwell, 2003; Mileva et al., 2009). During vibration, the mechanical action of the oscillatory motion produces a rapid change in the length of the muscle-tendon complex, which stimulates the primary endings of Ia muscle afferents, and to a lesser extent the Golgi afferent (Ib), leading to excitation of α–motoneurons of the homonymous motor units (Martin and Park, 1997a; Roll et al., 1989). Whilst segmental structures modulate the initial stages within the motor feedback loop in response to vibration, central projections from supraspinal structures are also important in generating the efferent neural response to afferent input (Lewis et al., 2001; Rothwell and Rosenkranz, 2005; Chez and Krakauer, 2000). For example, increased corticospinal excitability has been demonstrated during high-frequency direct vibration (Munte et al., 1996; Kossev et al., 1999; Rosenkranz and Rothwell, 2003) and more recently during low-frequency WBV (Mileva et al., 2009). Accordingly, modifications in Ia muscle afferent activity and corticospinal responses may be important neuromuscular mechanisms that contribute to the observed effects of acute low-frequency WBV exercise.

Increases in neural drive, motor unit synchronisation and recruitment have been reported to account for the increases in muscle force output following acute exposure to WBV exercise (Nordlund and Thorstensson, 2007; Rittweger, 2010). Acute low-frequency WBV has been shown to induce transient increases in the electrical activity of the muscle being vibrated during submaximal isotonic and isometric contractions (25-45

Hz) (Roelants et al., 2006; Hazell et al., 2007) and during maximal power based movements (Mileva et al., 2006). However, the acute use of low-frequency WBV as a method to potentiate neuromuscular excitability remains unclear (Nordlund and Thorstensson, 2007) with limited study focused on the corticospinal pathway.

TMS can be used to assess human corticospinal excitability during voluntary contractions, making it possible to measure the corticospinal control to a muscle (Hallett, 2007). If the intensity of the TMS stimulus is appropriate, it will depolarize presynaptic neurons that project onto corticospinal neurons to activate the muscle of interest. The subsequent transient muscle response can be recorded by sEMG and quantified as the MEP (Hallett, 2007). TMS has been used to study the effects of high-frequency direct vibration and more recently during WBV (Kossev et al., 1999; Mileva et al., 2009; Munte et al., 1996; Rosenkranz and Rothwell, 2003) on corticospinal excitability.

Single pulse TMS measures corticospinal output from the M1 to spinal motoneurons, and as such evokes an excitatory and inhibitory response within the corticospinal pathway (Werhahn et al., 2007). The SP, which is a pause in ongoing EMG activity following the TMS evoked MEP, is an example of an inhibitory phenomena within the corticospinal pathway (Rothwell et al., 1991). The duration of the SP can last anywhere between 50 ms to 300 ms following stimulation, and provides a measure of the strength of inhibition in cortical and spinal circuits (Terao and Ugawa, 2002). The mechanism of the SP is complex and not well defined, although, some spinal and cortical mechanisms have been suggested. The initial component of the SP (i.e. up to 50 ms) is produced by spinal mechanisms, such as Renshaw recurrent inhibition and after-hyperpolarisation (Inghilleri et al., 1993). The latter component, presumably arises as a result from the activation of inhibitory cortical neurons projecting onto corticospinal cells within M1 (Bertasi et al.,

2000). With single pulse TMS, the duration of the SP is thought to reflect GABA mediated inhibition modulated by inhibitory neurons that use $GABA_B$ as their neurotransmitter (Werhahn et al., 2007). Recently, Binder et al. (2009) reported an increase in the duration of the SP in an antagonist muscle flexor carpi radialis during high-frequency direct vibration and a reduction in the agonist extensor carpi radialis. Further, intracortical inhibition (SICI) tested by TMS was also reduced in the target muscle during vibration of the FDI muscle, demonstrating that corticospinal output was modulated by vibration (Rosenkranz and Rothwell, 2003). However, there is currently no data that has measured the effect of low-frequency WBV on the duration of the SP.

Although several studies have demonstrated modifications in corticospinal excitability *during* high-frequency vibration (Kossev et al., 1999; Munte et al., 1996), there is limited data on the effects of low-frequency WBV on corticospinal excitability. In the only study to date, Mileva et al. (2009) assessed the acute effect of WBV on corticospinal responses evoked by single and paired pulse TMS of a lower limb muscle and demonstrated facilitated MEPs *during* vibration. Therefore, the aim of this study was to determine the acute corticospinal responses (neural conduction time, MEP amplitude and SP duration) to a single bout of WBV exercise applied to the upper body utilising a vibration protocol practiced by athletes (Roelants et al., 2006). Given that previous evidence suggests, increased corticospinal excitability and increased cortical inhibition *during* low-frequency WBV (Mileva et al., 2009), it was hypothesized that acute exposure of the upper limbs to low-frequency WBV would increase corticospinal excitability and reduce the duration of the SP. The hypothesis of a shorter SP duration was based upon the inhibitory circuitry that mediates SICI being different from the neurons that are involved in the SP.

7.2 Methods

7.2.1 Participants

Ten healthy male participants (mean age 28.4 ± 5.9 years) participated in the study and had no known history of peripheral or neurological impairment. Written informed consent was obtained from the participants and ethical approval was granted from the university human research ethics committee.

7.2.2 Organisation of the study

Participants performed two interventions, namely, a static hold in a push-up position with WBV (WBV +) and without WBV (WBV-), in a randomised balanced order with 48 h separating each intervention. Participants were familiarised with the experimental procedures and equipment prior to their first testing session, undertook testing at the same time of day and were instructed to refrain from partaking in any vigorous physical activity 24 h prior to the testing interventions. Prior to each intervention, and 30 s post intervention, each participant completed a neurophysiological test that involved TMS over the left M1 projecting to the spinal motoneuron pool innervating the right BB.

