

**Functional magnetic resonance imaging (fMRI) and electromyography (EMG) of
neuro-physiological adaptations associated with cross-education of a complex
strength task**

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By

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Abstract

Cross-education of strength is a neural adaptation defined as the increase in strength of the untrained contralateral limb after unilateral training of the opposite homologous limb. The neural mechanisms of the effect have remained elusive, although it appears to be a motor learning adaptation. Despite cross-education of strength being an inter-limb effect, no previous study has determined the influence of handedness and the direction of transfer (dominant to non-dominant or the reverse). Arguably, this is partly responsible for massive variation in the literature regarding the magnitude of the effect. The primary purpose of this document is to attempt to determine the central and peripheral neuro-physiological mechanisms controlling cross-education of muscular strength. Prior to determining the mechanisms of the effect, the influence of handedness and the preferred direction of transfer for cross-education of strength must be addressed. The secondary purpose is to determine the preferential direction of transfer of cross-education of strength in order to isolate the circumstances in which the effect is more pronounced. Two experiments were necessary to meet these objectives.

Experiment 1: The purpose was to determine the effect of the direction of transfer on cross-education in right-handed individuals. **Methods:** Thirty-nine strongly right-handed females were randomized into a left-hand training (LEFT), right-hand training (RIGHT), or non-training control (CON) group. Strength training was 6 weeks of maximal isometric ulnar deviation, 4 times per week. Peak torque, muscle thickness (ultrasound), and electromyographic (EMG) activity were assessed before and after training in both limbs. **Results:** The change in strength in the untrained limb was greatest in the RIGHT group (39.2%; $p < .01$), whereas no significant changes in strength were observed for the untrained

limb of the LEFT group (9.3%) or for either of the CON group limbs (10.4% and 12.2%). Strength training also increased trained limb strength in the LEFT (41.9%, $p < .01$) and the RIGHT (25.9%; $p < .01$) groups. Training groups increased trained limb muscle thickness (RIGHT and LEFT combined: 4.1%) compared to CON (-4.0%) ($p < .01$). There were no changes in muscle thickness of untrained limbs compared to CON. There were no significant changes in trained limb agonist or antagonist EMG activation with training. Changes in untrained limb EMG were not different compared to CON. **Conclusions:** Cross-education with hand strength training occurs only in the right-to-left direction of transfer in right-handed individuals. Cross-education of arm muscular strength is most pronounced to the non-dominant arm.

Experiment 2: The purpose of this study was to determine the central and peripheral mechanisms of cross-education of strength after actual and imagery training. **Methods:** Thirty-three strongly right-handed females were randomized into an actual training, imagery training, or non-training control group. A sub-sample of 8 subjects (4 actual, 4 imagery training) had brain activity during exercise assessed with functional magnetic resonance imaging (fMRI). Strength training was 6 weeks of maximal isometric handgrip ulnar deviation (Biodex) of the right arm, 4 times per week. Peak torque (Biodex), muscle thickness (ultrasound), agonist-antagonist EMG, and fMRI were assessed before and after training. **Results:** Actual training was highly effective for increasing strength in trained (45.3%; $p < .01$) and untrained (47.1%; $p < .01$) limbs. Imagery training and control groups had no increases in strength for either arm. Muscle thickness increased only in the trained arm of the actual group (8.4%; $p < .001$). After actual training, there was an increase in activation of contralateral sensorimotor cortex and left temporal lobe during actual

contractions with the untrained left arm ($p < .001$). Actual training was associated with a significantly greater change in agonist muscle activation pooled over both limbs, compared to the imagery and control groups ($p < .05$). **Conclusion:** Cross-education of strength is only significant after actual training, indicating that peripheral feedback is necessary for the effect. Cross-education of strength is accompanied by changes in cortical activation indicative of motor learning and the retrieval of memory of movement acquired by the trained limb.

General Conclusion: The neuro-physiological mechanism of cross-education of strength is that changes in cortical activation indicative of motor learning occur in both brain hemispheres after unilateral training. Cross-education of strength is influenced by strength asymmetries related to handedness, and the preferential direction of transfer is from dominant to non-dominant limb. Cross-education is a motor learning adaptation also reliant on peripheral feedback during training.

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Dedication

This thesis is dedicated to my wife Danielle and to my mother Grace, and father Gerald. To my wife Danielle, for handling our three little kids every day while I worked, and for her love and support. To my mother and father, for their encouragement and support, help with kids and the occasional ride home or borrowed car during my schooling.

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Glossary

Alpha (α) Motoneuron: A motoneuron that innervates extrafusal muscle fibres (muscle fibres outside muscle spindles).

Basal Ganglia: The basal ganglia are a group of structures that involve the initiation and maintenance of motor function. They include substantia nigra, putamen, globus pallidus, caudate nucleus, and subthalamic nucleus.

Brainstem: The brainstem encompasses three structures: the medulla, pons, and midbrain. The brainstem processes sensation from skin and joints in the head, neck and face.

Broca's Area: Broca's area is involved with motor aspects of speech production. It is usually located in the ventral premotor cortex of the dominant hemisphere that directs speech (usually left).

Central Sulcus: A consistent sulcus that extends from the medial surface of the cerebral hemisphere to the lateral fissure. It separates the frontal and parietal lobes.

Cerebellum: The cerebellum plays a major role in modifying motor activity in response to sensory feedback. It is divided into a right and left hemisphere, and includes three distinct layers of cortex: the Purkinje layer, the molecular layer, and the granular layer.

Cingulate Motor Area: The most medial and superior part of the primary motor area bound by the longitudinal fissure.

Commissure: Connection of nerve fibres between cerebral hemispheres.

Contralateral: Structures on opposite sides of the body.

Corpus Callosum: A large commissural bundle of axons that join the right and left cerebral hemispheres of the brain.

Corticospinal Tract: The corticospinal tract is comprised of upper motor neurons in motor cortex which relay signals to lower motor neurons in the spinal cord.

Cross-education: Performance improvement (i.e. strength, skill execution, endurance) of the untrained limb after a period of unilateral practice (i.e. strength training, skill learning, endurance training) of the homologous contralateral limb.

Diamagnetic: Diamagnetic materials repel magnetic fields (reduce the intensity). Most body tissues are diamagnetic.

Distal Inhibition: Activation of inhibitory interneurons by descending signal from motor cortex or brainstem.

Electromyography (EMG): A technique used to estimate muscle activation by picking up the electrical activity of muscles during contraction.

Electromyostimulation (EMS): A technique used to artificially activate muscle, usually to elicit maximal activation.

Frontal Association Area: The frontal association area is comprised of the prefrontal cortex, and determines affective reactions to situations based on past experience. It is also involved in monitoring behaviour, judgment and foresight.

Frontal Lobe: The most anterior lobe of the cerebral hemisphere. It consists of cortex anterior to the central sulcus and superior to the lateral fissure.

Gamma (γ) Motoneuron: A motoneuron that innervates intrafusal muscle fibres (muscle fibres inside muscle spindles).

Golgi Tendon Organ: A muscle receptor that regulates muscle tension. Activation of Ib afferents from Golgi tendon organs will inhibit or terminate contraction of the muscle in order to prevent injury.

Gyrus: The crest of a convolution in the cerebral cortex, often appearing as rounded folds. Gyri help to identify regions of cortex in the brain.

Interlateral Transfer: The transfer of skill-learning from the practiced limb to the unpracticed limb. Also referred to as Bilateral Transfer or Intermanual Transfer.

Interneuron: A neuron that receives input from neurons and transmits output to other neurons. Interneurons can be excitatory or inhibitory.

Ipsilateral: Structures on the same side of the body.

Medullary Pyramid: The section of the brainstem where the medulla converges before connecting with the spinal cord. The medullary pyramid is the location of decussation of the corticospinal tracts.

Mirror Neurons: Mirror neurons are activated during the observation of previously acquired movements. Mirror neurons are thought to be located in ventral premotor cortex and secondary somatosensory area (parietal lobe).

Muscle Spindle: Muscle receptors that interpret and control muscle length. Activation of Ia afferents from muscle spindles causes contraction of the muscle in order to prevent injury. Muscle spindles consist of intrafusal muscle fibres.

Occipital Lobe: The most posterior lobe in the cerebral hemisphere. It is bound by the parietal-occipital fissure.

Paramagnetic: Paramagnetic materials attract magnetic fields (enhance the intensity).

Deoxyhemoglobin is paramagnetic.

Parietal Lobe: The central lobe of the cerebral hemisphere. It is bound anteriorly by the central sulcus and posteriorly by the parietal-occipital fissure.

Plasticity: Increase or decrease in of synaptic activity for short or long periods following activity. Plasticity has been strongly linked to learning and may involve new synapses or growth of new tissue.

Postcentral Gyrus: A strip of cortex on the surface of the cerebral hemisphere running parallel and immediately posterior to central sulcus. See primary somatosensory area.

Precentral Gyrus: A strip of cortex on the surface of the cerebral hemisphere running anterior and parallel to central sulcus that defines the primary motor area.

Prefrontal Cortex: See Frontal Association Area.

Premotor Cortex: The higher motor area of the cerebral cortex. It includes the premotor area and supplementary motor area.

Premotor Area: Acts in conjunction with supplementary motor area in programming skilled motor programs. It is located just anterior to primary motor area.

Primary Motor Area: The primary motor area includes the precentral gyrus. Each area represents the contralateral side of the body and is somatotopically organized. It includes the primary motor cortex.

Primary Somatosensory Area: The primary somatosensory area occupies the postcentral gyrus. Each area represents the contralateral side of the body and is somatotopically organized. It includes the primary somatosensory cortex.

Reciprocal Inhibition: Reciprocal inhibition involves signal from agonist muscle afferents onto Ia inhibitory interneurons, which generate inhibition of the antagonist muscle. It is also known as feedforward inhibition.

Recurrent Inhibition: Recurrent inhibition involves direct feedback to α -motoneurons without activation of the afferent loops, through the activity of Renshaw cells. Recurrent inhibition is a form of feedback inhibition.

Renshaw Cell: Renshaw cells are interneurons that can be activated by supraspinal input, muscles afferents and branches from α -motoneurons. They are involved in Recurrent Inhibition.

Semantic Memory: The aspects of cognition that include the knowledge acquired about the world around us, such as facts, concepts, and beliefs (Martin, 2001). Semantic memory also includes information about object and word meaning.

Somatosensory Association Area: This area integrates general sensory information from primary somatosensory area and from thalamus. It is located just posterior to postcentral gyrus.

Sulcus: The groove between two gyri in the cerebral cortex.

Supplementary Motor Area: Along with the premotor area, supplementary motor area functions in elaborate motor programming for more skilled voluntary movements.

T₂* Decay: T₂* Decay refers to the behaviour of ensembles of ensembles (mesoscopic level) of transverse spins and is reversible by radio frequency pulses in MRI. Since it is reversible, the signal from T₂* Decay is used to detect the BOLD response in fMRI.

T₂ Relaxation: T₂ Relaxation refers to the behaviour of a single ensemble (microscopic level) of transverse spins and is not reversible by radio frequency pulses in MRI.

Temporal Association Area: Integrate sensory information from auditory, visual and somatosensory areas and project to the frontal association area. Anterior regions of the temporal association area play a role in memory function.

Temporal Gyrus: The superior, middle and inferior temporal gyri make up the temporal lobe.

Temporal Lobe: The most inferior lobe in the cerebral hemisphere, located just inferior to the lateral fissure.

List of Abbreviations

AIP- Anterior Intraparietal Sulcus (in primates)

BOLD- Blood Oxygen Level Dependent

CBF- Cerebral Blood Flow

CIMT- Constraint-Induced Movement Therapy

CMA- Cingulate Motor Area

CMRO₂- Cerebral Metabolic Rate of Oxygen Consumption

CMRR- Common Mode Rejection Ratio

CNS- Central Nervous System

EMG- Electromyography

EMS- Electromyostimulation

F5- Ventral premotor cortex (in primates)

fMRI- Functional Magnetic Resonance Imaging

LFPs- Local Field Potentials

LTD- Long-term Depression

LTP- Long-term Potentiation

M1- Primary Motor Cortex

MAV- Mean Absolute Value

MVC- Maximal Voluntary Contraction

MUA- Multi-unit Activity

PET- Positron Emission Tomography

PMC- Premotor Cortex

RF- Radio Frequency

SMA- Supplementary Motor Area

S1- Primary Somatosensory Cortex

S2- Secondary Somatosensory Cortex

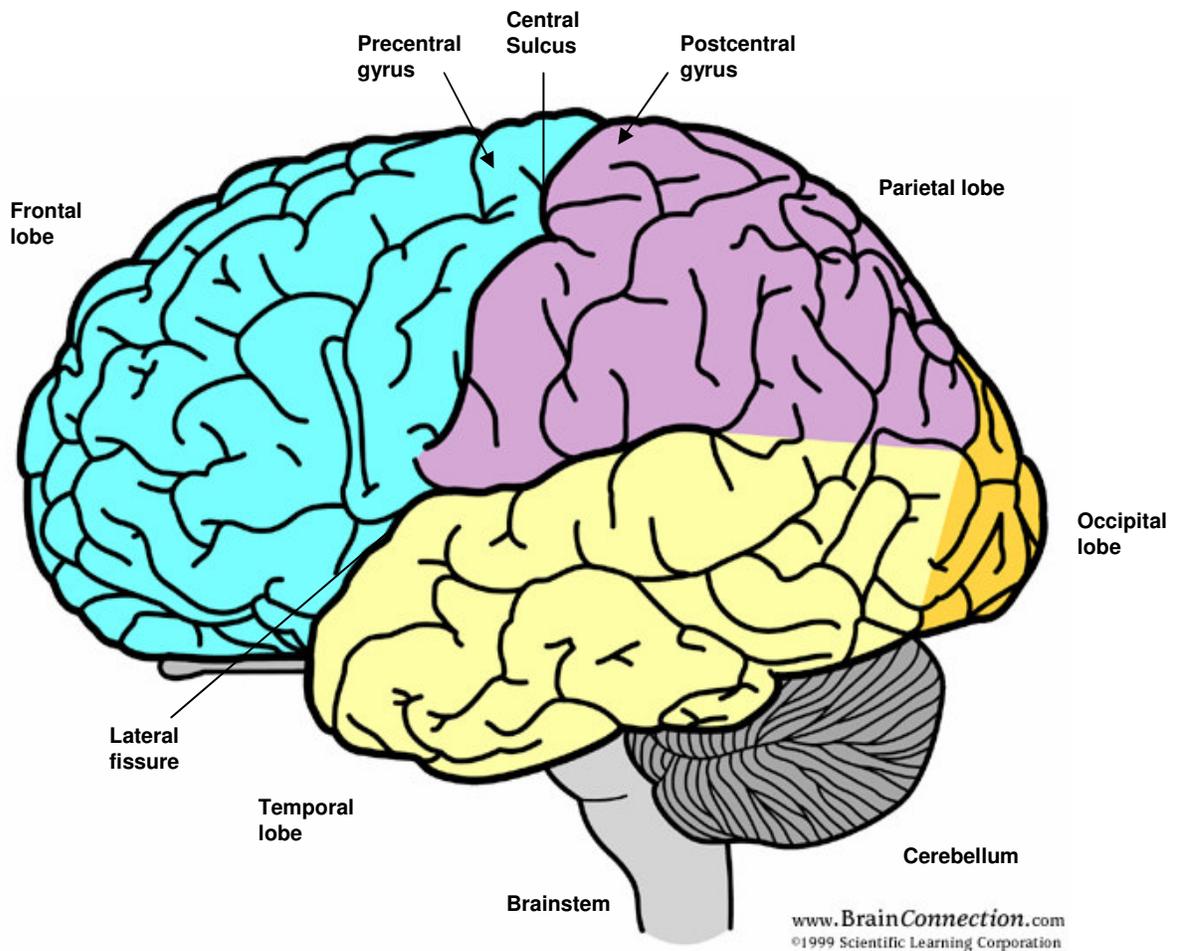


Figure 1.1 Basic surface anatomy of the brain.

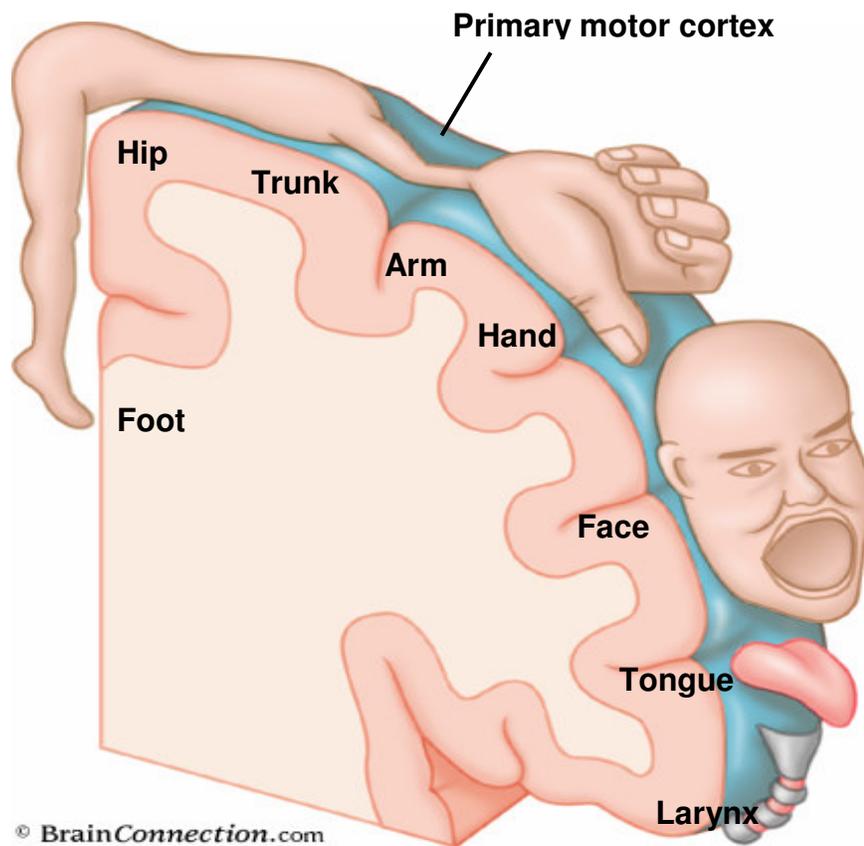


Figure 1.2 Motor homunculus of the human body. The homunculus shows a disproportionate somatotopically organized map of the area of motor cortex devoted to each body part.

Chapter 1: Introduction and Review of Literature

1.1 Introduction

As far back as the late nineteenth century, it has been documented that performance improvements are observed in the untrained limb after unilateral exercise training of the opposite homologous limb (Scripture et al., 1894). This ‘transfer’ phenomenon between limbs was later referred to as cross-education (Cook et al., 1933a). The definition of cross-education has followed an unusual path, and somewhat depends on the area of literature (i.e. motor control or exercise physiology). A global definition of cross-education is the performance improvement (i.e. strength, skill execution, endurance) of the untrained limb after a period of unilateral practice (i.e. strength training, skill learning, endurance training) of the homologous contralateral limb. Scripture et al. (1894) described cross-education of strength following unilateral exercise training, whereas early experimental psychology literature studied cross-education of a motor skill (Cook et al., 1933a). Historically, cross-education of strength and cross-education of skill have been studied by scientists with different expertise, and arguably this has led to separation in terminology. Physiologists have streamlined the research into strength transfer continuing with the term ‘cross-education’ (Hellebrandt, 1947; Moritani and deVries, 1979; Stromberg, 1986; Hortobágyi et al., 1997; Farthing and Chilibeck, 2003a), while experimental psychologists and motor control experts have focused on transfer of skill referring to it as ‘bilateral transfer’, ‘interlateral transfer’, or ‘intermanual transfer’, or just simply ‘transfer’ (Cook et al., 1933; Hicks, 1974; Elliott and Roy, 1981; Parlow and Kinsbourne, 1989; Thut et al., 1996; Teixeira and Caminha, 2003). In fact, some motor control researchers prefer the term ‘interlateral transfer of strength’ when discussing strength transfer (Teixeira and Caminha, 2003), claiming ‘cross-education’ is a term used in older literature (Parlow and Kinsbourne, 1989). The discrepancy in

the literature is quite obvious in that transfer studies in exercise physiology rarely report or discuss the findings of motor control skill transfer studies, and vice-versa.

More recently in exercise physiology, the definition of cross-education has included transfer of muscular strength and transfer of motor skill learning to the untrained muscle (Zhou, 2000). Of course, transfer of any skill to the untrained limb following training is a neural adaptation, since skill learning occurs without any structural changes in muscle. Skill learning is often accompanied by adaptations in trajectory and velocity of movement, and precise timing of agonist-antagonist muscle activations. Transfer of strength is thought to be similar as it occurs in the absence of muscle hypertrophy in the untrained limb (Zhou, 2000). In the present document cross-education refers to the transfer of strength to the untrained limb. Part of the purpose of this document is to address how strength transfer and skill transfer are likely related and may be controlled by similar motor learning mechanisms; therefore, the discrepancy in the literature may be unnecessary- the only relevant part of the definition of cross-education being the characteristics of the task being transferred (i.e. strength vs. skill).

More than fifty years ago, Hellebrandt (1951) speculated that the neural mechanisms of cross-education originated in the brain via communication between cortical hemispheres. However, the neural mechanisms controlling cross-education have continued to remain elusive. As with most other neural adaptations to training, neural adaptations associated with cross-education have mainly been assessed at the executor level (peripheral nervous system), and the central mechanisms controlling the effect have been difficult to affirm. For obvious reasons, central nervous system (CNS) adaptations to physical training, especially in the brain, have been difficult to assess. Continually advancing non-invasive methods of detecting CNS activity in humans such as Functional Magnetic Resonance Imaging (fMRI) allow for CNS assessment in

conjunction with peripheral assessments. Non-invasive assessment of cortical adaptation with training or motor learning is a relatively recent development, with techniques such as fMRI only emerging in the last fifteen years (Ogawa et al., 1990).

Before the neural mechanisms of cross-education of strength can be pursued, a gap in the current literature regarding handedness and the preferential direction of transfer (i.e. from dominant to non-dominant or the reverse) must be addressed. Transfer direction and handedness with various manual motor tasks has been addressed in the motor control literature (Parlow and Kinsbourne, 1989; Gordon et al., 1994; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996; Latash, 1999; Criscimagna-Hemminger et al., 2003) but no study to date has determined the influence of handedness or footedness on the direction of transfer of cross-education of strength. Arguably, this is part of the reason for the gross variation that exists in the literature in terms of the magnitude of effect. Findings range from no cross-education (Ebersole et al., 2002) up to as high as 104% (Hortobágyi et al., 1999) depending on the specific protocol. If cross-education of strength and cross-education of skill are controlled by similar mechanisms, than they may be subject to similar effects of handedness and the transfer direction.

The primary objective of this document is to attempt to determine the central and peripheral neuro-physiological mechanisms controlling cross-education of muscular strength, and compare them to candidate mechanisms previously proposed for cross-education of strength, and neural mechanisms of motor learning. The secondary objective, which must be met in order to meet the primary objective, is to determine the preferential direction of transfer of cross-education of strength in order to isolate the circumstances in which the effect is more pronounced. Two experiments are necessary to meet these objectives. The first experiment will examine the direction of transfer of cross-education in right-handed individuals using a manual

strength task, along with peripheral nervous system assessment. The second experiment will incorporate the direction of transfer from the first experiment which resulted in highest magnitude of effect, and will examine central and peripheral neural adaptations accompanying cross-education of strength.

1.2 Review of Literature

1.2.1 Cross-education

The magnitude of cross-education of strength is thought to be related to the magnitude of strength increase of the trained muscle; and is approximately 35-60% of the strength increase achieved in the trained muscle (Munn et al, 2004; Zhou, 2000). Regardless of the magnitude, there is definitive asymmetry between the strength increase in the trained and untrained limbs in most cases. The amount of strength transfer seems to depend on many factors- including the characteristics of the motor task (i.e. familiar or unfamiliar), training duration and intensity, training volume, contraction type (eccentric, concentric or isometric; actual versus imagined; voluntary or stimulated), contraction velocity, muscle group, and the restriction of movement/activation in the non-training limb during training. The majority of cross-education studies in exercise physiology have used resistance training protocols (Smith, 1970; Moritani and deVries, 1979; Houston et al., 1983; Davies et al., 1985; Parker et al., 1985; Cabric and Appell, 1987; Cannon and Cafarelli, 1987; Narici et al., 1989; Carolan and Cafarelli, 1992; Housh et al., 1992; Kannus et al., 1992; Weir et al., 1995; Hortobágyi et al., 1996a; Hortobágyi et al., 1997; Seger et al., 1998; Hortobágyi et al., 1999; Tracy et al., 1999; Shima et al., 2002; Ebersole et al., 2002; Farthing and Chilibeck, 2003a) while others have used unilateral muscular endurance training (Shields et al., 1999) or range of motion exercise (Stromberg, 1986). Cross-education of

strength is greater in untrained individuals with little resistance training experience (Weir et al., 1995; Hortobágyi et al., 1996a; Hortobágyi et al., 1997; Hortobágyi et al., 1999; Tracy et al., 1999), and has shown specificity to training (Hortobágyi et al., 1997; Farthing and Chilibeck, 2003a).

There exists no obvious relationship between the duration and intensity of training and the magnitude of cross-education (Zhou, 2000), but studies with longer training duration typically show greater transfer. The highest magnitude of cross-education with voluntary training (77%) was shown after 12 weeks of training (Hortobágyi et al., 1997). Most of the literature shows significant strength transfer following five or more weeks of training (Cannon and Cafarelli, 1987; Davies et al., 1985; Kannus et al., 1992; Hortobágyi et al., 1997; Tracy et al., 1999; Shields et al., 1999; Shima et al., 2002; Farthing and Chilibeck, 2003a). The majority of cross-education studies use training intensities above 60% of maximal voluntary contraction (MVC) (Zhou, 2000) but comparisons can be difficult unless the same contraction type is used. Contraction type is known to influence muscle activation and force during muscle contraction (Hortobágyi and Katch, 1990a; Westing et al., 1990; Westing et al., 1991; Aagaard et al., 2000; Seger and Thortensson 2000; see reviews by Stauber, 1989; Kellis and Baltopoulos, 1995) and muscle hypertrophy with training (Farthing and Chilibeck, 2003b). When comparing studies using the same contraction type for training, cross-education is greater when contractions of maximal intensity were required (Davies et al., 1985; Housh et al., 1992; Hortobágyi et al., 1997; Tracy et al., 1999).

Studies comparing contraction types show that eccentric rather than concentric or isometric training produces more cross-education (Hortobágyi et al., 1997; Seger et al., 1998). Eccentric training protocols also consistently show greater overall strength increases than

concentric or isometric (Colliander and Tesch, 1990; Higbie et al., 1996; Hortobágyi et al., 1996a; Hortobágyi et al., 1996b; Hortobágyi et al., 1997; Farthing and Chilibeck, 2003b), likely due to greater force production (Hortobágyi and Katch, 1990; Westing et al., 1990; Farthing and Chilibeck, 2003b) combined with muscle stretch during contraction. Greater force combined with muscle stretch leads to inherent muscle damage consistent after periods of eccentric training (Gibala et al., 1995; Chen and Hsieh, 2001). Despite these considerations, most cross-education of strength studies use isometric training (Davies et al., 1985; Parker, 1985; Cabric and Appell, 1987; Jones and Rutherford, 1987; Carolan and Cafarelli, 1992; Kannus et al., 1992; Weir et al., 1995; Oakman et al., 1999) conceivably because it is easier to restrict the movement of the non-training limb during static as compared to dynamic contractions. Dynamic contractions also present further limitations to EMG and are often normalized to peak isometric EMG (Hortobágyi et al., 1997) or maximal evoked motor response (Cannon and Cafarelli, 1987; Shima et al., 2002).

Our recent work compared eccentric training at high velocity (180°/s [3.14 rad/s]) and low velocity (30°/s [0.52 rad/s]), and found only high velocity training induced cross-education (Farthing and Chilibeck, 2003a). Since high velocity eccentric contractions are very unfamiliar to most individuals, we speculated more substantial motor learning was occurring with high velocity eccentric training leading to greater cross-education. Thus, the degree of task familiarity may be important for cross-education of strength, perhaps related to untrained individuals showing more cross-education. Consistently, studies employing more unfamiliar tasks seemingly show a greater effect (Hortobágyi et al., 1997; Hortobágyi et al., 1999). Intuitively, if individuals are already trained for the task, how much more neural adaptation can be exhibited? Moritani

and deVries (1979) have shown that neural factors contribute negligibly to strength gain beyond 6 weeks of training.

The importance of task familiarity for cross-education is supported by studies using muscle stimulation. Training procedures using electrically stimulated contractions or electromyostimulation (EMS) appear to increase the magnitude of cross-education (Cabric and Appell, 1987; Hortobágyi et al., 1999). EMS training is very unfamiliar to the vast majority of individuals, and even with pre-study familiarization trials cross-education of strength was as high as 104% (Hortobágyi et al., 1999). Despite bypassing any descending signal to initiate movement- as is the case with EMS- participants were obviously still able to use neural information gained through the evoked contractions for feedback and memory pertaining to future movement with the untrained limb. These findings are consistent with recent theory suggesting cross-education is related to the strength increase achieved in the training limb (Zhou, 2000; Munn et al., 2004). EMS produces greater muscle activation per contraction than voluntary contraction training and accelerates strength gain in the trained limb (Hortobágyi et al., 1999) therefore it should also produce more cross-education.

1.2.2 Cross-education of Strength and Interlateral Transfer of Skill

The suggestion that task familiarity influences cross-education of strength may also provide linkage to interlateral transfer of skill. As mentioned above, interlateral or bilateral transfer refers to transfer of skill learning between limbs. Interlateral transfer has been shown with various motor tasks such as pointing (Elliott and Roy, 1981), tracking (Hicks et al., 1983), drawing and writing (Hicks, 1974; Parlow and Kinsbourne, 1989), mirror writing (Latash, 1999), mirror tracing (Cook, 1933a & 1933b), learned dynamics of reaching (Criscimagna-Hemminger

et al., 2003), and maze learning (Stoddard and Vaid, 1996). Skill transfer is commonly asymmetrical as a function of the direction of transfer- from right to left or left to right (Stoddard and Vaid, 1996), and the handedness of the subject (Parlow and Kinsbourne, 1989). In other words, the skill may or may not transfer depending on whether the left or right limb was used for the initial trail. The majority of studies support interlateral transfer in the right to left direction (primarily in right-handed individuals) (Parlow and Kinsbourne, 1989; Gordon et al., 1994; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996; Latash, 1999; Teixeira, 2000-experiment 1; Criscimagna-Hemminger et al., 2003; Teixeira and Caminha, 2003), but there are studies that support the reverse direction (left to right) (Hicks, 1974; Parlow and Kinsbourne, 1990; Taylor and Heilman, 1980; Teixeira, 2000-experiment 2), both directions (Morton et al., 2001), or neither direction (Teixeira, 1993; Kitazawa et al., 1997).

1.2.2.1 Models of Transfer, Lateralization, and Handedness

Historically, three models have been used to explain the findings of transfer studies: the access model (Taylor and Heilman, 1980), the proficiency model (Laszlo et al., 1970) and the cross-activation model (Parlow and Kinsbourne, 1989). The access model is based on findings that the right hand of right-handed subjects benefits more from contralateral hand learning. This theory suggests motor engrams (motor programs) are stored in the dominant left hemisphere regardless of the hand used, and therefore the right hand has preferential access to the information (Thut et al., 1996). The proficiency model operates on the premise that motor engrams are stored unilaterally in the opposite brain hemisphere (Thut et al., 1996). Theoretically, the more effective engram will be stored when acquisition is with the more proficient system (left hemisphere of right-handers) and is more beneficial for learning in the

opposite side (through commissural fibres). However, studies showing prevalence of right to left transfer in split-brain patients (severed corpus callosum) (Criscimagna-Hemminger et al., 2003) seem to refute the proficiency model, although corpus callosum is not the only possibility for communication between opposite cortex. The cross-activation model hypothesizes the storage of dual engrams- one in each hemisphere. Therefore the acquisition of a task with the more proficient system would provide a better stored engram for the opposite side. This model would also assume a role of commissural fibres during task acquisition- but not during subsequent performance of the opposite side. Thus, both the proficiency model and the cross-activation model support the right to left direction of transfer.

A more recent model applied to transfer studies is based on the transferability of the type of information required for movement at the task level (cortex) and the manipulator level (muscles) (Imamizu and Shimojo, 1995). Spatial information (as perceived by the brain) must be transformed into joint position and rate of change of joint angle information (for muscles) in order for movement to occur. Imamizu and Shimojo (1995) suggest that if learning occurs at the task level, perfect transfer will occur because the necessary information is only based on spatial coordinates. On the other hand if learning occurs at the manipulator level, little or no transfer will occur because joint torque and rate of change of joint angle information will differ for right and left limbs. Finally, if learning involves both the task and manipulator levels, then intermediate transfer will occur.

Predicting the direction of interlateral transfer may depend on the characteristics of the task and handedness. Interlateral transfer studies are lopsided with entirely or majority right-handed subjects (Taylor and Heilman, 1980; Hicks et al., 1983; Teixeira, 1993; Gordon et al., 1994; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996; Thut et al., 1996; Latash, 1999;

Teixeira, 2000; Morton et al., 2001; Criscimagna-Hemminger et al., 2003; Teixeira and Caminha, 2003). Further to this, caution should be taken in assuming that declared handedness or determined handedness via questionnaire is a good method for determining hand preference for a given novel task (Steenhuis and Bryden, 1999). This confound could account for some inconsistency in the findings of interlateral transfer studies. Prior related experience and the characteristics of the task could dictate greater non-preferred hand proficiency or ambidexterity- both especially common in left-handed individuals (Steenhuis and Bryden, 1999). For example, left-hand proficiency might be shown in a right-handed individual for a unilateral catching task, especially if the person has prior baseball or softball experience.