7.2.3 Whole-body vibration condition (WBV+)

Participants were exposed to vertical sinusoidal WBV. In accordance with previous research, the vibration frequency was set at 35 Hz with a peak-to-peak amplitude of 4 mm (Roelants et al., 2006). Participants were required to position themselves on top of a commercial WBV platform (vibroGym, Australia) in a conventional static push-up

position (Figure 7.1a) with their hands positioned according to their bi-acromial width (Gross et al., 1993; Fees et al., 1998) with the elbow flexed 10^0. To negate the possibility of discomfort to the volar aspect of the hands, a thin foam matt (10 mm) was placed over the machine. Whilst in this position, participants were exposed to three sets of 60 s bouts of vertical sinusoidal vibration, separated by a 60 s recovery period. Prior to and immediately after the vibration bout, TMS was applied to the contralateral M1 projecting to the spinal motoneuron pool innervating the right BB muscle at AMT and 20% above AMT.

7.2.4 Without whole-body vibration condition (WBV-)

During the WBV-, a custom made wooden box, with a 2 cm clearance was placed over the WBV platform (with a 2 cm block for the participants to place their feet on) to ensure that the vibration machine could be set to the exact same parameters as for the vibration condition (without the vibration stimulus reaching the participants limbs), with the participants in the same static push-up position (Figure 7.1b). TMS was applied prior to and following the WBV- condition.

Figure 7.1a. Participant set up illustrating push-up position during the WBV+ trial.

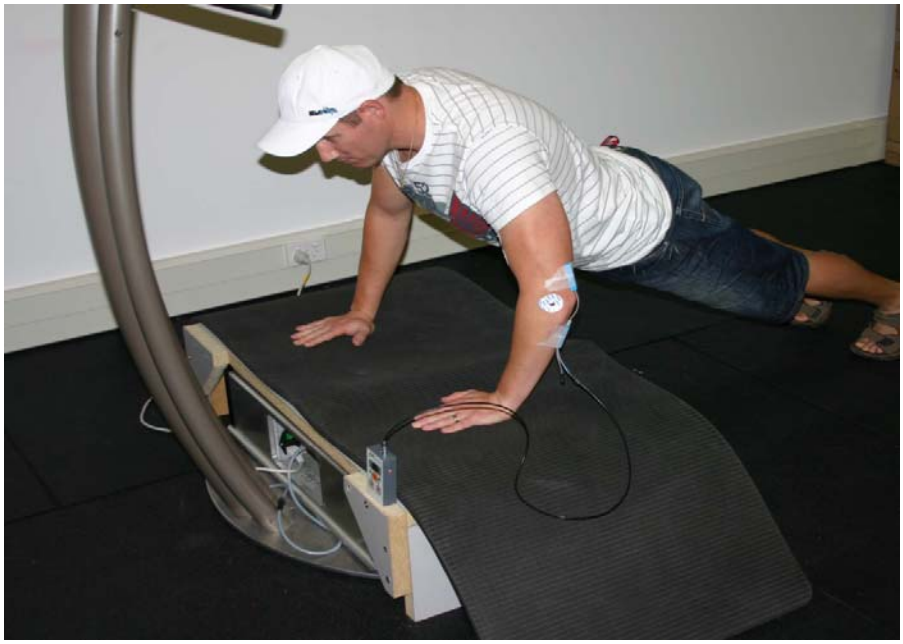

Figure 7.1b. Participant set up illustrating push-up position during the WBV- trial. Note custom wooden box overlaying the WBV platform as described in section 7.2.4.

7.2.5 Electromyography and transcranial magnetic stimulation

Surface EMG activity and TMS evoked MEPs were recorded from the right BB muscle using bipolar Ag-AgCl electrodes**.** Refer to sections 4.2.3 (page 106) and 5.2.5 (page 136) for a more detailed description of the methods employed.

7.2.6 Data and statistical analyses

All MEPs collected (n = 10, two sets of five 500 ms recordings, were displayed and averaged online for visual inspection as well as stored off-line for further analysis (refer to sections 4.2.3 [page 104] and 5.2.5 [page 134] for a more detailed description of the methods employed). Latency, MEP peak-to-peak amplitude and SP duration were analysed according to the methods described in sections 4.2.7 (page 109) and 5.2.6 (page 135). All data were first screened for normal distribution. In order to have sufficient data to test for questions of normality, all MEP parameters (AMT and 20% above AMT) were used to establish the distributional properties. Shapiro-Wilk tests demonstrated that MEP amplitude at AMT and 20% above AMT were not normally distributed, (SW = 0.84 p = 0.04; SW = 0.82, p = 0.02, respectively). As a result of this violation, Wilcoxon Signed Ranks analyses were performed to compare the effect between conditions (WBV + vs. WBV-) and time (pre vs. post) on corticospinal excitability and inhibition. Data is presented as means (± SD) and for all comparisons, a significance level of $p < 0.05$ was employed.

7.3 Results

7.3.1 Latency period

There were no significant differences in latency period at AMT between conditions at baseline (pre WBV- 13.2 ± 1.1 ms; pre WBV + 13.2 ± 0.9 ms, $p = 1.00$) or 20% above AMT (pre WBV- 13.1 ± 1.3 ms; pre WBV + 13.1 ± 0.8 ms, $p = 0.81$). Post testing between conditions also revealed no significant differences in latency duration at AMT (post WBV- 13.0 ± 1.0 ms; post WBV+ 13.2 ± 0.9 ms, $p = 0.78$) and at 20% above AMT (post WBV- 13.2 ± 0.9 ms; post WBV + 12.9 ± 0.9 ms, $p = 0.34$).