Lateralization of function between brain hemispheres could also explain why some tasks transfer preferentially in one direction or the other depending on the characteristics of the task. Usually in right-handed subjects the right hand is advantaged when tasks are more difficult or require more accuracy, speed, and timing (Roy and Elliott, 1986; Elliott et al., 1993), perhaps related to the finding that the right hand seems to be advantaged for processing feedback with and without visual information (proprioceptive) (Roy et al., 1994). The right-hand/left hemisphere system is also thought to be less variable in terms of motor output (Annett et al., 1979; Carson et al., 1993). However, more recent studies have found diminished asymmetry between right and left hands for skills requiring spatial precision (increased difficulty), indicating a greater involvement of the right hemisphere for spatial information processing (Maraj et al., 1998; Bryden and Roy, 1999). The question remains as to whether the right hand advantage is due to nature or nurture. Heath and Roy (2000) found that exhaustive left hand practice dissipated asymmetry between hands for an aiming task in a right-handed subject. Kinematic measures were nearly identical following training, and no transfer to the right hand was

observed. The greatest improvement for the left hand with practice was during deceleration of movement, indicating enhanced utilization of response-produced feedback (proprioception or visual feedback). The advantaged right hand system may be due to more practice associated with 'living in a right-hand world', rather than biological difference between brain hemispheres. Left-handed subjects have shown more willingness to use their non-preferred hand, suggesting that left-handers may have adapted to an environment better suited for right-handers (Mamolo et al., 2005). Also, if nature is responsible for the right hand advantage, one might expect increasing asymmetry through the life span. However, recent research indicates adults show reduced asymmetry between hands as compared to younger age categories (Bryden and Roy, 2005).

Whether strength transfer is similar to skill transfer in regards to the influence of task characteristics and handedness is yet to be determined. Most cross-education studies have attempted to control for the effect of dominance by training muscle groups on the same side of the body across subjects regardless of handedness or footedness. Although no study has directly compared cross-education of strength in both directions, it appears that a greater effect is observed when training specific muscles of the left side of the lower body (77-104%) (Hortobágyi et al., 1997; Hortobágyi et al., 1999). Cross-education of strength has been shown in both directions across the literature despite the lack of consistently reporting the dominant side.

Prevalence for the right to left or the left to right direction of transfer for cross-education of strength may be more obvious when upper body muscle groups are trained (especially hands), since most skill transfer studies use manual tasks and show asymmetry with transfer direction (Parlow and Kinsbourne, 1989; Gordon et al., 1994; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996; Latash, 1999; Criscimagna-Hemminger et al., 2003). Training of dominant upper body muscle groups can exaggerate strength asymmetry between homologous muscles (Teixeira

and Caminha, 2003). Further to this, the determination of handedness has been reliable (Bryden, 1977), whereas distinguishing footedness or leggedness has proved more difficult (Vanden-Abee, 1980). More recently, footedness questionnaires have been used in conjunction with handedness questionnaires to determine that footedness is a better predictor of language lateralization (Elias and Bryden, 1998). Of the studies that report training the dominant or non-dominant side, results are mixed. Cross-education with training of the dominant side has ranged from 11% to 43% (Davies et al., 1985; Carolan and Cafarelli, 1992; Shields et al., 1999), whereas cross-education with training of the non-dominant side has ranged from no effect up to 16% (Housh et al., 1992; Ebersole et al., 2002). Of the studies that reported randomizing whether the dominant side would be trained or untrained, cross-education ranged from 7.8% to 13% (Shima et al., 2002; Farthing and Chilibeck, 2003a).

Forming a clear hypothesis about the direction of transfer and the influence of the dominant side of the body on cross-education of strength is difficult due to discrepancies in training protocol across the literature (i.e. training duration, task complexity, contraction type and intensity, muscle group, upper or lower body). If cross-education is proportional to the strength gain of the trained muscle (Munn et al., 2004; Zhou, 2000), then training the weaker left side of the body will likely result in greater strength gains and proportionately greater cross-education. Depending on the task characteristics such as complexity (multi-jointed, speed, neuromuscular timing), preferential right to left cross-education of strength might be predicted based on the aforementioned right hand advantage (Roy et al., 1994).

1.2.3 Cross-education and Imagery Training

Motor imagery has shown similar cortical activation patterns as actual movement (Cunnington et al., 1996; Porro et al., 1996; Schnitzler et al., 1997; Lotze et al., 1999; Leonardo et al., 1995; Binkofski et al., 2000; Romero et al., 2000; Thobois et al., 2000; Naito et al., 2002). Motor imagery and motor preparation have suitably been called functionally equivalent processes (Jeannerod, 1994). Motor imagery includes activation in contralateral areas of the precentral gyrus (specifically primary motor cortex-M1) (Porro et al., 1996; Schnitzler et al., 1997; Leonardo et al., 1999), cingulate motor area (CMA) (Naito et al., 2002), supplementary motor area (SMA) (Cunnington et al., 1996; Deiber et al., 1998; Lotze et al., 1999; Naito et al., 2002), premotor cortex (PMC) (Leonardo et al., 1999; Lotze et al., 1999; Romero et al., 2000; Binkofski et al., 2000), and superior parietal lobe (Thobois et al., 2000), ipsilateral cerebellum (Porro et al., 1996; Thobois et al., 2000; Naito et al., 2002), and both inferior lateral sides of the cerebellum (Ryding et al., 1993); and ipsilateral areas of cortex including M1, SMA, and PMC, parietal cortex and prefrontal cortex (Roth et al., 1996; Schnitzler et al., 1997; Binkofski et al., 2000; Gerardin et al., 2000).

While the influence of handedness is apparent for interlateral transfer, the importance it has for motor imagery is unclear. Studies including right hand imagery tasks with right-handed subjects have shown decreased M1 and primary somatosensory cortex (S1) activity, but similar SMA and PMC activation compared to actual movement (Deiber et al., 1997; Schnitzler et al., 1997; Deiber et al., 1998; Lotze et al., 1999; Romero et al., 2000). Motor imagery and actual movements appear to show similar activations in regions relevant for movement preparation and planning, but areas more involved in movement execution (M1) or feedback (S1) are suppressed with imagery. With particular relevance to transfer studies, motor imagery with right hand movement does not appear to activate homologous contralateral brain regions as with left

(Thobois et al., 2000). Unfortunately, very few studies have compared right and left hand imagery. Thobois et al. (2000) found contralateral M1 was activated only with right hand imagery in right-handers, whereas prefrontal cortex was activated only during left hand imagery, and cerebellum was activated regardless. Bilateral activation was shown in SMA and superior parietal lobe with only left hand imagery. The authors speculated greater overall brain activation with left hand imagery in right-handers may reflect a difficulty for motor imagery with the non-dominant hand. This could be related to the influence of handedness for interlateral transfer of skills (Parlow and Kinsbourne, 1989), and may provide support for the access model described earlier (Thut et al., 1996). As the access model might predict, motor programs associated with imagery could be stored only in the left hemisphere regardless of the hand used, and therefore the right hand has preferential access to the information. Intuitively, better motor imagery could be expected with the dominant hand.

A small number of studies have experimented with imagery training protocols (Yue and Cole, 1992; Herbert et al., 1998; Zijdwind et al., 2003; Ranganathan et al., 2004). Conflict exists as to whether imagery training can result in significant strength increase and cross-education. Yue and Cole (1992) found imagery training nearly as effective for strength and cross-education as actual training (Imagery- 22% trained, 10% untrained; Actual- 30% trained, 14% untrained) whereas Herbert et al. (1998) found no effect of imagery training. Adjusting for a small strength increase in the control group, Zijdwind et al. (2003) attributed approximately 20% strength increase to imagery training. Variation across studies could be related to differences in training modality. Herbert et al. (1998) report right hand training, whereas Yue and Cole (1992) report left hand training, and Zijdwind et al. (2003) report bilateral lower leg training. Yue and Cole (1992) seem to support the access model in that left hand acquisition was

beneficial for strength and transfer, but they conflict with the majority of transfer studies which support preferential right to left transfer (Parlow and Kinsbourne, 1989; Gordon et al., 1994; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996). Further, the findings of Yue and Cole (1992) suggest cross-education of strength must involve key influence from the task level (brain), since imagery training eliminates any influence from the manipulator level (muscles) and produces cross-education similar to actual training. However, as Imamizu and Shimojo (1995) contend, if only the task level is involved in transfer between limbs imagery training should result in perfect transfer- roughly double the cross-education effect shown by Yue and Cole (1992). If the manipulator level is important for cross-education, actual training should result in greater transfer than imagery. Relative to the trained limb, Yue and Cole (1992) found similar cross-education with imagery and actual training. This area warrants further study since the findings of Yue and Cole (1992) are apparently difficult to replicate (Herbert et al., 1998) and so few imagery training studies exist.

There is apparent need for studies where imagery training is examined in conjunction with functional imaging techniques to determine neuro-physiological adaptation. Given the similarity in brain activation patterns reported previously with imagery and actual movement, imagery training might involve similar cortical adaptations as actual training. Theoretically, the proportion of strength increase associated with neural factors with training (Moritani and deVries, 1979) could be partly induced by imagery alone. Changes in cortical activation using functional imaging techniques has not been examined before and after imagined resistance training, although it has been examined after motor imagery practice (Lotze et al., 1999; Jackson et al., 2003). Intuitively, for imagery training to be effective for strength and cross-education, CNS adaptation must be involved since the periphery should not be experiencing activation or

relaying feedback. However, studies have shown some small activation (above resting) of target musculature with motor imagery which can be removed with practice (Lotze et al., 1999) or prompting (Zijdewind et al., 2003).

1.2.4 Cross-education, Motor Imagery, and Semantic Memory

There could be an important link between semantic representations of movement within the cortex and cortical activations associated with motor imagery and/or unilateral movement. Semantic memory refers to “the aspects of cognition that include the knowledge acquired about the world around us, such as facts, concepts, and beliefs” (Tulving, 1983; Martin, 2001). Perhaps more central to aspects of motor function, semantic memory also includes the information stored in our brains about object and word meaning (Martin, 2001). Martin argues that semantic memory has its representations mainly in the left temporal lobe region (Martin, 2001), although prefrontal cortex (D’Esposito et al., 1998), bilateral temporal lobe activations (Kable et al., 2002) and hippocampus have also been linked to memory (Kupfermann, 1991).

Martin et al. (1995) attributed activation in the left middle temporal gyrus as retrieval of motion knowledge, since this region is just anterior to the region associated with motion perception (Puce et al., 1998). Imagining actions also has been associated with middle temporal lobe activation and PMC activation (Gerardin et al., 2000) indicating motor imagery must be cognitively processed from stored information. For instance, imagery of movement while using a handgrip dynamometer could not be done if no prior knowledge of the movement exists. However, if applicable knowledge about other handgrip devices (staple gun, glue gun) is present, artificial construction of the movement could be produced based on associative knowledge. Imagery neurons have been described in response to imagery of previously viewed stimuli in the

middle temporal lobe, which may represent the retrieval of picture information from memory (Kreiman et al., 2000). In addition to imagining motion or objects, seeing a word or hearing a word representing the object or motion, or even hearing a sound associated with motion (e.g. footsteps) or an object (e.g. ball bouncing) will also result in semantic memory activations (Martin, 2001). Martin (2001) also suggests that features and attributes defining an object in semantic memory are stored in perceptual and motor systems active when we first experienced the object. This might explain why activated areas in ipsilateral cortex in response to unilateral movements are similar to the contralateral activation, and why imagined movements show very similar activation patterns as actual movements. Martin (2001) went further, contending that knowledge about the sequence of motor movements associated with the use of objects is stored near the motor systems activated when the object is manipulated. Imagery of moving objects with the right hand has been associated with ventral premotor cortex activation similar to what is observed when subjects were naming tools (Martin et al., 1996; Gerardin et al., 2000). This indicates that motor function is systematically arranged in the cortex to provide efficient retrieval of information needed to process appropriate movement, allowing quick response if necessary. If semantic representations play a role in cross-education and imagery, it might be reflected by activation in temporal lobe regions associated with motion perception. Cross-education of strength could be controlled by bilateral semantic representation of an altered motor plan. In the case of motor imagery, semantic representations of movement stored in cortex could be responsible for kinesthetic sensations and neural activity during imagery training and could lead to strength gain.

Perhaps closely linked to semantic representation of movement are mirror neurons (Rizzolatti et al., 1996a; Rizzolatti et al., 1998; Buccino et al., 2001). Mirror neurons might play

a role in ipsilateral activation with unilateral movement, and could be relevant for cross-education. Prefrontal and parietal regions are activated during imagery of someone else performing a given task (Ruby and Decety, 2001; Buccino et al., 2001). Mirror neurons encoded for a particular task are activated during observation of the same actions being performed by another (Murata et al., 1997; Rizzolatti et al., 1998; Buccino et al., 2001). Ventral premotor cortex (F5) in the primate shows strong associations with regions activated in anterior intraparietal sulcus (AIP) (Rizzolatti et al., 1998), which is also activated during object grasping and presentation (Sakata et al., 1995). Although these findings are mainly in primates, humans show evidence of a similar ‘observation/execution matching system’ while observing movement (Rizzolatti et al., 1996b; Binkofski et al., 1999; Buccino et al., 2001). Human fMRI work has also shown ventral premotor cortex (Brodmann’s area 44, Broca’s area) and secondary somatosensory cortex (S2) activation during object manipulation with the fingers (Binkofski et al., 1999) providing evidence for a similar parietal-frontal projection as described in primates (Rizzolatti et al., 1998). Binkofski et al. (1999) suggested that activation in anterior intraparietal sulcus (S2) in humans likely corresponds to AIP activation in primates. Activation of Broca’s area in humans may imply encoding of lexical information (relating to words or the vocabulary of a language) about the object being manipulated- perhaps in semantic memory.

Evidence of parietal-frontal interactions with object manipulation in humans and primates has led researchers to develop models representing a ‘mirror neuron system’ within the cortex (Oztop and Arbib, 2002). The concept of the mirror system might be pertinent for skill acquisition, especially in terms of evaluating aspects or sequences of performing a task properly based on the observation of another. Mirror neurons could provide the basis for storage of images about previously acquired movement, but not novel tasks since the task has not yet been

acquired. A 'hand-state hypothesis' has been presented implicating the motor system in recognizing an action in terms of appropriate feedback or 'hand-state' data from the control of manual object grasping (Oztop and Arbib, 2002). The hypothesis operates on the notion that 'hand state' provides retrievable data required to formulate a grasp movement appropriate for the particular position and shape of an object. The mirror system may reflect an understanding of visually presented actions through the ability to transfer hand state data from one hand to the other (Oztop and Arbib, 2002). Buccino et al. (2001) have also demonstrated the role of the mirror system for other actions such as foot, mouth, and jaw movements. They observed somatotopically organized activation of premotor cortex with each different motor observation. Mirror neurons may be involved in movement information encoding in humans and are activated with subsequent observation of the movement. Hence, a familiar unilateral movement could activate relevant mirror neurons in both cortical hemispheres. Perhaps directly related to cross-education and imagery training, ipsilateral mirror neurons might be observing or gaining an understanding of movement while it is being executed by the opposite side. Of course, this implies a strong contribution of acquiring visual information during the movement. It is also clear that mirror neurons are likely related to semantic memory in some manner. Observing movement is probably associated with object and movement comparison with stored semantic knowledge. Reasonably, the benefit of these comparisons is accessible for both limbs in the case of unilateral acquisition.

1.2.5 Mechanisms of Cross-education of Strength

The neuro-physiological mechanisms controlling cross-education of strength are probably related to those controlling interlateral transfer of skills. The particular neural adaptation is some

form of motor learning, but the problem is that the neural basis of motor learning has remained elusive and is still the topic of extensive study (Willingham, 1998; Ioffe, 2004). Intuitively, motor learning research has concentrated on adaptation in areas of the brain relevant for movement including motor and premotor areas, sensory areas, basal ganglia, and cerebellum (Ioffe, 2004). Historically, much of what we know about the contributive role of brain areas has come from animal lesion studies (Ioffe, 2004). More recently, functional imaging techniques (i.e. PET, MRI) have made it possible for in depth study in humans, where lasting changes in activation patterns of brain structures have been demonstrated with motor learning (Ioffe, 2004). The proposed mechanisms of motor learning have centered around modifications in neural output, new synapses, adaptation of networks or populations of synapses through long-term potentiation (LTP) and/or long-term depression (LTD), and changes in cortical processing (Sanes and Donoghue, 2000). The difficulty in applying mechanisms of motor learning to cross-education of strength is the query of how neural information gained from training one limb is easily transferred to the untrained limb. This problem has led to speculation about whether this information is transferred in the brain and spinal cord (CNS), or in peripheral neural circuits.

1.2.5.1 Plasticity in the Brain

When lasting or permanent adaptation occurs in cortical and sub-cortical structures in response to repetitive stimuli it is referred to as plasticity. Plasticity results in the formation of new synapses or connections in the brain, and can lead to a larger area of activation in relevant cortex with motor learning (Pascual-Leone et al., 1994; Karni et al., 1995; Pascual-Leone et al., 1995). Motor learning has been associated with permanent plasticity or LTP/LTD within neural networks mediating the execution of a particular task (see reviews by Sanes and Donoghue,

2000; Sanes, 2003). Cross-education of strength could involve plasticity in brain areas relevant for the untrained limb, although no study to date has used functional imaging to determine if this is the case. Motor learning of skilled tasks and sequences has shown evidence of plasticity in M1 (Karni et al., 1995; Sanes and Donoghue, 2000; Sanes, 2003), PMC and SMA (Grafton et al., 1995; Grafton et al., 2002), basal ganglia (Jueptner et al., 1997) and cerebellum (Jueptner et al., 1997; Sakai et al., 2002).