7.3.2 Corticospinal excitability

There were no significant differences for the percentage of stimulator output at AMT between conditions (WBV- 46.8 ± 3.5%; WBV + 47.0 ± 3.4%; $p = 0.34$). Similarly, there was no difference at 20% above AMT between conditions (WBV- 66.8 ± 3.3%; WBV + 67.0 ± 4.8%; $p = 0.37$). Figures 7.2 and 7.3 display the mean peak-to-peak amplitudes of MEPs evoked at AMT and at 20% above AMT for each condition (WBV- vs. WBV +) and time (pre vs. post). There were no significant differences in mean MEP amplitude at AMT between conditions at baseline (pre WBV- 0.71 ± 0.25 mV; pre WBV + 0.69 ± 0.23 mV; $p = 1.00$). Further, there were no significant differences between conditions at baseline for MEP amplitude at 20% above AMT (pre WBV- 2.1 ± 1.3 mV; pre WBV + 2.2 ± 1.4 mV; $p = 0.54$). Post testing analyses were performed between conditions (i.e. post WBV- vs. post WBV +), with no significant differences for MEP amplitude at AMT (post WBV- 0.70 ± 0.21 mV; post WBV + 0.69 ± 0.22 mV; $p = 0.65$) and 20% above AMT (post WBV- .2.2 ± 1.4 mV; post WBV + 2.0 ± .1.3 mV; $p = 0.88$) being observed.

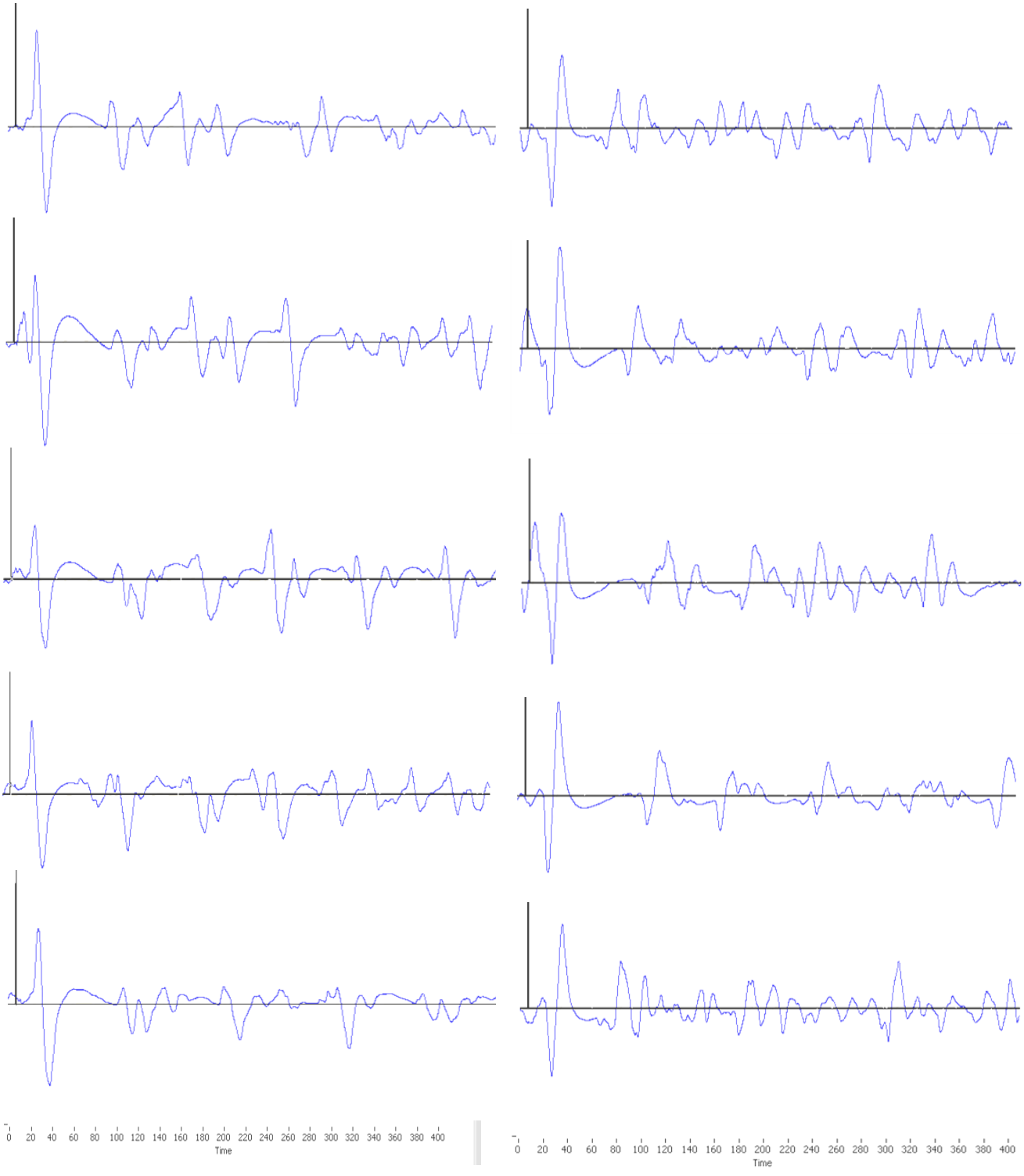

Figure 7.2. Example of five raw MEP sweeps (400 ms) from one participant's right BB during the TMS trials pre (traces on the left) and post (traces on the right) WBV+.

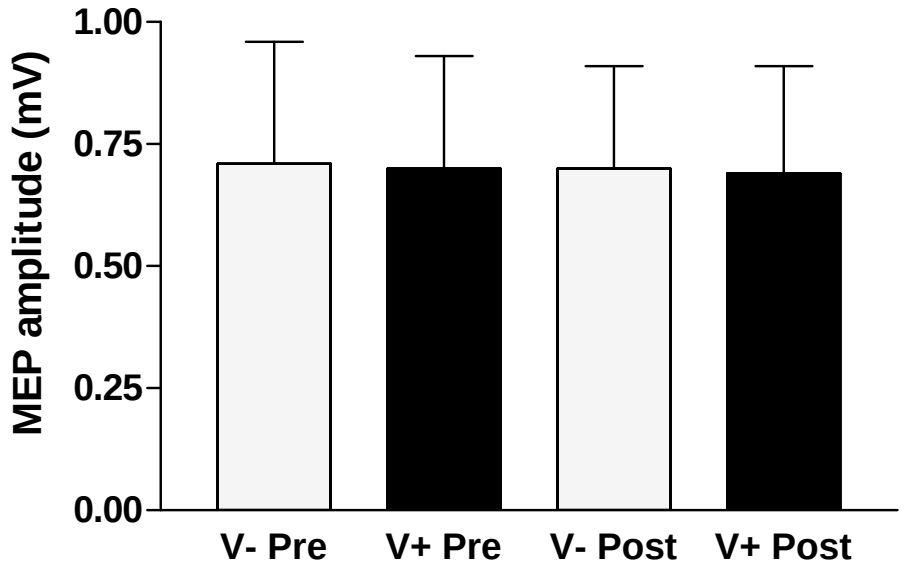

Figure 7.3. Mean (± SD) MEP amplitudes (*n* = 10) obtained from right BB prior to and immediately following no WBV (V-, light bars) and with WBV (V+, black bars) conditions at AMT. No significant differences in MEPs where observed between conditions pre and post WBV.

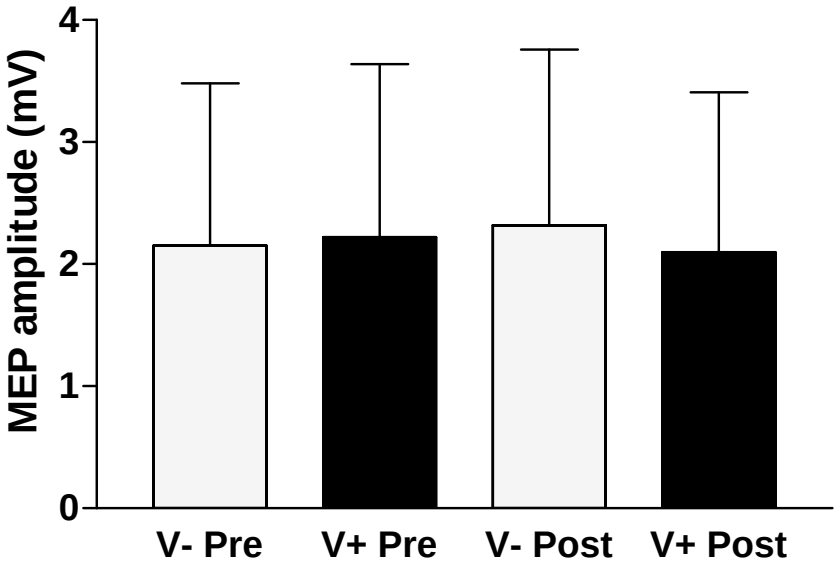

Figure 7.4. Mean (± SD) MEP amplitudes (n = 10) obtained from right BB prior to and immediately following no WBV (V-, light bars) and with WBV (V+, back bars) conditions at 20% above AMT. No significant differences in MEPs where observed between conditions pre and post WBV

7.3.3 Corticospinal inhibition

There were no significant differences in the duration of the SP at 20% above AMT between conditions at baseline (pre WBV- 116.8 ± 12.4 ms; pre WBV+ 118.3 ± 11.9 ms, $p = 0.14$, Figure 7.5). Similarly, post testing analyses did not show significant differences for SP duration between conditions (post WBV- 117 ± 12.8 ms; post WBV + 112.2 ± 12.5 ms, $p = 0.95$).

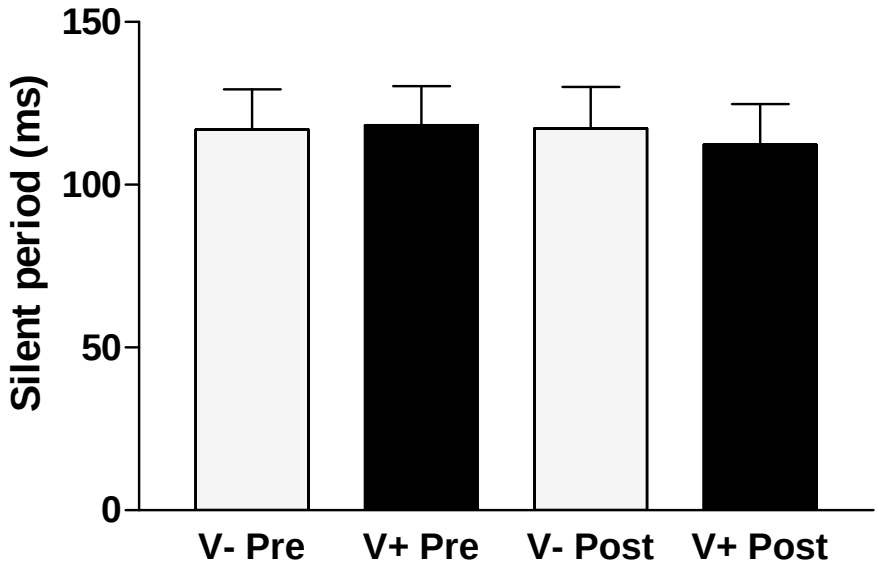

Figure 7.5. Mean (±SD) data showing right BB SP duration (n = 10) values obtained from single-pulse TMS at 20% above AMT prior to and immediately following no WBV (V-, light bars) and with WBV (V+, black bars) conditions. There were no significant differences in SP duration between any of the conditions.