Further evidence suggests plasticity can be associated with increased or decreased activation in the brain. Several functional imaging studies have shown cortical reorganization or shifting activations with motor learning (Jueptner et al., 1997; Shadmehr and Holcomb, 1997; Van Mier et al., 1998; Pearce et al., 2000; Staines et al., 2002; Ward et al., 2003). Therefore, plasticity may be associated with new activations in previously inactive regions (LTP) or deactivation of previously active regions (LTD). Ward et al. (2003) showed evidence of functional reorganization with re-learning during stroke recovery. Patients with poor recovery of motor skills displayed irrelevant motor cortex activation during hand grip movement as compared to patients with good recovery. Re-learning was associated with decreased functional activation. Cross-education of strength could involve plasticity in a similar way, perhaps by changing how activated brain regions are lateralized in response to unilateral training.

Plasticity in M1 could be particularly relevant for cross-education of strength as it has been shown to play a role in the early consolidation of learning motor skills (Muellbacher et al., 2002). When M1 activity is disrupted, performance improvements or practice changes are impaired (Ziemann et al., 2001; Donchin et al., 2002; Muellbacher et al., 2002; Sohn et al., 2002). Motor adaptation in M1 is also thought to include LTP and LTD. LTP would imply that the excitatory synaptic potential in M1 would be elevated in response to learning over days or

weeks, whereas LTD would imply the opposite effect to M1 neurons that might interfere with task acquisition. In a practical sense, LTP and LTD may improve coordination of movement by increasing activity of M1 neurons associated with descending signal to agonists, and decreasing activity of M1 neurons projecting to antagonists (decreasing co-activation). Decreased co-activation has been documented as a potential motor learning adaptation for strength tasks (Aagaard et al., 2000). Evidence of this adaptation might be reflected in synaptic plasticity within M1 with motor learning (Rioult-Pedotti et al., 2000).

Plastic changes in sub-cortical structures such as cerebellum and the basal ganglia could also be relevant for cross-education of strength. The cerebellum is known to reflect LTP and LTD with motor learning (Ito, 2000; Sanes, 2003) and is also involved in temporal processing of movement (Ivry, 1997; Ivry and Spencer, 2004). Cerebellar plasticity could lead to more precise timing of agonist, antagonist, or synergist muscle activation resulting in improved coordination. Motor learning in the cerebellum is evidenced by changing levels of inhibition to Purkinje fibers (the only output neurons from cerebellum) from mossy and climbing fibers (cerebellar excitatory afferent fibers) in cerebellar circuits (Ghez, 1991). Ito (1984) suggested that the climbing fibers depress the activation of granule cells (synapse with Purkinje fibers via parallel fibers) in cerebellum in response to a novel task. With a novel task, high levels of error signal will be sent to the cerebellum through climbing fibers. Once the task is learned, activity of climbing fibers on granule cells diminishes (decreased error). As summarized by Ito (2000), LTD is reflected in the interaction between climbing fibers and granule cells. When climbing fiber impulses reach the Purkinje cells at the same time as input from granule cells, the activity of granule cells on the Purkinje cells is persistently suppressed. In this way, LTD is thought to be a memory mechanism in the cerebellum and contributes to motor learning (Ito, 2000).

Another major function of the cerebellum is to compare actual movement with intended in order to shape ongoing movement and improve accuracy (Ghez, 1991). This feedback mechanism is likely active in motor learning through activity of climbing fibers. Error signals are thought to drive the process of LTD in the cerebellum, reshaping cerebellar circuits in the direction that minimizes error associated with movement (Ito, 1989). Similar to M1, impairing cerebellar activity also impairs learning response (Ito, 2000). Neural adaptation with cross-education of strength could involve cerebellar LTP and LTD, especially if the task is complex and requires extensive rehearsal in order to master.

The role of the basal ganglia in motor learning cannot be overlooked, and their contribution to movement is far from simplistic. Basal ganglia nuclei including caudate, putamen, and striatum have shown plasticity in response to motor sequence learning (Grafton et al., 1995; Jueptner et al., 1997). Perhaps the best summary of the contribution of basal ganglia to movement is its involvement in information processing needed for planning and triggering movement and organizing postural adjustments (Ghez and Gordon, 1995). The basal ganglia receive input from all other cortical regions and project to the thalamus before returning to premotor areas and M1 (Ghez, 1991; Latash, 1998). Importantly, the basal ganglia show firing rate changes primarily after the initiation of movement, suggesting a more important role for the continuation and modulation of movement while it is ongoing (Latash, 1998).

Basal ganglia are also thought to be linked with the cerebellum in motor learning (Doya, 2000), but participate more in reinforcement-based learning rather the error-based learning more relevant for the cerebellum (Doya, 2000). The reward signal in the basal ganglia is encoded in the dopaminergic fibres of the substantia nigra in response to reinforcing stimuli (Schultz, 1998; Doya, 2000). Reward based activity in basal ganglia could be part of LTP with motor learning,

but contingent upon error-based learning in the cerebellum (i.e. movement must be scanned for error before reinforcement can be given). Doya (2000) is not the only author to suggest a link between the basal ganglia and the functions of the cerebellum. The basal ganglia have also been linked to temporal processing in a pacemaker and gating role (Ivry and Spensor, 2004), although controversy exists over the precise contribution to timing.

The basal ganglia could be part of the link between plasticity in M1 and cerebellum. Theoretically, successful movement could be determined by cerebellum and when the signal is relayed to the basal ganglia nuclei, plasticity could lead to permanent alterations in stored motor programs in M1. In this way, plasticity in basal ganglia would be relevant for cross-education of strength. Functional MRI studies have shown bilateral activation of basal ganglia nuclei with unilateral hand movements (Gerardin et al., 2000). Perhaps with unilateral movement, the basal ganglia restrict projections to ipsilateral M1 (resting limb), but still relay commands through the thalamus and ipsilateral premotor areas normally associated with ongoing movement or movement acquisition.

1.2.5.2 Bilateral Cortical Activation

The interaction between cortical hemispheres during unilateral movement is a potential mechanism for transfer of strength or skills between limbs. Bilateral activation of M1, PMC, and SMA has been demonstrated previously with unilateral movement (Kristeva et al., 1991; Toma et al., 1999; Ehrsson et al., 2000; Liu et al., 2000; Gerardin et al., 2000; Binkofski et al., 2000; Nirkko et al., 2001). SMA might have particular importance for cross-education, since it is involved in complex movement programming and motor planning (Ghez and Gordon, 1995) and mediating intrahemispheric connections (Rouiller et al., 1994). Nirkko et al. (2001) found that

regardless of which side of the body was moving, left SMA and PMC were always more activated than right- perhaps indicating left hemisphere dominance. Kim et al. (1993) reported left motor cortex activation in both right and left-handed subjects with left limb movement, providing further evidence for the idea of left hemisphere motor dominance (Taylor and Heilman, 1980). However, a more recent study by Borowsky et al. (2002) shows strong evidence of strict contralateral control (14/16 subjects) using a touch paradigm. The two remaining subjects, who did not show an obvious contralateral advantage, reported using a verbal mediation strategy which likely contributed to activation in the ipsilateral cortex. As such, there seems to be conflicting evidence for the existence of left hemisphere motor dominance. The left hemisphere does seem to show strong dominance for language in both left and right-handed individuals, not surprisingly exaggerated with execution of speech (Kupfermann, 1995). Older literature suggests most people are left hemisphere dominant for language regardless of handedness (Rasmussen and Milner, 1977). Ninety-six percent of right-handers and 70% of left-handers show left hemisphere dominance for language (Rasmussen and Milner, 1977). In relation to the dominant hand, right-handers exhibit far more consistency toward contralateral hemisphere dominance for language than left-handers (Rasmussen and Milner, 1977). Together, this evidence seems to support the access model, assuming a more prevalent role of the left hemisphere for motor learning, providing preferential access for the right hand for future movement. The idea of language dominance in the left hemisphere could provide support for the link between semantic memory and movement (left temporal lobe) discussed earlier (Martin, 2001). Earlier praxis models also support the link between semantic memory and movement suggesting the operation of two subsystems: a conceptual system and a production system (Roy, 1983), where the former provides perception and language knowledge for action, and the latter provides the mechanism

for execution. More recent research by Joshi et al. (2003) confirms a link between language and movement, in that apraxia (loss or impairment of the ability to execute complex movements or gestures) was consistently observed in individuals with primary progressive aphasia (a slowly progressive language deficit). Interestingly, apraxia after left hemisphere stroke correlates with the presence of aphasia and other cognitive deficits (Zwinkels et al., 2003).

1.2.5.3 Adaptations in Muscle Activation Patterns

Several studies have documented that maximal activation during muscular contractions may be limited by neural inhibition or incomplete activation, especially during eccentric contractions at high velocity, serving as a protective mechanism to prevent injury (Westing et al., 1990; Westing et al., 1991; Aagaard et al., 2000; Seger and Thortensson 2000; see reviews by Stauber, 1989; Kellis and Baltopoulos, 1995). Further, training results in more complete activation of motor units (Aagaard et al., 2000). Adams et al. (1993) demonstrated incomplete activation by estimating muscle activity using MRI (muscle proton spin-spin T_2 relaxation time). They found untrained subjects could only activate approximately 70% of muscle during maximal voluntary contraction. Motor learning with training seems to lead to increased muscle activation, and is the likely mechanism for strength increase without hypertrophy. Increased muscle activation may also be involved in cross-education of strength. Previous research has shown cross-education of strength is accompanied by increased EMG activity (Moritani and deVries, 1979; Yue and Cole, 1992; Hortobágyi et al., 1997), reflecting increased motor unit recruitment in the untrained limb.

Neural integration within the nervous system is a very complex process and leads to speculation about neuro-physiological adaptation with task acquisition. Motor unit nuclei are

inhibited or excited by corticospinal tract neurons in ventral roots of the spinal cord (grey matter), or by local interneurons as part of peripheral neural circuits (Ghez and Gordon, 1995). Inhibition descending from cortex and terminating in corticospinal tracts called distal inhibition (Martin and Jessell, 1995). Reciprocal inhibition refers to signal from agonist muscle afferents to Ia inhibitory interneurons, resulting in inhibition of the antagonist muscle (Martin and Jessell, 1995). Recurrent inhibition occurs through the activity of Renshaw cells which feedback to α -motoneurons directly without activation of the afferent loops (Enoka, 2002). Practically, these neural integration scenarios can produce varying levels of inhibition/excitation resulting in increased or decreased force during muscular contraction. For instance, a fixed level of excitatory input with less inhibitory input to α -motoneurons will increase force production to a similar extent as increasing efferent excitatory input alone. Muscle force also increases when less afferent input is relayed to interneurons by muscle receptors, or where more inhibitory input is relayed to the antagonist α -motoneuron by local interneurons or motor cortex. These scenarios demonstrate how seemingly infinite combinations of excitatory and inhibitory input can increase contraction force (Agostino et al., 1992). The question of which mechanism is preferentially controlled by the CNS during movement has been the target of many motor control theorists for years (Latash, 1993). Many of these theories aim to solve Bernstein's problem of degrees of freedom or motor redundancy, also known as motor 'abundance' (Latash, 1993). In other words a motor task can be performed with the same joint torques and with the same end result using seemingly infinite combinations of γ -motoneuron, α -motoneuron, and muscle afferent activity (Prilutsky and Zatsiorsky, 2002).

Improvement in agonist-antagonist coordination leading to more complete activation of the agonists may account for cross-education of strength. In terms of neuro-physiological

mechanisms, agonist activation or agonist-antagonist interaction has been the focal point of most studies on cross-education of strength (Moritani and deVries, 1979; Carolan and Cafarelli, 1992; Weir et al., 1994; Hortobágyi et al. 1997; Hortobágyi et al., 1999; Ebersole et al., 2002; Shima et al., 2002). Most studies have reported an increase in untrained agonist muscle activation with cross-education (Hortobágyi et al. 1997; Hortobágyi et al., 1999; Shima et al., 2002). Carolan and Cafarelli (1992) found 16.2% cross-education of strength, coupled with a 13% decrease in antagonist co-activation. Greater inhibition of the antagonist muscle group during agonist contraction would obviously decrease opposition for the intended movement, increasing force production. Co-activation is mediated by the CNS and spinal interneuron integration of muscle afferents. Interneurons stimulated by muscle afferents synapse with other α -motoneurons innervating the antagonist muscle groups (Ghez and Gordon, 1995). Ia afferent input from agonist muscle spindles causes excitation of the agonist and inhibition of the antagonist. Conversely, Ib afferent input from the agonist Golgi tendon organ causes inhibition of the agonist and excitation of the antagonist. Therefore high afferent input to the spinal cord from muscle spindles (regulates muscle length) and Golgi tendon organ (regulates muscle tension) during contraction would lead to agonist-antagonist co-activation (Ghez and Gordon, 1995). This may explain why incomplete activation is apparent with eccentric training (Aagaard et al., 2000; Seger and Thortensson 2000) since muscle force production is greater (Hortobágyi et al., 1990a; Farthing and Chilibeck, 2003b), and the muscle is undergoing forced stretch during contraction. These conditions likely result in high afferent activity from muscle spindles and Golgi tendon organ. Refer to Figure 1.3 for an illustration of the influence of Ia and Ib afferents and recurrent inhibition on agonist-antagonist coordination.

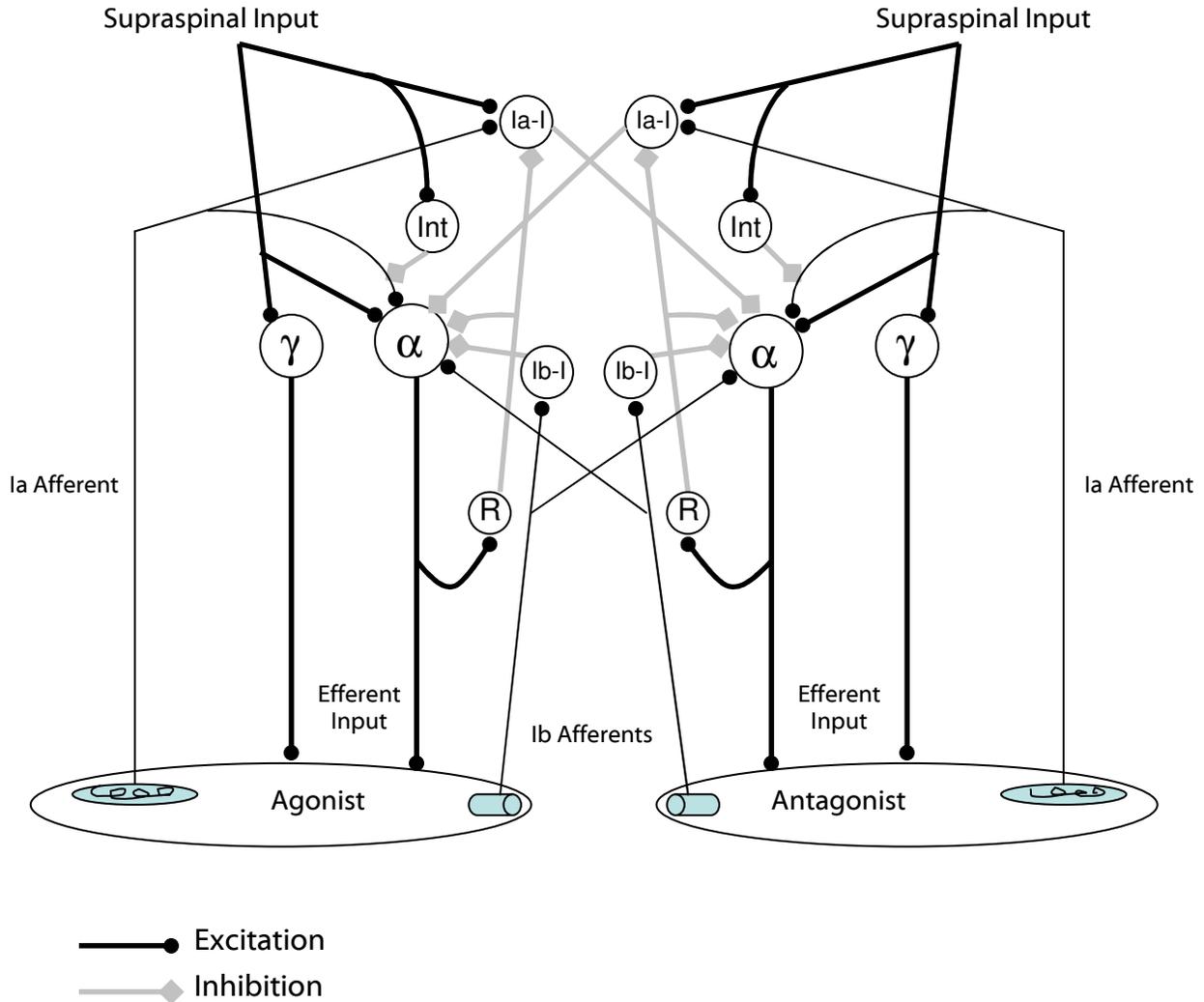


Figure 1.3 The influence of muscle afferents and recurrent inhibition on agonist-antagonist coordination. Activity of Ia and Ib afferents influences the integration of alpha (α) and gamma (γ) motoneuron inputs through Ia interneurons (Ia-I) and Ib interneurons (Ib-I). Supraspinal input can inhibit muscle afferents through interneurons (Int). Recurrent inhibition via Renshaw cells (R) influences agonist-antagonist coordination without supraspinal input. Adapted from Enoka, 2002, page 305, figure 6.65.