7.4 Discussion

With good evidence to demonstrate that afferent stimulation (via direct high-frequency vibration) augments corticospinal excitability (Rosenkranz and Rothwell, 2003; Ridding et al., 2000; McDonnell and Ridding, 2006), it was hypothesised that low-frequency WBV exercise may also modulate corticospinal excitability through stimulation of the primary endings of muscle spindles, thus increasing muscle activation. This is the first study to examine the effects of low-frequency WBV applied to the upper body on corticospinal excitability. The main findings of the study are that when compared to a WBV- (sham) condition that required the same exercise to be performed with the WBV machine activated, but without the vibration stimulus reaching the participants, acute exposure to WBV did not modulate the excitability of the corticospinal tract or the spinal motoneuron pool innervating BB.

Although it has been reported that acute exposure to low-frequency WBV may alter neuromuscular excitability (Cardinale and Bosco, 2003), this study found no difference in the size of the descending corticospinal volley at AMT and at 20% above AMT immediately following WBV, demonstrating that motoneuronal activity remained unaffected. These findings are in agreement with previous studies that have examined the post-vibratory effect on corticospinal excitability using both high-frequency direct muscle and tendon vibration (Munte et al., 1996; Kossev et al., 1999; Steyvers et al., 2003) and low-frequency WBV (Mileva et al., 2009).

Potential mechanisms for no change in corticospinal excitability immediately following vibration may be due to changes in spontaneous discharge rate of Ia muscle afferents (Ribot-Ciscar et al., 1998). It has been observed that a decrease in spindle discharge rate occurs immediately following vibration and that this decrease is consistent

with the decreases seen in the H-reflex following vibration (Hultborn et al., 1987; Arcangel et al., 1971). Within the WBV literature, theoretical considerations have suggested that the mechanisms for improved muscle activation and performance are due to increased excitatory input from Ia muscle afferents, as a result of the tonic vibration reflex (TVR). The findings from this study and that of Mileva et al. (2009), demonstrate that the post-vibratory effect of low-frequency WBV are unlikely to be as a result of the TVR. Recent studies have tried to assess the effect of acute low-frequency WBV on motoneuron excitability (H-reflex) demonstrating acute exposure had no significant effect on the motoneuron pool (Hopkins et al., 2009; Armstrong et al., 2008; McBride et al., 2010). Since the present results have observed no difference in the size of the descending corticospinal volley immediately following WBV, the findings support the notion that acute WBV exercise does not preferentially affect the motoneuron pool.

In the present study, it was hypothesised that low-frequency WBV exposure would reduce the duration of the SP, reflecting reduced corticospinal inhibition, however, the duration of the SP remained unaffected following WBV at 20% above AMT and this was consistent to the finding reported by Mileva et al. (2009) who also demonstrated no significant difference in intracortical inhibition immediately following WBV. However *during* WBV they did observe a significant difference in intracortical inhibition. Changes in cortical inhibition during vibration exposure have been suggested to occur as a result of input from Ia muscle afferents, however, the present findings suggest that the discharge rate of Ia muscle afferents during the post-vibratory period remained unaffected and, as such, has had no effect on the strength of inhibitory elements within the corticospinal pathway projecting to the spinal motoneuron pool innervating the BB muscle.

A limitation to the present study was that corticospinal activity was not measured during exposure to low-frequency WBV, thus making it difficult to make direct comparisons to previous research (Mileva et al., 2009). However, the research question was to investigate corticospinal mechanisms to account for post-WBV performance changes reported previously (Hazell et al., 2007; Mileva et al., 2006; Roelants et al., 2006). The present study adds to the suggestion of muscle dampening (Luo et al., 2005) by demonstrating that a vertically based floor vibration stimulus of 35 Hz and 4 mm amplitude has no post-effect on corticospinal excitability and inhibition, showing the effects of WBV may be distinct to those of direct high-frequency vibration.

The results observed may also be explained from the exposure time and intensity of the low-frequency WBV protocol used. The exposure time used may have been too long, as previous studies have reported exposure times of greater than 30 s results in decreased muscle activation, most likely due to reduced Ia muscle afferent input (Eklund and Hagbarth, 1966; Hultborn et al., 1987). Nonetheless, all parameters utilised in this study fall within the ranges routinely used by other acute low-frequency WBV studies that have reported increased muscle activation (Delecluse et al., 2005; Mileva et al., 2009; Hazell et al., 2007; Issurin and Tenenbaum, 1999). The recovery period allocated between bouts was also consistent with recent findings using the same low-frequency WBV parameters (30-35 Hz, 4 mm amplitude) as the present study (Da Silva-Grigoletto et al., 2009). The number of sets prescribed is consistent with other studies, however, these variables were for the lower limb as currently there are no studies that have assessed WBV on the upper body (Nordlund and Thorstensson, 2007). Therefore, even though this study utilised a low-frequency WBV protocol that has previously elicited positive effects (in the lower limb), in this study it may not have been appropriate in eliciting corticospinal responses (in all

participants) in the primary agonist (BB) that was targeted during the vibration exposure. Furthermore, with only one other study examining the upper-body (whilst standing on the WBV machine) (Hazell et al., 2007), employing targeted individualised vibration parameters may be required in order to obtain a more consistent finding. However, the novel aspect of this study was that a sham WBV intervention was used to reduce any placebo effect of WBV, by having participants complete the same exercises under the exact same conditions (i.e. with the WBV turned on and set to the exact same parameters). Previous studies have simply had participants to perform the control interventions with the machine turned off, thus not replicating a true experimental control condition.

7.5 Conclusion

Using a control condition that required the exact same exercise task to be performed as the WBV task, and using a vibration intensity that has customarily been used in previous studies that have reported significant effects, does not preferentially affect corticospinal excitability and inhibition when compared to a control condition. Although previous studies using low-frequency WBV and direct high-frequency vibration have demonstrated facilitated corticospinal output *during* the vibration exposure, studies demonstrating significant differences in corticospinal excitability and inhibition immediately following vibration remain elusive. Based upon the present findings, acute WBV exercise applied to the upper body does not alter the functional properties of the corticospinal pathway projecting to the spinal motoneuron pool innervating the BB.

CHAPTER EIGHT

General Discussion

The primary objective of this thesis was to systematically investigate the short-term development of strength via corticospinal mechanisms following isometric, isotonic, cross-education and acute WBV exposure. This chapter will present an integrated discussion outlining how the major findings of each study described within this thesis contributes to the overarching research question regarding the corticospinal responses, measured by the correlated activity of pairs of active single motor units and the technique of TMS, following short-term strength training. Specifically, the discussion will focus on the effect that different types of strength training have on strength development, MEP amplitude and SP duration. The discussion will conclude with a section that recommends the future direction of research in this area.

Chapter 3 (study 1) showed in an intrinsic hand muscle that the strength of motor unit synchronisation and motor unit discharge rate was not influenced by short-term strength training. As chapter 3 was not able to identify the neural mechanism for the large increase in strength (54%), chapter 4 (study 2) used TMS to determine the corticospinal responses in the same muscle (FDI) using the same strength training protocol as chapter 3. Although the strength training program did not yield the same large increase in strength that was observed with study 1, with an improvement of 34%, study 2 did show a reduction in corticospinal inhibition (SP). Given the finding of reduced corticospinal inhibition in a hand muscle following isometric strength training, subsequent studies addressed the effect of heavy load controlled isotonic strength training on corticospinal excitability and inhibition. Specifically, chapters 5 (study 3) and 6 (study 4) observed a significant increase in strength and corticospinal excitability of the trained and untrained limb respectively. This reflects a functional change in the strength of corticospinal projection onto the spinal motoneuron pool innervating the trained and untrained musculature. However, unlike

chapter 4, there were no significant changes in corticospinal inhibition observed in chapters 5 and 6. Study 5 of this thesis (chapter 7) investigated the corticopsinal responses following acute WBV resistance exercise, reporting WBV exercise does not preferentially modulate corticospinal excitability and inhibition when compared to a sham (no vibration) condition.

The collective results of this thesis suggests that the corticospinal responses observed following strength training are dependent on the type of strength training performed and muscles trained. For example, strength training in a hand muscle was shown to affect the excitability of inhibitory circuits projecting to the spinal motoneuron pool innervating the FDI muscle; conversely, strength training of an upper limb muscle affects the excitability of interneurons projecting onto corticospinal cells that descend onto spinal motoneurons controlling the BB muscle. Acute exposure to WBV did not preferentially modulate corticospinal excitability or inhibition. Based upon these findings, the corticospinal responses are specific to the type of strength training performed and the muscles subjected to training as two different populations of neurons confined within the corticospinal pathway have been affected by different strength training methods.

Although chapters 3 and 4 used the exact same strength training program and muscle, strength training did not influence the corticospinal control of single motor units. An important mechanism that contributes to motor unit synchronisation is the corticospinal pathway (Farmer et al., 1997). However, chapter 3 showed that motor unit synchronisation was not influenced by short-term strength training. This finding was unexpected, as it was hypothesised that motor unit synchronisation and discharge rate would increase and this would account for the observed change in strength. Several studies have observed increased motor unit discharge rates following a period of isometric strength training (Van

Cutsem et al., 1998; Kamen and Knight, 2004), however only one previous study has proposed increased synchronisation of motor units to account for increases in strength following strength training (Milner-Brown et al., 1975). The results from chapter 3 are consistent with the observations from a simulation study that reported motor unit synchronisation does not influence the maximal force producing capacity of a muscle (Yao et al., 2000). As such, the data presented in chapter 3 supports the notion that the central mechanisms that influence motor unit synchronisation (i.e. common inputs from the branching of last order corticospinal neurons) are not related to the activation pattern of the FDI that influence its force generating capacity. Although it was hypothesised in chapter 3 that isometric strength training would increase motor unit synchronisation and coherence, the findings from chapter 4 support the notion that at least in the FDI muscle, changes in strength are influenced by reduced corticospinal inhibition and not changes in motor unit synchronisation and coherence.

Although, this thesis found a decrease in corticospinal inhibition in a hand muscle and an increase in corticospinal excitability in a gross muscle, the corticospinal responses appear to be as a result of the specific requirements of the strength training itself. In chapters 3, 4, 5 and 6, the strength training method employed a training protocol that was designed to challenge the participants. Specifically, in chapters 3 and 4, participants' were instructed to abduct their index finger against a maximal load for 3 s, whereas in chapters 5 and 6, participants were required to lift a heavy load (80% of 1RM) and adhere to a particular timing to perform each repetition (4 s elbow extension/ 3 s elbow flexion) was manipulated in an attempt to make a relatively simply movement more challenging. The specific repetition protocols were prescribed to stimulate the neuromuscular system and alter corticospinal output.

The changes in corticospinal inhibition and excitation found in this thesis are similar to the changes often observed in the skill training literature. The change in both corticospinal excitability and inhibition within this thesis, reflects a functional change in the strength of existing corticospinal cells that project onto the spinal motoneuron pool innervating the trained muscles. The adjustment in the excitability of the corticospinal pathway observed is most likely as a result of a change in the level of GABAergic mediated inhibition. Chapter 4 hypothesised that strength training would increase MEP amplitude, reduce corticospinal inhibition, and increase strength. The results of chapter 4, despite not showing a change in MEP amplitude, support an increase in the excitability of the inhibitory circuits, thereby reducing the SP duration, and improving the net excitatory drive onto the spinal motoneuron pool innervating the FDI. This study demonstrated that the strength training program in the hand had affected a specific population of GABAergic cortical neurons. $GABA_B$ are the most widely distributed GABAergic cortical neurons in the M1 (Watanabe et al., 2002). Activation of $GABA_B$ results in the generation of an inhibitory post synaptic potential which hyperpolarises the postsynaptic neuron and makes it more difficult for the initial axon segment to reach the firing threshold required for the generation of an action potential in corticospinal cells (Krnjević and Schwartz, 1967). This is an important physiological process, as it's thought that this type of inhibition allows for fine tuning of a movement, thus improving the selective activation of the appropriate muscle for a particular movement (Ridding et al., 1995b; Zoghi et al., 2003). Therefore, the changes in inhibition reported have "released" corticospinal cells from inhibition and enhanced the net drive to the FDI, resulting in increased activation of the muscle. Given that chapter 3 was unable to determine what mechanisms were responsible for the large increase in strength following short-term strength training, it appears that changes in

corticospinal inhibition may in part explain the increase in strength observed in the FDI muscle.