Co-activation is not a new concept in the literature, although its purpose was not always clear. Enoka (1997) described it as a protective strategy when there is uncertainty or unfamiliarity about a given task- common in any unfamiliar or complex experimental conditions. Therefore task complexity and unfamiliarity is likely to have a drastic effect on muscle activation. Complex resistance training exercises (i.e. multi-joint) have been shown to produce more incomplete agonist activation in comparison to simple exercises (i.e. single-joint) (Chilibeck et al., 1998). More complete activation after training is a peripheral candidate mechanism for cross-education of strength, but exactly how the body conveys this information to the opposite side of the body is still unclear. As referenced to earlier, plasticity in the brain may be linked to the mechanism.

1.2.5.4 Increased Excitability of the Contralateral Musculature

Hortobágyi et al. (1999) argue that afferent activity from activated muscles during unilateral movement could increase excitability of the contralateral musculature. They found electromyostimulation (EMS) training more effective for cross-education than voluntary training, and proposed that neurons innervating contralateral muscle fibers could be activated through pain receptors and skin sensory afferents active during EMS. They further suggested EMS training produced greater excitation of Group Ia afferents (muscle spindles)- which would result in agonist excitation and antagonist inhibition within the contracting limb, and agonist inhibition and antagonist excitation in the contralateral limb (described as the crossed extension reflex- Rothwell 1987). Hortobágyi et al. (1999) theorized that Group Ia excitation might strengthen excitatory synaptic transmission in the contralateral musculature leading to better strength performance. However, if the crossed-extension reflex was responsible for increased excitability of the contralateral muscles, the contralateral antagonistic muscle group and not the homologous

muscle group would be expected to show increased activation. Some research has shown modulation of cortical excitability in both hemispheres after unilateral fatiguing muscle activity (Bonato et al., 1996), but our recent work revealed very negligible activation of the contralateral homologous musculature during unilateral training (Farthing and Chilibeck, 2003a). Some activation of the muscle might be expected if excitability was increased during contraction of the opposite limb. Worthy of mention, descending motor axons from motor cortex can directly excite spinal motor neurons as well as send collaterals to Group Ia inhibitory interneurons (Ghez and Gordon, 1995). Therefore, motor signal from both local and higher motor centers can independently influence muscle activation, and the mechanisms controlling cross-education of strength could be controlled by a combination of cortical adaptation and inter-limb communication at the spinal level.

Recent research by Aagaard et al. (2002) provides evidence for increased motor unit excitability after a period of resistance training (assessed by the Hoffmann reflex and supra-maximal evoked V-wave). Unilateral resistance training may increase motor unit excitability for both limbs and this could be a potential mechanism of cross-education of strength. V-wave increase is thought to reflect heightened efferent motoneuron activity (Aagaard et al., 2002) or reflex potentiation (Sale, 1988). The H-reflex reflects spinal loop excitability at rest and the V-wave (V1) reflects spinal loop excitability during volitional activation (Duchateau and Enoka, 2002). The V-wave is essentially a variant of the H-reflex, but is recorded during MVC. The potential contribution of increased muscle excitability to cross-education of strength awaits further research. To our knowledge no study has measured untrained muscle motor unit excitability by H-reflex or V-wave before and after unilateral resistance training.

1.2.5.5 Corticospinal Tract Impulses

Corticospinal tracts could be the CNS location where motor control information is relayed from one side of the body to the other. Lateral corticospinal tract nerves (~75% of total tract) conduct impulses from the motor cortex of the brain to motor neurons in the spinal cord and descend contralaterally, after decussating at the medullary pyramid in the brainstem. However, approximately 25% of the corticospinal tract descends ipsilaterally as part of the ventral corticospinal tract (Ghez and Gordon, 1995). The lateral corticospinal tracts project to the contralateral motor nuclei of the ventral horn and to interneurons in the intermediate zone (Martin and Jessell, 1995). Ventral corticospinal tracts descend more medially and project bilaterally at the appropriate level of the spinal cord to the medial cell group controlling axial muscles (Martin and Jessell, 1995). The ventral tracts are apparently involved in posture stabilization by controlling axial musculature, or at least are involved in the integration of descending signals targeting axial muscles. Activity in the ventral corticospinal tract has been proposed as a mechanism for cross-education by causing co-activation of homologous muscles (Hellebrandt, 1951). During unilateral movement the ventral corticospinal tracts could provide motor control information about postural stabilization that is easily applied to the opposite side of the body. Studies have shown negligible activity of the opposite homologous musculature during training (Hortobágyi et al., 1997; Farthing and Chilibeck, 2003a), and several studies have shown no significant muscle hypertrophy (Houston et al., 1983; Narici et al., 1989; Hortobágyi et al., 1996; Hortobágyi et al., 1997; Farthing and Chilibeck, 2003a), but no study to date has assessed the activation of postural or trunk muscles with cross-education of strength.

The ventral corticospinal tracts could also contribute to motor learning in higher levels of the nervous system through interaction with the reticular formation in the brainstem. Aside from

being involved in postural maintenance, the reticular formation is highly active for integration of various neural inputs and is responsible for both excitatory and inhibitory connections with spinal and motor neurons through the reticulospinal tract and is actively involved in motor learning (Ghez and Gordon, 1995). Relative to inter-limb effects such as cross-education, neural drive patterns could be reprogrammed in both cortical hemispheres through the reticular formation, leading to improved agonist-antagonist coordination in both limbs after unilateral training.

1.2.6 Origins of fMRI

The rationale of fMRI operates on a fairly simple premise- it identifies brain regions that are preferentially utilizing oxygen during the execution of a given task (i.e. cognitive or motor) or when responding to stimulus (i.e. visual, auditory). However, the method by which MRI signal is converted into functional activation maps is quite complex. fMRI is contingent upon the blood-oxygen-level-dependent (BOLD) signal, first described by Ogawa et al. (1990). The origins of BOLD come from the effect of oxygen transfer in the brain on the MRI signal. In fMRI, the signal comes from ensembles of ensembles (mesoscopic level) of Hydrogen protons from water (Sarty, 2004). Thulborn et al. (1982) first observed that the molecular change from oxyhemoglobin (diamagnetic) to deoxyhemoglobin (paramagnetic) decreased signal intensity by causing shortening of the transverse magnetization relaxation time (T_2 relaxation) of water protons in the blood. The use of MRI for functional brain imaging emerged with the realization that cerebral blood flow (CBF) changed out of proportion with the exchange of oxygen in the brain, and fluctuating levels of deoxyhemoglobin could be detected. Ogawa et al. (1990) later discovered the T_2^* shortening effects of deoxyhemoglobin, and coined 'BOLD'. BOLD signal in

fMRI is detected from the effects of deoxyhemoglobin on T_2^* Decay (mesoscopic level) (Sarty, 2004). The paramagnetic property of deoxyhemoglobin allows it to be used as an indigenous contrast agent, causing an inhomogeneous magnetic field (Forster et al., 1998). This in turn causes dephasing of the frequency of the surrounding proton spins, and decreased signal intensity (Forster et al., 1998). Signal intensity will increase by up to 5% at 1.5T (T= tesla, i.e. magnet strength) in areas with low deoxyhemoglobin levels (or high oxyhemoglobin; areas of activation) (Connelly et al., 1993). Therefore, BOLD is essentially an indirect measure of neural activity since activated brain regions will be characterized by greater oxygen use and increased regional CBF (Arthurs and Boniface, 2002).

MRI signal itself is generated by Hydrogen protons in the body tissue being imaged by tipping the precession of the spins away from the direction of the main magnetic field using precisely timed and targeted radio frequency (RF) pulses. The timing of pulse sequences and gradient reversals in fMRI imaging can influence the sensitivity of the magnetic susceptibility effects of deoxyhemoglobin, or the ability to detect changes in T_2^* decay (Forster et al., 1998). For instance, spin-echo sequences refocus the signal (using a 180° RF pulse at a precise time after the initial 90° RF pulse) in order to record the signal. Gradient-echo imaging techniques use gradient reversal for refocusing instead of a 180° RF pulse, and thus are more sensitive to the effects of deoxyhemoglobin (Forster et al., 1998). The goal of all fMRI sequences seems to be decreasing acquisition time without sacrificing spatial resolution and BOLD sensitivity. Since functional data (BOLD response) is detected with less spatial resolution than anatomical images, activation maps are usually overlaid onto high resolution T_1 weighted anatomical images (axial, coronal or sagittal), or rendered into 3D and overlaid onto an average brain (Talairach ellipsoid). A registration problem with this technique creates a margin of error (4-5mm) in determining the

anatomical location of activated brain regions, which can be somewhat reduced by blurring the functional data.

Since the BOLD signal is dependent on the presence of deoxyhemoglobin, it is physiologically dependent on the hemodynamic response to brain activity. Thus, BOLD signal is related to CBF and the cerebral metabolic rate of oxygen consumption ($CMRO_2$). When BOLD signal is detected by MRI, cerebral blood flow (CBF) to an activated brain region changes disproportionately to the change in oxygen consumption (Kim and Ugurbil, 1997). To elaborate, when a brain region is activated the immediate consumption of oxygen causes an initial increase in the level of deoxyhemoglobin. Once oxygen is depleted from the tissue, the demand for oxygen for continued activation causes an increase in CBF. Along with the increase in CBF is an increase in oxyhemoglobin to the tissue. This influx usually super-cedes the oxygen demands of the tissue and oxygenated blood floods the tissue, thus decreasing the signal generated from deoxyhemoglobin and increasing BOLD signal intensity (Raichle, 2001). Paradoxically, regions of activation in fMRI are characterized by increases in oxyhemoglobin and decreases in deoxyhemoglobin. The relationships described above indicate that despite originating from deoxyhemoglobin, the BOLD response function most resembles that of CBF, at least in time course of change (refer to Figure 1.4).

Given all this, what does the BOLD signal represent from a neuro-physiological perspective? Active brain cells consume oxygen and are metabolically active, but does BOLD reflect increased energy expenditure or neural output, or is it detecting cortical processing of brain tissue? Logothetis et al. (2001) addressed the dilemma of what is detected by BOLD in fMRI. They simultaneously measured BOLD and intracortical cell recordings in monkeys, and concluded that BOLD response was highly correlated to local field potentials (LFPs) as

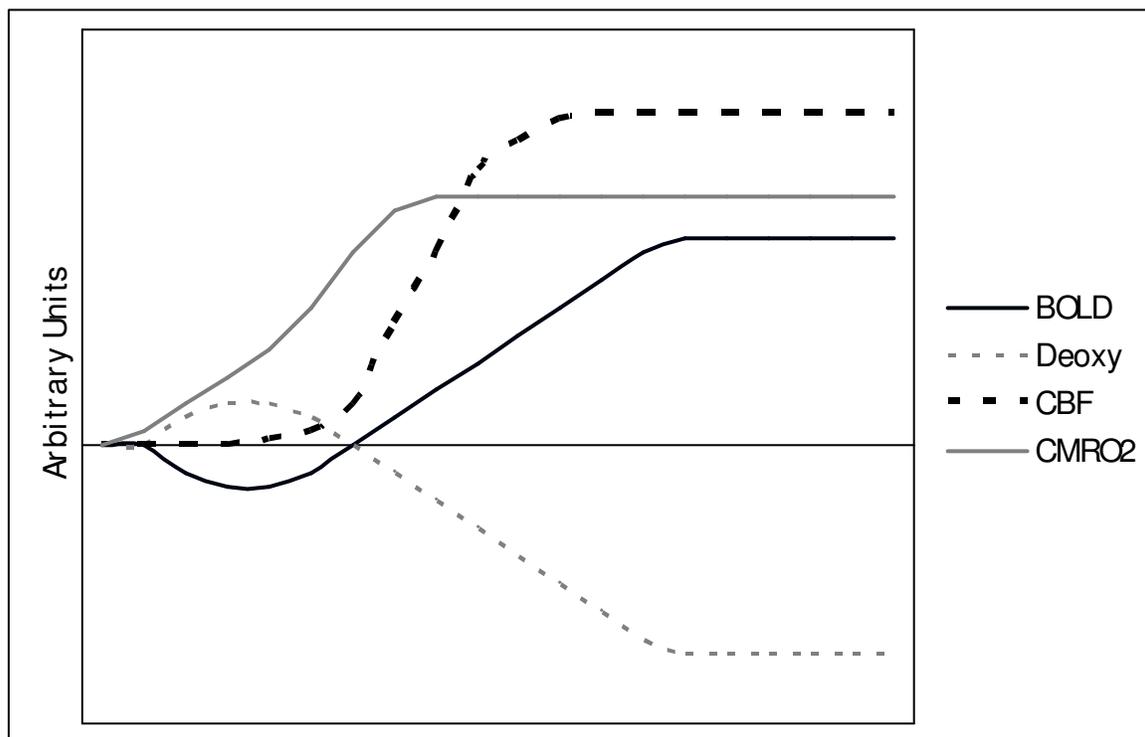


Figure 1.4 The relationship between BOLD and the hemodynamic response. BOLD function is most similar to CBF and is inversely proportional to changes in deoxyhemoglobin. Adapted from Sarty (2004).

compared to single and multi-unit activity (MUA). As outlined by Logothetis et al. (2001), LFPs reflect a weighted average of the input signal to a neural population, whereas MUA reflects the output of a neural population. In the experiment, only LFPs remained elevated for the duration of stimulus, and showed a stronger increase in response to stimulus than MUA. Logothetis et al. (2001) concluded that BOLD reflects the input and cortical processing in an activated region (including excitatory and inhibitory interneurons) rather than only output activity (MUA), and therefore is a better representation of total neural activity. Consistently, a recent review by Lauritzen and Gold (2003) concluded that CBF and BOLD reflect afferent input function including all aspects of pre and post-synaptic processing in active regions, and not efferent output activity.

Despite the findings of Logothetis et al. (2001), there is still speculation about the ability for fMRI BOLD to detect the activity of populations of neurons (Arthurs and Boniface, 2002). Even at the voxel level, fMRI is still detecting vastly numerous neurons. Controversy exists as to whether fMRI can distinguish between small activity changes in large populations of neurons, or large changes in small populations of neurons (Arthurs and Boniface, 2002). Assuming fMRI signals represent the activity of populations of neurons, it would be sensitive to adaptations in synchronization and firing rate (Chawla et al., 1999), but might not detect neural reorganization or plasticity where overall firing activity in neural populations is unaltered (Arthurs and Boniface, 2002). More recent research by Arthurs and Boniface (2003) concluded that BOLD correlated highly with somatosensory evoked potential amplitude, suggesting that fMRI signals reflect underlying electrophysiology in the brain.

Functional MRI is used in the present project as a method of detecting central nervous system adaptation after a period of unilateral arm training, as reflected by changes in activation

patterns. The high spatial resolution of fMRI is desirable for detecting subtle changes in activation within a given brain region. Cortical plasticity cannot be proven using fMRI, but brain regions displaying changes in activation will be presented as indicators of central nervous system adaptation in response to training.

1.2.7 Statement of the Problem

Cross-education of strength has conclusively been attributed to neural mechanisms since strength gain in the untrained limb occurs with no morphological change (Moritani and deVries, 1979; Garfinkel and Cafarelli, 1992; Seger et al., 1998; Farthing and Chilibeck, 2003a). However, the neuro-physiological mechanisms of cross-education of strength have remained elusive. No study to date has examined cortical adaptation in conjunction with cross-education of strength. Peripheral neural adaptations have been shown in both limbs in response to unilateral training (Carolan and Cafarelli, 1992; Hortobágyi et al., 1997; Hortobágyi et al., 1999; Shima et al., 2002), but these are not consistent across studies and exactly how the information is transferred to the untrained limb is unknown. As mentioned previously, before the neural mechanisms of cross-education of strength can be pursued, the influence of handedness and the direction of transfer must be determined in order to isolate the circumstance in which the effect is most pronounced. Two experiments are required to attempt to determine the neuro-physiological mechanisms behind cross-education of strength. Experiment 1 focuses on the potential role of handedness and the direction of transfer for cross-education of strength. The purpose of experiment 1 is to determine the preferential transfer direction in right-handed individuals, and to determine peripheral neural adaptations in agonist/antagonist activation (EMG) with cross-education of strength.

The purpose of experiment 2 is to examine the nervous system changes associated with cross-education of strength at both the central (fMRI) and peripheral (EMG) level of the nervous system after actual and imagery training. A secondary purpose of experiment 2 is to determine the effectiveness of imagery training for strength and cross-education. Comparing actual and imagery training is also necessary to determine the importance of the role of peripheral feedback for cross-education of strength. Experiment 2 uses the preferred direction of transfer for cross-education of strength in right-handers as determined by Experiment 1.

1.2.8 Hypotheses

1.2.8.1 Experiment 1

1. Cross-education will be greater with left hand training in right-handers based on the theory that cross-education is related to the strength increase in the trained limb (Zhou, 2000; Munn et al., 2004) and training the weaker left limb will likely produce greater strength increase in the trained limb.
2. Agonist-antagonist activation patterns will adapt in a manner beneficial for force production in the desired direction of movement (i.e. increased agonist activation and/or decreased antagonist co-activation).

1.2.8.2 Experiment 2

1. Cross-education of strength will be associated with changes in activation in the brain as evidence of motor learning, and peripheral adaptations in agonist-antagonist coordination beneficial for the desired direction of movement (i.e. increased agonist and/or decreased antagonist activation).

2. In agreement with the findings of Yue and Cole (1992), imagery training will be effective for increasing strength in both the trained and untrained (cross-education) limb.
3. Imagery training will show changes in activation as evidence of motor learning, and peripheral adaptations in agonist-antagonist coordination beneficial for the desired direction of movement.
4. Cross-education of strength and imagery training will be associated with retrieval of semantic memory of movement.

Chapter 2: Experiment 1

Experiment 1 has recently been published in a peer-reviewed exercise physiology journal. Therefore, it is presented as a module in its published form with the exception of the some minor wording changes that were necessary for the conversion to graduate thesis format. The introduction section below repeats key aspects of the review of literature directly pertinent to the purpose of the experiment.

2.1 Introduction

Scripture et al. (1894) described cross-education as the performance improvement in the untrained limb following a period of unilateral exercise training. Early experimental psychology literature also described cross-education as interlateral transfer of a motor skill (Cook et al., 1933a). More recently it has been accepted that cross-education can include the transfer of muscular strength to the untrained homologous muscle following a period of unilateral training, and the transfer of motor skill learning to the untrained muscle (Zhou, 2000). In the present investigation cross-education is referred to as the transfer of strength to the untrained muscle. The magnitude of cross-education of strength is thought to be related to the magnitude of strength increase of the trained muscle; and is approximately 35-60% of the strength increase achieved in the trained muscle (Zhou, 2000; Munn et al., 2004).

Cross-education of strength may depend on the direction of the effect (i.e. from right trained muscle groups to homologous left untrained muscle groups or from left trained muscle groups to homologous right untrained muscle groups) or training of muscle on either the dominant or non-dominant side. Interlateral transfer, defined as the transfer of skill learning following unilateral practice, commonly shows an asymmetrical direction of transfer, either from

right to left or left to right (Stoddard and Vaid, 1996), and may depend on handedness (Parlow and Kinsbourne, 1989). Particular motor tasks transfer in only one direction (Criscimagna-Hemminger et al., 2003), either direction (Morton et al., 2001), or not at all (Teixeira, 1993) depending on the complexity of the chosen skill. However, most interlateral transfer studies support the dominant to non-dominant direction of transfer (Parlow and Kinsbourne, 1989; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996; Thut et al., 1996; Latash, 1999; Criscimagna-Hemminger et al., 2003; Teixeira and Caminha, 2003;). Most cross-education studies have attempted to control for the effect of dominance by training muscle groups on the same side of the body across subjects regardless of handedness.

Muscle activation patterns as determined by electromyography (EMG) of the agonist muscle have been well documented in cross-education studies (Ebersole et al., 2002; Hortobágyi et al., 1997; Hortobágyi et al., 1999; Moritani and deVries, 1979). Most studies have reported an increase in untrained agonist muscle activation coupled with cross-education (Hortobágyi et al., 1997; Hortobágyi et al., 1999; Shima et al., 2002). However, Carolan and Cafarelli (1992) measured agonist and antagonist muscle co-contraction, and found that hamstring co-activation was decreased in the untrained limb after unilateral knee extensor training. Regardless, a training induced increase in force production can occur with increased agonist activation (Hortobágyi et al., 1997; Hortobágyi et al., 1999), decreased antagonist activation (Carolan and Cafarelli, 1992), or increased activation of one or more synergists within a muscle group (Aagaard et al., 2000; Rabita et al., 2000; Shima et al., 2002).

The purpose of the present investigation was to determine the effect of the imposed direction of transfer on the magnitude of cross-education in right-handed individuals. The major hypothesis is that in right-handed individuals, the magnitude of cross-education of strength

would differ with right-hand and left-hand training. If cross-education is proportional to the strength gain of the trained muscle (Zhou, 2000; Munn et al., 2004), then one would predict that training the weaker left side of the body would result in greater strength gains and proportionately greater cross-education. Therefore, a second hypothesis of this study is that cross-education would be greater with left-hand training than right-hand training. A secondary purpose of this study was to examine the muscle activation patterns of both the agonist and antagonist muscles and compare it to the adaptations in muscle activation previously associated with cross-education of strength (Carolan and Cafarelli, 1992; Hortobágyi et al., 1997; Hortobágyi et al., 1999). Since cross-education is a neural adaptation (Zhou, 2000), a third hypothesis is that cross-education of strength would be associated with the peripheral nervous system as changes in muscle activation patterns which would assist force production in the desired direction of movement (i.e. increased agonist activation and/or decreased antagonist activation).

2.2 Methods

2.2.1 Subjects

Ethical approval for the experiment was given by the University of Saskatchewan's biomedical review board for research in human subjects, and all participating subjects gave their informed consent (Appendix C). Thirty-nine right-handed females with little prior resistance training experience in the previous year volunteered for participation in the study. The subject pool was restricted to one gender for purposes of reducing between-subject variation. Prior to any physical assessment, all subjects reported prior resistance training experience if any, declared handedness, and then completed the Waterloo Handedness Questionnaire (WHQ) to

determine the degree of handedness (Bryden, 1977). A score of +20 indicates strong right-handedness, whereas a score of -20 indicates strong left-handedness. Subjects were excluded from the study, if they did not obtain a positive score on the handedness questionnaire. Two subjects from the right-training group and one subject from the left-training group dropped out of the study prior to training.

2.2.2 Design

Prior to the testing protocol, all subjects were familiarized with the testing environment and protocol. Each subject performed two or three low intensity practice repetitions of the strength task to become familiar with the motor requirements. This was to alleviate some of the learning effect that might be attributed to the testing protocol. Subjects later returned to the testing lab for assessment of right and left limb muscle thickness of the posterior medial forearm, followed by right and left limb isometric ulnar deviation peak torque with simultaneous measurement of muscle activation by EMG. Once pre-testing was completed, subjects were randomized into one of three groups: left-training (n=13), right-training (n=12), or control (n=14). Subjects had a mean age of 20.8 ± 0.4 yrs, mass of 65.0 ± 1.5 kg, height of 167.0 ± 1.1 cm, training experience of 3.0 ± 0.6 months, and handedness score of 17.4 ± 0.4 , with no differences between groups. The left-training group trained only their left hand and the right-training group trained only their right hand, whereas the control group did not train. Since the control group had two untrained limbs, the arm that would be designated trained or untrained for statistical comparisons was randomly selected (Farthing and Chilibeck, 2003a). Once training was complete, all participants were again assessed for muscle thickness, isometric peak torque, and EMG in both the trained and untrained limb.

2.2.3 Muscle Thickness

Muscle thickness was measured using B-Mode ultrasound (Aloka SSD-500, Tokyo, Japan) and was completed on both the right and left posterior medial forearm (flexor carpi ulnaris and flexor digitorum superficialis) before and after training. Muscle thickness was assessed prior to any strength assessment. To ensure that the position of the muscle thickness measurements was consistent across subjects, a mark was drawn on the midline of the forearm one-fifth of the distance down from the olecranon process to the distal head of the ulna. Another mark was drawn directly perpendicular and medially 2-3 cm away. This distance varied across subjects depending on the size of their forearm. The perpendicular point would correspond to where the centre of the ultrasound probe would be placed on the bulk of the muscle on the posterior medial forearm. Great care was taken using overhead transparency film, anatomical landmarks (olecranon) and blemishes (moles, scars) on the skin to ensure that identical sites were measured on each testing occasion (Farthing and Chilibeck, 2003a). Reproducibility of the muscle thickness measures were completed on ten subjects 5-7 days apart. Coefficients of variation were 1.4% and 1.5% for the right and left posterior forearm, respectively.

2.2.4 Strength

Isometric ulnar deviation peak torque was assessed on a Biodex isokinetic dynamometer (Biodex System 3, Biodex Medical Systems, Shirley, N.Y.) before and after training for both the right and left arm. The Biodex chair was fully reclined so that the participant was placed in the supine position and the arm was fully extended at the elbow joint. This was done to minimize the contribution of total body movement to peak torque. The hand was pronated in line with the forearm midline to put the hand into neutral position. The task involved the combination of

handgrip strength and ulnar deviation. Therefore, participants were instructed that a forceful handgrip contraction combined with ulnar deviation at the wrist joint produced the most force in the required direction of movement. Participants were prompted with the statement: “Try to twist the handle forward and downwards”. Stabilization belts were fastened across the shoulders and the arm was positioned on a pad and fastened with a Velcro strap. The Biodex wrist attachment was fastened to the dynamometer, and the handle grip was rotated and positioned vertically, perpendicular to the ground. Isometric ulnar deviation was chosen because it is an unfamiliar movement and would maximize the cross-education effect. The exact hand position for the task and the Biodex dynamometer set-up is illustrated in Figure 2.1. Each subject’s Biodex chair and handle positions were recorded and kept on file for the training program. Immediately prior to assessment, each subject was again reminded of the required direction of torque production. Once the subject was positioned, they completed four maximal 2-second isometric contractions, each separated by 30 seconds of rest. The highest peak torque value achieved was used for comparison. Reproducibility of isometric torque was completed on ten subjects 5-7 days apart. Coefficients of variation for the task were 4.9% and 5.8% for the right and left arm, respectively.

2.2.5 Electromyography

Maximal isometric muscle activation as assessed by EMG was collected for the right and left arm during each of the four repetitions on the Biodex for both the primary agonist (flexor carpi ulnaris) and the primary antagonist (brachioradialis). Raw data (volts) were collected using a two-lead EMG (Bagnoli-2, Delsys Inc., Boston, MA) and later converted to mean absolute value (MAV) using the accompanying software (EMGworks, version 2). A reference electrode

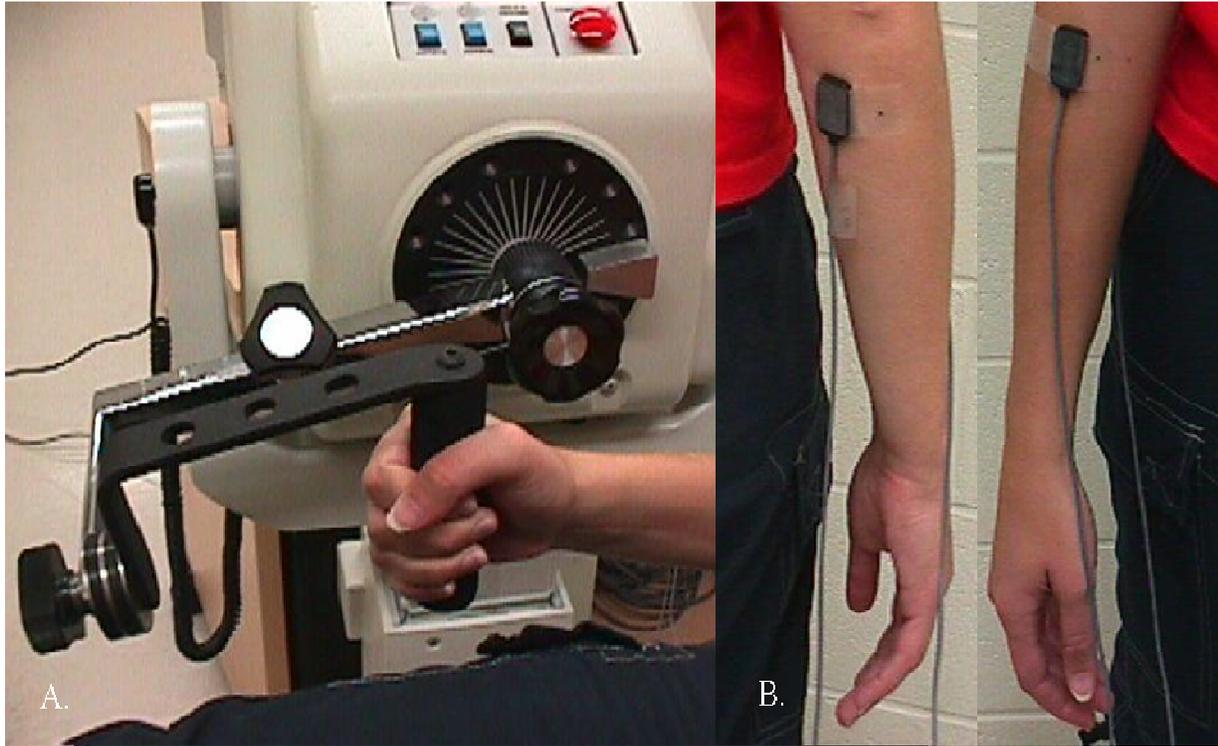


Figure 2.1 Illustration of the Biodex isometric handgrip ulnar deviation strength task set up (A) and EMG electrode placement (B).

(ground wire) was applied to the kneecap with a single conductor. The EMG main amplifier unit included single differential electrodes with a bandwidth of 20 ± 5 Hz to 450 ± 50 Hz, a 12 dB/octave cut-off slope, and a maximum output voltage frequency range ± 5 volts. The overall amplification or gain per channel was 1000 dB. The system noise was $< 1.2 \mu\text{V}$ (rms) for the specified bandwidth. The electrodes were two silver bars (10 mm x 1 mm diameter) spaced 10 mm apart, with a Common Mode Rejection Ratio (CMRR) of 92 dB. The sampling rate was 1024 Hz. The land-marking procedure for the EMG electrode placement was similar to the muscle thickness measures. A mark was drawn on the midline of the forearm one-fifth of the distance down from the olecranon process (or elbow skin crease for the antagonist) to the distal head of the ulna (wrist skin crease for the antagonist). Another mark was drawn directly perpendicular and medially (laterally for the antagonist) 2-3 cm away. This distance varied across subjects depending on the size of their forearm. The perpendicular point would correspond to where the centre of the EMG lead would be placed (Figure 2.1).

In order to compare the amount of muscle activation in the non-training arm to the training arm during training, agonist EMG data was collected for both limbs during one training set five weeks into training. This was done to verify whether the subjects were activating both arms during unilateral training.

Reproducibility of the EMG measurements was completed on ten subjects 5-7 days apart. Coefficients of variation for the left agonist, left antagonist, right agonist, and right antagonist were 13.0%, 17.6%, 15.4%, and 14.1% respectively.

2.2.6 Training Program

The training groups completed six weeks of unilateral isometric ulnar deviation training four times per week for a total of 24 training sessions. Individuals were not allowed to complete post testing until they completed at least 21 of 24 training sessions; therefore, the training program extended into the seventh week for some subjects due to imperfect compliance. The training program was progressive, beginning with 2 sets of 8 repetitions and progressing up to 6 sets of 8 repetitions by the second week. A taper down to 3 sets was used for the last two training sessions to facilitate recovery from any overtraining (Gibala et al., 1994). All subjects trained on the Biodex in identical fashion as described for testing. Each isometric contraction was 2-seconds long and was separated by 2-seconds of rest and was cadenced by a metronome. The rest interval between sets was 30 seconds. The primary researcher was present during the training sessions and provided verbal encouragement. All subjects were allowed to view their real time torque production during training to provide a measure of performance feedback.

2.2.7 Statistics

Strength and muscle thickness data were analyzed using a Group (left, right, control) x Time (pre, post) x Arm (trained, untrained) multivariate analysis (SPSS version 11.5) appropriate for multiple dependent variables with repeated measures. Percent change for strength and muscle thickness was determined by subtracting the post-training from the pre-training score, dividing by the pre-training score and multiplying by 100. This was analyzed using a Group x Arm multivariate analysis to help simplify the results and to allow comparison of the relative magnitude of cross-education. Univariate ANOVA and relevant one-way ANOVA and paired t-tests followed if multivariate significance was found. EMG activation was analyzed using a Group (left, right, control) x Time (pre, post) x Arm (untrained, trained) x Muscle (agonist,

antagonist) ANOVA with repeated measures on the last three factors. EMG was not included in the multivariate analysis because of an additional factor in the design (agonist, antagonist).

Tukey's Post hoc test was used where appropriate. Significance was set at $p < 0.05$.

2.3 Results

2.3.1 Strength and Muscle Thickness

As could be expected with strongly right-handed participants, the left arm was significantly weaker than the right arm for all subjects before and after training, $t(38) = -13.014$, $p < 0.01$ and $t(38) = -8.682$, $p < 0.01$, respectively. There was a significant Group x Time x Arm multivariate interaction for strength and muscle thickness, $\Lambda(4,70) = 0.435$, $p < 0.01$. Univariate ANOVA for strength revealed a significant Group x Time x Arm interaction $F(2,36) = 3.510$, $p < 0.05$. There were significant increases in strength over time for the training arm of the left-training group, $t(12) = -3.836$, $p < 0.01$, the training arm of the right-training group $t(13) = -3.386$, $p < 0.01$, the designated training arm of the control group, $t(13) = -3.154$, $p < 0.01$, and the untrained arm of the right-training group $t(11) = -5.506$, $p < 0.01$. The data for the change in strength over time are presented in Table 2.1.