Given the finding from chapter 4, it was hypothesised in chapters 5 and 6 that isotonic strength training of an upper limb muscle would increase corticospinal excitability, reduce corticospinal inhibition and increase muscle strength. The finding of no significant differences in SP duration was also unexpected, particularly for chapters 5 and 6, because of the importance of GABA-mediated inhibition in the acquisition of motor skills. However, in light of this, there are no current strength training studies that have investigated the role of corticospinal inhibition in strength development. Although the strength training employed in chapters 5 and 6 focused on controlling the repetition time in an attempt to make the biceps curl exercise more challenging, this had a greater effect on the excitability of interneurons that project onto corticospinal cells, most likely modulated by peripheral feedback mechanism. In accordance with previous research (Hortobágyi et al., 1996), the slow and controlled nature of each repetition performed throughout the strength training intervention may have increased peripheral feedback and provided a mechanism for increased corticospinal excitability, as described in chapters 5 and 6. Therefore, providing the participants with a repetition timing cycle for each phase and using a free weight has added some degree of difficulty to a relatively simple movement and possibly made it more challenging for the participant's to control the movement. Therefore, despite chapters 4, 5 and 6 using a repetition cycle that was designed to make the exercises more challenging, the corticospinal pathway was differentially modulated, and thus the corticospinal responses to strength training appear to be influenced by the type of muscle subjected to training.

The increased excitability of the corticospinal pathway observed in chapters 5 and 6 were due to potential mechanisms such as; changes in cortical synapse number, synaptic strength, unmasking of silent synapses and shifting the strength in functional connectivity between hemispheres (Carroll et al., 2001a; Nielsen and Cohen, 2007). Adjustments in synapse number are likely to reflect enhanced postsynaptic potentials within the contralateral M1 and corticospinal pathway as demonstrated by enhanced MEPs at and above AMT. Modifications in functional connectivity have also been demonstrated through neural mechanisms associated with cross-education strength training (chapter 6). The changes in corticospinal excitability of the contralateral untrained M1 projecting to the spinal motoneuron pool innervating the left BB, reported in chapter 6, demonstrated increased excitability of existing intrinsic horizontal corticospinal connections confined to layer II and III of the M1. The moderate, yet significant correlations detected between the change in corticospinal excitability confined to both the left and right M1 and the increase in strength of the left BB reported in chapter 6 provides evidence for a change in strength of functional connectivity between the hemispheres, supporting the motor irridation hypothesis (Todor and Lazarus, 1986). The repetitive bilateral M1 activation throughout the heavy load strength training intervention has resulted in an increase in the size of the TMS evoked MEPs from both M1, demonstrating a functional change in the strength of corticospinal connectivity between hemispheres (Hortobágy et al., 2003; Zijdewind et al., 2006; Perez et al., 2008). This finding supports the notion that strong unilateral contractions, which results in bilateral M1 activation, has increased corticospinal excitability of the right M1 through adaptive changes in interhemispheric pathways, most likely modulated by transcollasal pathways (Wassermann et al., 1998; Foltys et al., 2003; Hortobágyi, 2005; Carroll et al., 2006; Farthing, 2009).

Since a significant part of the corticospinal pathway is indirectly attached to the spinal motoneuron pool via spinal interneuronal networks, the findings from this thesis cannot exclude the contribution of functional changes that may have occurred at a segmental level (as M-waves were only conducted in chapter 4), especially when the descending volleys evoked by TMS are influenced by changes in transmission in spinal networks. The results of this thesis would support, in part, some form of adaptation within spinal cord circuits, given the moderate correlations reported for the changes in corticospinal excitability and changes in strength. This is particularly evident for the findings from chapter 3. Although there were no changes in motor unit behaviour following training (i.e. synchronisation, recruitment threshold or discharge rate), there may have been modifications in reflex physiology. This would be consistent with recent isometric strength training studies that have demonstrated increased synaptic efficacy of Ia afferents, increased corticospinal drive (V-wave) and increased number of excitatory synapses onto the spinal motoneuron pool following training (Del Balso and Cafarelli, 2007; Fimland et al., 2009a; Fimland et al., 2009b).

Since chapters 4, 5 and 6 have demonstrated modulation of the corticospinal pathway following different types of strength training, chapter 7 specifically investigated whether WBV exercise, which is a relatively new method of sports conditioning (Rittweger, 2010) would also preferentially modulate the corticospinal pathway. The impetus for this chapter was based upon the observations reported in the literature (Bosco et al., 1998; Cochrane & Stannard, 2005), that acute exposure to WBV increases muscle function (i.e. increased power output) as a result of increased neuromuscular excitability. Further, several studies have investigated the effect of direct high-frequency vibration on motor unit synchronisation and corticospinal excitability and inhibition (Munte et al., 1996;

Kossev et al., 1999; Shinohara, 2005; Rosenkranz et al., 2007). As reported in chapter 7, WBV did not influence corticospinal excitability or inhibition when compared to a sham condition. Although these studies have used a sham condition when studying the effects of WBV, several studies have simply had participants to stand on the WBV machine whilst the machine is turned off (Cochrane et al., 2004; Bosco et al., 1999; Cochrane & Stannard, 2005). However, in this thesis, the sham condition required the participants to complete the exact same protocol as for the WBV condition, with the only difference being that the vibration stimulus did not reach the participants. It was thought that this randomized cross-over design would reduce any placebo effect. A significant limitation to chapter 7 was that MEPs were not obtained during vibration, which makes it difficult to determine the physiological effects of WBV on corticospinal output and to make any comparisons to the recent study performed by Mileva et al. (2009) on lower limb muscles. Furthermore, recent data suggests that the effects of WBV on the neuromuscular system are more favourable when individual frequencies and amplitudes are applied (Di Giminiani et al., 2009). Although chapter 7 used a protocol that has elicited positive neuromuscular responses for the lower limb (Roelants et al., 2006), the results of chapter 7 lend support to the suggestion that the prescription of individual frequencies is important and as such future WBV studies should prescribe individual frequencies and amplitudes and also measure the corticospinal responses during and after WBV.