Univariate ANOVA for muscle thickness revealed a significant Group x Time x Arm interaction $F(2,36) = 20.905$, $p < 0.01$. Muscle thickness of the training arm of the left-training group increased significantly over time, $t(12) = -3.197$, $p < 0.01$. The untrained arm of the left-training group and the designated trained arm of the control group significantly decreased over time, $t(12) = 4.138$, $p < 0.01$ and $t(13) = 4.473$, $p < 0.01$, respectively. Muscle thickness data is presented in Table 2.1.

		Right-training Group		Left-training Group		Control Group	
		(n = 12)		(n = 13)		(n = 14)	
		Pre	Post	Pre	Post	Pre	Post
Strength (N·m)	Untrained	12.3±0.64	17.1±1.6*	18.9±1.0	20.3±0.9	16.4±1.5	18.1±1.7
	Trained	17.9±0.7	22.6±1.7*	11.9±0.8	16.2±1.2*	16.7±1.4	18.5±1.5*
Muscle Thickness (cm)	Untrained	2.86±0.09	2.83±0.09	3.07±0.07	2.92±0.06*	2.97±0.11	2.90±0.08
	Trained	2.93±0.10	2.99±0.09	3.00±0.08	3.16±0.07*	2.99±0.09	2.80±0.07*

Table 2.1 Maximum isometric strength and muscle thickness as a function of test (pre and post) and arm (trained and untrained) for each group (Mean ± SE). *Significantly different than corresponding pre value ($p < 0.01$).

The percent changes for strength and muscle thickness revealed a significant Group x Arm multivariate interaction $\Lambda(4,70)=0.382, p<0.01$. Univariate ANOVA for strength revealed a significant Group x Arm Interaction $F(2,36)=7.871, p<0.01$. Tukey's post hoc test revealed that the relative change for the untrained arm of the right-training group ($39.2\pm 7.8\%$) was significantly greater than the untrained arm of the left-training group ($9.3\pm 4.9\%$; $p<0.05$) and both control group arms ($10.4\pm 5.0\%$; $p<0.05$, and $12.3\pm 4.7\%$; $p<0.05$). The percent change for the training arm of the left-training group ($41.9\pm 13.2\%$) was also significantly greater than the untrained arm of the left-training group ($p<0.01$) and both control arms ($p<0.05$). The relative magnitude of strength change for both the trained and untrained arms is presented in Figure 2.2.

Univariate ANOVA for muscle thickness percent change revealed a significant Group x Arm interaction, $F(2,36)=18.316, p<0.01$. Tukey's post hoc test revealed that muscle thickness percent change for the trained arm of each training group was significantly greater than the designated trained arm of the control group ($p<0.05$). There was no significant difference between groups for muscle thickness change in the untrained limb.

2.3.2 Electromyography (EMG)

The analysis of mean absolute value (MAV) EMG during strength testing was completed on 31 of 39 subjects. Eight subjects' data were excluded due to excessive noise, or poor signal acquisition. Analysis of the data (MAV) revealed a significant Time x Arm x Muscle interaction $F(2,28)=6.019, p<0.05$. Post hoc analysis revealed that EMG activity of the untrained agonist decreased significantly over time pooled across groups, $t(30)=2.117, p<0.05$. The magnitude of decrease in EMG activity of the untrained agonist muscle was not significantly different between

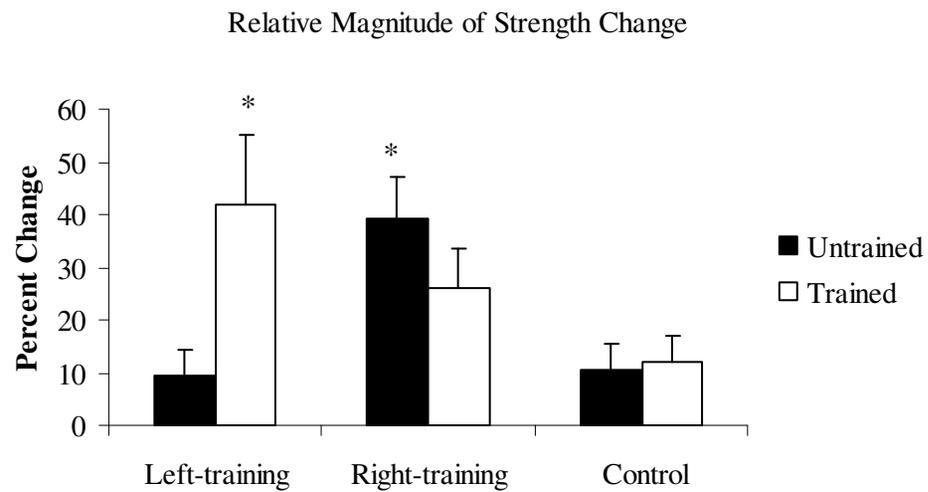


Figure 2.2 Relative magnitude of strength change for the trained and untrained arms for all groups. *Percent change for the untrained arm of the right-training group and the training arm of the left-training group significantly greater than the untrained arm of the left-training group and both control group arms ($p < 0.05$).

training and control groups over time. No significant changes were shown for trained agonist muscle or the antagonist muscle of either arm. EMG activity (MAV) is presented in Table 2.2.

Agonist EMG activity (MAV) in both arms during a typical training set was completed on 22 of 25 training subjects. For the left-training group, agonist EMG activity in the non-training arm and the training arm averaged 16.7% and 96.9% of the corresponding pre training peak isometric EMG activity, respectively. For the right-training group, agonist EMG activity in the non-training arm and training arm averaged 6.7% and 90.8% of the pre training peak isometric EMG activity, respectively.

2.4 Discussion

This study was the first to examine the effect of the direction of transfer on cross-education of strength. The most important finding from this experiment is that cross-education occurred only after training the dominant hand in right-handed individuals, and that no cross-education occurred after training the non-dominant left hand. This was contrary to the hypothesis which predicted cross-education would be greater if the left hand was trained because recent reviews of studies on cross-education suggest that the amount of cross-education is proportional to the increase in strength in the trained contralateral homologous muscle (Zhou, 2000; Munn et al., 2004). Since the left hand is weaker it was also hypothesized that it would improve most with training and cross-education would be proportionate to this increase in strength. Despite a greater improvement in the training arm with left hand strength training, cross-education was greater with right hand training (Figure 2.2). The findings of this study are supported by cross-education studies that have trained upper body muscle groups; specifically those that have trained distal muscle groups (Shields et al., 1999; Teixeira and Caminha, 2003). Shields et al. (1999) reported

		Right-training Group (n = 11)		Left-training Group (n = 9)		Control Group (n = 11)	
		Pre	Post	Pre	Post	Pre	Post
Agonist (volts)	Untrained	0.318±0.034	0.254±0.020*	0.248±0.030	0.237±0.040*	0.323±0.040	0.289±0.028*
	Trained	0.263±0.026	0.340±0.035	0.269±0.021	0.311±0.029	0.288±0.023	0.261±0.017
Antagonist (volts)	Untrained	0.030±0.004	0.056±0.026	0.044±0.010	0.049±0.013	0.038±0.010	0.038±0.007
	Trained	0.031±0.003	0.048±0.011	0.038±0.008	0.042±0.004	0.031±0.008	0.034±0.006

Table 2.2 Maximal isometric muscle activation (EMG) as a function of test (pre and post), arm (trained and untrained) and muscle (agonist and antagonist) for each group (Mean ± SE). *Significant time main effect (all groups pooled) ($p < 0.05$).

a 43% increase in muscular endurance of the untrained left hand after right handgrip endurance training. The muscle group trained and the level of cross-education in this study is most similar to our training paradigm and resulting cross-education of strength (39%). Unfortunately, no study has reported training the left handgrip or forearm. Studies that report training the non-dominant arm (upper arm or hand muscles) either do not report any cross-education (Housh et al., 1992), or show a much smaller effect (11%) which is not compared to a control group (Davies et al., 1985). The concern of reporting significant cross-education without comparing the effect to a control group is duly noted (Munn et al., 2004). Familiarity to the testing procedures can create a mild learning effect as we have shown in the control group in our study (Figure 2.2).

In this study where all subjects were strongly right-handed, the left hand was weaker than the right hand for handgrip ulnar deviation peak torque. The obvious weakness of the left arm in right-handers may be a contributing factor to the effect of the direction of transfer on cross-education. Previous studies of laterality have shown that the dominant hand is stronger and more skilled compared to the non-dominant hand (Steenhuis and Bryden, 1999). Based on this finding, the left hand was likely less coordinated for the task than the right hand in this study, and thus may have had more potential for adaptation in neural coordination. This is supported by the finding that despite similar muscle thickness between the left and right arms within groups, torque production was much lower in the left arm for both groups prior to training (Table 2.1). In lieu of this, cross-education of strength may only occur in one direction (i.e. right to left) for all upper body tasks in right-handed people. Few studies of cross-education have reported the dominant limb, and no previous study has compared the direction of transfer. A host of interlateral transfer studies support superior transfer of complex or unfamiliar motor skills from the dominant to the non-dominant hand (Parlow and Kinsbourne, 1989; Imamizu and Shimojo,

1995; Stoddard and Vaid, 1996; Thut et al., 1996; Latash, 1999; Criscimagna-Hemminger et al., 2003; Teixeira and Caminha, 2003;). With particular relevance to our findings, Parlow and Kinsbourne (1989) found that in right-handers, the left hand benefited more from opposite hand training (inverted-reversed printing) than the right hand. Perhaps the complexity or unfamiliarity of the task is the determining factor for whether cross-education of strength is unidirectional. If so, the mechanisms controlling cross-education of strength would be very similar to those controlling cross-education of skills. Task complexity limits the ability of the nervous system to maximally activate the involved musculature prior to training (Aagaard et al., 2000). Strength training induces motor learning resulting in increased activation of the agonists and/or synergists (Aagaard et al., 2000; Shima et al., 2002), and decreased co-activation of antagonists (Carolan and Cafarelli, 1992). Interlateral transfer of strength to the untrained limb may also be caused by these changes in activation in the absence of muscle hypertrophy. If the task is sufficiently unfamiliar to both limbs, transfer will likely occur in either direction. If the task is less familiar to the non-dominant hand, then the task may transfer asymmetrically.

Another interesting finding of this experiment is that the magnitude of cross-education (39%) did not differ statistically from the magnitude of gain in strength in the trained arm (26%) for the right-training group. One other study has reported greater increase in strength of the untrained compared to trained contralateral homologous muscle (Hortobágyi et al., 1997). In the present study, the left hand increased in strength to a similar extent whether the left hand (42%) or the right hand (39%) was trained. One hypothesis of this study was that the neural adaptation responsible for these findings would be reflected as more complete agonist activation or decreased antagonist activation leading toward greater force production in the desired direction of movement. This hypothesis is not supported. The increase in strength over time for the trained

forearm is not coupled with an increase in agonist muscle activation, although both training groups exhibit an increasing directional trend (Table 2.2). The untrained forearm shows no difference in agonist activation compared to the control group (Table 2.2). Previous research is mixed as to whether there is increased agonist activation in conjunction with cross-education (Cannon and Cafarelli, 1987; Carolan and Cafarelli, 1992; Hortobágyi et al., 1997; Shima et al., 2002). Carolan and Cafarelli (1992) reported unchanged agonist activation countered by decreased co-activation of the antagonist leading to strength increase. Other studies of cross-education have demonstrated increased agonist activation in the untrained limb (Hortobágyi et al., 1997; Shima et al., 2002). In this study, the mechanisms through which strength increase occurred could be different between arms. Significant muscle hypertrophy (Table 2.1) and increased muscle activation (Table 2.1) in the trained forearm is shown in the present study. In the absence of similar adaptation in the untrained agonist, one can speculate the strength increment was caused by increased activation of synergist muscles (Aagaard et al., 2000; Shima et al., 2002) or changes in agonist motor-unit recruitment strategies not detected by the EMG analysis such as altered motor-unit conduction velocity, number of active motor-units, and motor-unit discharge rate (Farina et al., 2004).

Another explanation for the lack of increase in agonist activation (as measured by EMG) in conjunction with increased strength of untrained contralateral homologous muscle is that the neural adaptation associated with cross-education originates in areas of the CNS such as motor cortex or cerebellum and not in the peripheral nervous system. Recent research has noted that voluntary muscle contraction of one limb can evoke neural responses in cortical regions relevant for the opposite limb without an effect on the motor neuron pool and without an increase in peripheral nerve (H-reflex) excitability (Hortobágyi et al. 2003). Unilateral movement has also

been shown to elicit bilateral activation of the pre-motor and motor fields (Kristeva et al., 1991). Activation of these ipsilateral cortical areas may produce a learning effect for the opposite limb, especially if the premotor areas are activated. In the present experiment, no peripheral nervous system adaptation was detected by the EMG analysis, indicating that increased strength of the untrained contralateral muscles may have been induced by increased activation of areas of the CNS such as motor cortex (Hortobágyi et al., 2003).

A limitation of our study is that EMG data only provide an indirect measure of muscle activation unlike more direct techniques such as twitch interpolation. The particular task here involved multiple muscles due to the required combination of handgrip and ulnar deviation. This made it difficult to effectively use interpolated twitch to gain an estimate of maximal motor unit recruitment. The handgrip-ulnar deviation task was chosen because it is an unfamiliar movement and the aim in this study was to obtain a high degree of cross-education. Previous research has indicated that less familiar tasks elicit a higher amount of cross-education (Farthing and Chilibeck, 2003a). In choosing the unfamiliar task of the current study to maximize cross-education the ability to use the twitch interpolation technique was limited.

Other limitations of EMG data limit the conclusions that can be drawn from our results. Signal amplitude cancellation can be as high as approximately 85% during maximal fatiguing contractions, and can vary as a function of subcutaneous tissue, number of motor units, and conduction velocity (Keenan et al., 2005). Other factors that can influence the surface EMG include skin-electrode impedance, location of electrodes over the muscle, muscle fiber shortening, crosstalk between muscles, shift of the muscle relative to the detection system, number of recruited motor units, and motor unit synchronization (Farina et al., 2004). Variation in any of these parameters from pre to post training could limit the results. This is reflected in the

modest reproducibility for our EMG measurements where repeated measures had coefficients of variation ranging from 13.0 to 17.6%. Considering these limitations, it is difficult to conclude with certainty that the EMG results indicate a true altered input to either the trained or untrained agonists or antagonists.

The major conclusion of this study is that cross-education with isometric hand strength training occurs only in the right to left direction of transfer in right-handed individuals, and is not coupled with increased activation of the agonist or decreased activation of the antagonist in the untrained limb. Another finding of this study is that similar strength increases can be induced in the left limb with either left or right hand isometric training in right-handed individuals. Cross-education of strength does not occur with an increased maximal EMG activity indicating that neural adaptations may occur in higher brain centers such as the motor cortex. This possibility is addressed as part of Experiment 2.

Chapter 3: Experiment 2

3.1 Introduction

Previous literature attributes cross-education of strength to neural mechanisms since there is no evidence of morphological change accompanying strength increase in the untrained limb (Moritani and deVries, 1979; Garfinkel and Cafarelli, 1992; Seger et al., 1998; Zhou, 2000; Farthing and Chilibeck, 2003a). However, the exact neuro-physiological mechanisms of cross-education of strength have remained elusive. Peripheral neural adaptations have been shown in both limbs in response to unilateral training- including increased agonist activation (Hortobágyi et al., 1997; Shima et al., 2002) and decreased antagonist co-activation (Carolan and Cafarelli, 1992). But these adaptations are not consistent across studies and exactly how the adaptation is transferred to the untrained limb is unknown. The theory that cross-education is controlled in CNS through communication between cortical hemispheres can be dated as far back as Hellebrandt (1951), yet no study to date has examined cortical adaptation with cross-education of strength.

The neuro-physiological mechanism controlling cross-education of strength is likely adjunct to motor learning. The mechanism of motor learning is thought to be neural plasticity in the brain, in regions including M1 (Pascual-Leone et al., 1994; Karni et al., 1995; Pascual-Leone et al., 1995; for reviews see Sanes and Donoghue, 2000; Sanes, 2003), PMC and SMA (Grafton et al., 1995; Grafton et al., 2002), and cerebellum (Jueptner et al., 1997; Sakai et al., 2002). Further evidence suggests motor learning also involves cortical reorganization (Jueptner et al., 1997; Shadmehr and Holcomb, 1997; Van Mier et al., 1998; Pearce et al., 2000; Staines et al., 2002; Ward et al., 2003). Particularly in M1, plasticity has been shown to play a role in the early consolidation of learning motor skills (Muellbacher et al., 2002). When M1 is disrupted during

learning, improvements are impaired (Ziemann et al., 2001; Donchin et al., 2002; Muellbacher et al., 2002; Sohn et al., 2002). In relation to strength tasks, increased or decreased activation in M1 could reflect improved coordination by increasing activity of neurons associated with descending signal to agonists, and decreasing activity of neurons projecting to antagonists (decreasing co-activation). Decreased co-activation has been documented using EMG in conjunction with cross-education of strength (Carolan and Cafarelli, 1992). However, the relationship between changes in cortical activation and changes in muscle activation patterns with cross-education of strength has never been examined.