8.1 Conclusion

The objective of this thesis was to undertake a systematic study of the neural adaptations to various methods of strength training with an emphasis on the corticospinal

pathway. This thesis has shown changes in corticospinal output that are reflective of the type of strength training performed and muscles subjected to training.

Despite this thesis having demonstrated increases in corticospinal excitability and decreases in corticospinal inhibition, it seems unlikely that these changes are primarily responsible for the rapid development of strength. Given that only single pulse TMS was used throughout this thesis, changes in presynaptic inhibition and motoneuron excitability were not investigated and cannot be excluded.

From the results of this thesis, several lines of future research can be identified to further the studies presented. Future studies should examine motor unit synchronisation and MEPs following strength training of the FDI simultaneously. This would help to provide a mechanism of adaptation following isometric strength training of the FDI that was not obtained in the findings in chapter 3. Future studies may also look at comparing the effects of similar strength training protocols (i.e. maximal isometric protocols) on the synchrony and coherence between proximal and distal muscles. An extension of experiments from Chapter 4 would be to quantify the effect of strength training on intracortical inhibition as this would provide valuable objective information regarding the role of cortical inhibitory circuits in the acquisition of strength. A limitation to the studies completed in this thesis was the University did not have the infrastructure to support a more resourced investigation into the cortical and subcortical effects of strength training. Therefore, future studies should employ the technique of paired pulse TMS. There is a need for a series of studies to examine the task-dependant effects of strength training on corticospinal excitability. This could be accomplished by comparing the effect of isometric strength training and isotonic strength training simultaneously. There are several lines of evidence that suggest that corticospinal control is task-dependant during skilled movements

(Flament et al., 1993; Aranyi et al., 1998; Tinazzi et al., 2002; Pearce and Kidgell, 2010) and recent observations have suggested that strength training may be considered a form of skill training, therefore an investigation into the task-dependant response is required (Carroll et al. 2002; Farthing, 2009; Zhou, 2000). Future research should also examine changes in movement representations following strength training. This would help clarify if a period of chronic strength training results in the alteration of cortical muscle representations within the M1 and would help demonstrate a link between the adaptations associated with skill and strength training. A closer examination of other neural pathways underlying the cross-transfer of strength, such as transcollosal and ipsilateral pathways is also required as it would provide objective data on the underlying neural pathways that modulate the cross-transfer of strength. A limitation to the studies presented in this thesis is that the corticospinal responses of antagonist muscles were not obtained, therefore to extend upon the findings in chapters 4, 5 and 6, future investigations should measure the change in TMS evoked MEPs and SP duration from antagonistic muscles. Finally, a closer examination of the training effects of using individualised WBV frequencies on upper and lower limb corticospinal responses is needed. Further investigations should examine the effect of WBV, placebo and control conditions on corticospinal responses. This would be valuable in determining the corticospinal responses to acute and longer term WBV training.

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APPENDICES

Appendix A: Edinburgh Handedness Inventory

Last Name..... First Names.....

Date of Birth..... Sex.....

Please indicate your preferences in the use of hands in the following activities by *putting + in the appropriate column*. Where the preference is so strong that you would never try to use the other hand unless absolutely forced to, *put + +*. If in any case you are really indifferent *put + in both columns*. Some of the activities require both hands. In these cases the part of the task, or object, for which hand preference is wanted is indicated in brackets. Please try to answer all of the questions, and only leave a blank if you have no experience at all of the object or task.

		LEFT	RIGHT
1.	Writing		
2.	Drawing		
3.	Throwing		
4.	Scissors		
5.	Toothbrush		
6.	Knife (without fork)		
7.	Spoon		
8.	Broom (upper hand)		
9.	Striking Match (match)		
10.	Opening box (lid)		
i.	Which foot do you prefer to kick with?		
ii.	Which eye do you use when using only one?		

L.Q. value* =

* the LQ value is the total number of +'s for the RIGHT hand boxes, less the total number of +'s for the left hand boxes, divided by the total +'s in both RIGHT and LEFT hand boxes.

Appendix B: Transcranial Magnetic Stimulation† (TMS) Adult Safety Screen

Name:
Date:
Age:

Please answer the following:

Have you ever:

Had an adverse reaction to TMS?	☐Yes	☐No
Had a seizure?	☐Yes	☐No
Had an electroencephalogram (EEG)?	☐Yes	☐No
Had a stroke?	☐Yes	☐No
Had a serious head injury (include neurosurgery)?	☐Yes	☐No
Had any other brain-related condition?	☐Yes	☐No
Had any illness that caused brain injury?	☐Yes	☐No
Do you have any metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork?	☐Yes	☐No
Do you have any implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines?	☐Yes	☐No
Do you suffer from frequent or severe headaches?	☐Yes	☐No
Are you taking any medications?	☐Yes	☐No
Are you pregnant, or is it possible that you may be pregnant?	☐Yes	☐No
Does anyone in your family have epilepsy?	☐Yes	☐No
Do you need further explanation of TMS and its associated risks?	☐Yes	☐No

*If you answered **yes** to any of the above, please provide details (use reverse if necessary):*

_____
_____
_____
_____
_____