Increased cortical activation is a plausible mechanism for neural adaptation in both limbs with unilateral training. After consolidation of a strength task with unilateral training, the untrained limb undeniably has access to the new information; otherwise transfer would not occur. The exact role of commissural fibres in communicating information across cortical hemispheres remains unclear. Relevant information about movement may actually be transferred to the opposite cortex (Parlow and Kinsbourne, 1989), or conceivably both hemispheres could have access to information stored in only one hemisphere (Thut et al., 1996). Further to this, changes in activation could occur in relevant regions of both hemispheres with unilateral acquisition. Several studies have shown bilateral activations in M1, SMA and PMC are commonly associated with unilateral movement (Kristeva et al., 1991; Toma et al., 1999; Ehrsson et al., 2000; Liu et al., 2000; Gerardin et al., 2000; Binkofski et al., 2000; Nirkko et al., 2001). Intuitively, cortical adaptation with cross-education of strength might be reflected by similar changes in activation in relevant areas of both contralateral and ipsilateral cortex.

Cross-education of strength has also been documented with imagery training (Yue and Cole, 1992). Few studies have experimented with imagery training (Yue and Cole, 1992; Herbert

et al., 1998; Zijdwind et al., 2003; Ranganathan et al., 2004), and conflict remains as to the effectiveness of imagery training for increasing strength. Yue and Cole (1992) found imagery training of the left hand was nearly as effective for strength and cross-education as actual training, whereas Herbert et al. (1998) found no effect of imagery training with the right hand. Zijdwind et al. (2003) reported a 20% increase in strength with bilateral imagery training of the lower legs. The findings of Yue and Cole (1992) suggest cross-education of strength must involve key influence from the task level (brain), since imagery training eliminates any influence from the manipulator level (muscles) and produced cross-education similar to actual training. However, Imamizu and Shimojo (1995) suggest that if only the task level is involved in transfer between limbs imagery training should result in perfect transfer (i.e. the same relative strength increase in both limbs). The amount of cross-education of strength shown by Yue and Cole (1992) after actual and imagery training (14% and 10%, respectively) was roughly half of the relative strength gain in the training limb (Actual- 30%; Imagery-22%). This suggests that the manipulator level also contributes to cross-education. In theory, if the manipulator level is important for cross-education, actual training should produce greater transfer than imagery due to sensory feedback.

In recent years, many functional imaging studies have experimented with motor imagery paradigms. Motor imagery has shown similar cortical activation patterns as actual movement (Cunnington et al., 1996; Porro et al., 1996; Schnitzler et al., 1997; Lotze et al., 1999; Leonardo et al., 1995; Binkofski et al., 2000; Romero et al., 2000; Thobois et al., 2000; Naito et al., 2002), leading some to equate motor imagery and motor preparation as functionally equivalent processes (Jeannerod, 1994). Motor imagery includes activation in areas including M1, SMA, PMC, CMA and cerebellum (Ryding et al., 1993; Cunnington et al., 1996; Porro et al., 1996;

Schnitzler et al., 1997; Deiber et al., 1998; Leonardo et al., 1999; Lotze et al., 1999; Binkofski et al., 2000; Romero et al., 2000; Thobois et al., 2000; Naito et al., 2002). Motor imagery and actual movements appear to show similar activations in regions relevant for movement preparation and planning, but areas more involved in movement execution (M1) or feedback (S1) are suppressed with imagery.

There is apparent need for functional imaging studies comparing unilateral actual and imagery training to determine the neural mechanisms controlling an increase in strength without muscle hypertrophy. Cross-education of strength and the increase in strength from imagery training are similar. Both situations involve an increase in strength without physical training. Given the similarity in brain activation patterns reported previously with imagery and actual movement, imagery training might involve similar cortical adaptations as shown for the untrained limb after unilateral actual training. Theoretically, a proportion of the increase in strength with training associated with neural factors (Moritani and deVries, 1979) could be induced by imagery alone. Cortical activation using functional imaging has not been examined before and after imagined resistance training, although it has been examined after motor imagery practice (Lotze et al., 1999; Jackson et al., 2003). Intuitively, for imagery training to be effective for increasing strength and cross-education, CNS adaptation must be involved since the periphery should not be experiencing activation or relaying feedback.

Cross-education of strength and imagery training could be dependent on memory of prior movement. Accessing semantic memory of movement could be reflected by cortical activation in temporal lobe associated with motor imagery and/or unilateral training. Semantic memory refers to the information stored in our brains about object and word meaning (Tulving, 1983; Martin, 2001), and is thought to be represented in left temporal lobe (Martin, 2001). Martin et al. (1995)

suggested activation in the left middle temporal gyrus reflects retrieval of motion knowledge. Interestingly, imagining actions has also been associated with middle temporal lobe and PMC activation (Gerardin et al., 2000) linking motor imagery to cognitive processing of stored information. Martin (2001) also suggested that features and attributes defining an object in semantic memory are stored in perceptual and motor systems active when we first experienced the object. This might explain why activated areas in ipsilateral cortex in response to unilateral movements are similar to the contralateral activation (Nirkko et al., 2001), and why imagined movements show very similar activation patterns as actual movements. Martin (2001) also contends that knowledge about the sequence of motor movements associated with the use of objects is stored near the motor systems activated when the object is manipulated. Imagery of moving objects and naming tools have both been associated with ventral PMC activation (Martin et al., 1996; Gerardin et al., 2000), which has also been linked to the ‘mirror system’ and observation of movement (Rizzolatti et al., 1996b; Binkofski et al., 1999; Buccino et al., 2001; Oztop and Arbib, 2002). Activation in ventral PMC in humans may imply encoding of lexical information (relating to words or the vocabulary of a language) about the object being manipulated- perhaps in semantic memory. Semantic memory might be pertinent for cross-education of strength, especially in terms of evaluating aspects of performing the task properly by comparing current movements with those previously acquired by the opposite limb.

The primary purpose of this experiment is to attempt to determine the neuro-physiological mechanisms controlling cross-education of strength, by assessing both peripheral and central neuro-physiological adaptation in response to unilateral training. Based on the premise that cross-education of strength is a form of motor learning, it is hypothesized that for both limbs central neural adaptation will involve changes in activation as evidence of motor

learning and peripheral adaptation will involve adaptations in agonist-antagonist coordination beneficial for the desired direction of movement. A secondary purpose is to determine the effectiveness of imagery training for strength and cross-education, also in conjunction with peripheral and central assessment. It is also hypothesized that imagery training will be effective for increasing strength and cross-education and will result in changes in activation in brain, and adapted agonist-antagonist coordination reflective of motor learning. As a final hypothesis, cross-education of strength and imagery training will be associated with retrieval of memory of prior movement.

3.2 Methods

3.2.1 Subjects

Ethical approval for the experiment was given by the University of Saskatchewan's biomedical review board for research in human subjects, and all participating subjects gave their informed consent (Appendix C). Thirty-four right-handed females with little prior resistance training experience in the previous year volunteered for participation in the study. A fault in data collection procedures caused one subject from the control group to be excluded from the study. During post-testing procedures, the subject reported misunderstanding the requirements of the task during pre-testing measures, and admitted the pre-test data was likely not representative. The data was considered unreliable and removed from the study at discretion of the primary researcher. Therefore, thirty-three subjects were used for the analysis in the study. A sub-sample of eight subjects participated in the MRI experiment (described below). The subject pool was restricted to one gender for purposes of reducing between-subject variation and previous studies in our lab have shown a trend for females to show greater cross-education of strength. Prior to

any physical assessment, all subjects reported prior resistance training experience if any, declared handedness, and then completed the WHQ to determine the degree of handedness (Bryden, 1977). As in experiment 1, subjects were excluded from the study, if they did not obtain a positive score on the handedness questionnaire (indicating right handedness). After completing the handedness questionnaire, all subjects completed the Vividness of Movement Imagery Questionnaire (VMIQ) (Isaac et al., 1985) to determine external and internal movement imagery ability. The VMIQ requires participants to give a vividness rating on a 5-point scale for 24 different movements, first imagining ‘watching somebody else’ performing the movement and then imagining ‘doing it yourself’. A rating of 1 corresponded to ‘perfectly clear and as vivid as normal vision’ and a rating of 5 corresponded to ‘no image at all’. Therefore, a score of 24 for external and 24 for internal items was a perfect score.

3.2.2 Design

Prior to the testing protocol, all subjects were familiarized with the testing environment and protocol. To alleviate some of the learning effect that might be attributed to the testing protocol, each subject performed two or three low intensity practice repetitions of the strength task to become familiar with the motor requirements. After height and weight assessment, subjects later returned to the testing lab for assessment of right and left arm muscle thickness of the posterior medial forearm, followed by right and left limb isometric ulnar deviation peak torque with simultaneous measurement of muscle activation by EMG. Once pre-testing was completed, subjects were randomized into one of three groups: actual training (n=12), imagery training (n=11), or control (n=10). The randomization procedure was modified slightly since the sub-sample of subjects participating in the MRI experiment (n=8) could not be assigned to the

control group as determined by the study design. This meant the remainder of subjects stood a greater chance of being assigned to the control group. All subjects trained their right arm as determined by experiment 1, where cross-education of strength occurred only after right-hand training. Since the control group had two untrained limbs, the arm that would be designated trained for statistical comparisons was the same as the training groups (i.e. right arm). Subjects had a mean (\pm SE) age of 20.8 ± 0.4 yrs, mass of 64.2 ± 1.5 kg, height of 166.6 ± 1.1 cm, training experience of 3.3 ± 0.5 months, handedness score of 17.1 ± 0.5 , VMIQ external score of 44.4 ± 3.2 , and VMIQ internal score 40.9 ± 2.2 . There were no baseline differences between groups except for mass, where the control group (68.3 ± 2.8 kg) was significantly heavier than the imagery training group (59.4 ± 2.0 kg) , $F(2, 30)=3.59$, $p<0.05$. Once training was complete, all participants were again assessed for muscle thickness, isometric peak torque, and EMG in both the trained and untrained limbs.

3.2.3 Muscle Thickness

The procedure for muscle thickness measurement was the same as Experiment 1 (Refer to Section 2.2.3).

3.2.4 Strength

The procedure for strength assessment was identical to Experiment 1 (Refer to Section 2.2.4)

3.2.5 Electromyography

The procedure for EMG acquisition was also the same as in Experiment 1 (Refer to Section 2.2.5)

3.2.6 Strength Training Program

Actual training consisted of six weeks of unilateral isometric ulnar deviation training of the right hand four times per week for a total of 24 training sessions. Individuals were not allowed to complete post testing until they completed at least 21 of 24 training sessions. The training program was progressive in nature beginning with 2 sets of 8 repetitions and progressing up to 6 sets of 8 repetitions by the second week of training. A taper down to 3 sets was used for the last two training sessions to facilitate recovery from any overtraining (Gibala et al., 1994). Training was completed on the Biodex in identical fashion as described for testing. Each isometric contraction was 2-seconds long and was separated by 2-seconds of rest and was cadenced by a metronome. The rest interval between sets was 30 seconds. The primary researcher was present during the training sessions and provided verbal encouragement. All subjects were allowed to view their real time torque production during training. This was done to provide a measure of performance feedback.

3.2.7 Imagery Training Program

Imagery training was identical to actual training with the obvious exception of muscle contractions. Imagery training was four times per week for six weeks for a total of 24 training sessions, and involved the same progression of training outlined for the actual training group. All imagery training sessions were completed on the Biodex. Subjects were positioned in the chair exactly the same as the testing procedures and were required to grasp the handle. Each imagined

contraction was 2-seconds long and was separated by 2-seconds of rest and was cadenced by the primary researcher using verbal prompts (i.e. “contract” and “relax”). Individuals were asked to imagine contracting their muscles when they heard the word “contract” and imagine relaxing their muscles when they heard the word “relax”. The primary researcher viewed a metronome to ensure that the 2-second cadence was kept. The metronome was silenced to avoid distracting the subjects during imagery. All subjects were encouraged to focus on a single point somewhere on the ceiling, and stay locked on the point until the training set was completed. The rest interval between sets was 30 seconds. Imagery training in the present experiment was internal imagery performed with eyes open to be consistent with the MRI environment where visual cues were used for prompting. Subjects were instructed to “imagine performing the maximal handgrip contraction with their right hand, feeling the sensations associated with contraction while keeping the hand still” (adapted from Porro et al., 1996). Prior to each training session, subjects were reminded to focus on the internal aspects of imagery (i.e. feelings and sensations of the particular muscle contraction) and avoid actual contraction of the muscles at all times.

3.2.8 MRI Experiment

Functional magnetic resonance imaging was used to assess cortical adaptation before and after unilateral actual and imagery training of the right hand. Subjects participating in the MRI experiment (n=8) were recruited only from the training groups (actual: n=4; imagery: n=4). No control subjects participated in the MRI experiment due to high cost and limited availability of the MRI. Procedurally, MRI scans were always completed prior to all other measures (i.e. strength, muscle thickness, and EMG). A special familiarization session was completed during the week prior to the pre-training MRI scan. Each subject was oriented with the requirements of

the MRI sequence using a specially constructed mock MRI contained near the MRI suite. The MRI itself was not available for familiarization due to clinical use during the week, but brief orientation to the MRI was also done immediately prior scanning. The mock MRI provided subjects with a good simulation of being inside an MRI with the head coil attachment. This was done to reduce potential discomfort or anxiety experienced by subjects during actual image acquisition, reduce the chance of head movement, and minimize MRI time. The mock MRI was equipped with the same computer software (E-prime) as the MRI itself to expose subjects to the prompts and instructions they would be viewing during actual imaging.

The MRI experiment consisted of four conditions: left actual, right actual, right imagery, and left imagery. The order of conditions was randomized for each subject and kept consistent for pre and post training MRI scans. Participants completed 5 sets of 8 repetitions for each condition. During each set, muscle contraction or imagery of contraction was alternated with rest to mimic a typical training set. When the word ‘contract’ appeared on screen, participants were to engage in the contraction until the word disappeared. The stimulus was the same for each condition (i.e. ‘contract’), regardless of whether real or imagined contractions were being performed. After eight repetitions were completed, a rest interval of 30 seconds was given, where participants viewed a fixation cross (+). This cycle was repeated until 5 sets were completed for the condition.

Maximal contractions could not be used in the MRI due to motion artifact caused by head movement. To minimize head motion with the task, participants were instructed to avoid sudden ‘jerking’ movements when contraction was initiated. This was facilitated by using ‘ramp’ contractions, with a smooth transition between contractions. This technique made the duration of contraction more arbitrary. Participants were also instructed to aim for a contraction intensity of

approximately 60% of maximum. Previous studies have shown that BOLD response does not vary with intensity of contractions corresponding to light and heavy resistance (Ludman et al., 1996). However, BOLD response density has been shown to increase with force exertion up to 50% MVC (Thickbroom et al., 1998). No study to our knowledge has determined the BOLD response to high intensity contractions such as 80% MVC or above. As an extra precaution, for all conditions, the uninvolved limb was rested across the participants' waist with the intention of restricting movement during contractions of the involved limb. For the imagery conditions, instructions were similar to imagery training as described above. Participants were instructed to grasp the handle and "imagine performing the maximal handgrip contraction with their right (or left) hand, feeling the sensations associated with contraction while keeping the hand still" (adapted from Porro et al., 1996).

The duration of contraction in the MRI (1.8 seconds) was slightly shorter than for training and testing (2 seconds). Pilot testing revealed that 2-second acquisition intervals for contractions in the MRI was too close to natural breathing rhythm and participants found it difficult to avoid synchronized breathing with the task (e.g. always exhaling during the contraction and inhaling during rest). Breathing or breath-hold in synchronization with the task was associated with time correlated activations in addition to activations normally associated with the task (data not shown). Previous fMRI studies have shown brain activations associated with the valsalva maneuver (similar to breath-hold; Henderson et al., 2002) and have also noted the influence of respiration on cerebral spinal fluid (CSF) flow through the cerebral aqueduct, where expiration directs CSF flow caudally and inspiration directs CSF flow cranially (Klose et al., 2000). Therefore, subjects were instructed to avoid breath-hold at any time and avoid synchronizing their breathing with the task. Piloting showed that this was facilitated by a slightly

shorter acquisition time for contractions in the MRI (1.8 seconds). As mentioned, the contraction duration in the MRI was more arbitrary due to the adjustments made to limit head motion (ramp contractions).

Isometric ulnar deviation of the right or left hand was made possible in the MRI with the construction of a specialized wooden apparatus. The apparatus was constructed so the position of the arm in relation to the body was very similar to the Biodex set-up, with the exception that the apparatus was made with handles for both hands. This was imperative for the MRI experiment so the apparatus would not have to be reversed and the subject repositioned in order to complete conditions with either hand. The Biodex attachment was mimicked by a wooden dowel of equal diameter pierced through a stack of wood blocks (for reinforcement) and glued down into a flat wood plank. The apparatus could be maneuvered up and down the MRI bed to accommodate different arm lengths, and was positioned so the participant was in neutral position and comfortable, and not forced into shoulder depression or elevation. The MRI set-up for isometric ulnar deviation with the wooden apparatus is shown in Figure 3.1.

All imaging procedures were completed with a 1.5-T Siemens Symphony Magnetic Resonance Imager. The experiment was a blocked design and was analyzed using the BOLDfold technique (Borowsky et al., 2002; Sarty and Borowsky, 2005). For each of the four conditions, 168 volumes of 12 slice axial single-shot echo planar images (EPI) were obtained (90° flip angle, TR=1800ms, TE =55ms, 64 x 64 acquisition matrix, 128 x 128 reconstruction matrix). The first 8 volumes were used for image stabilization, and the remaining 160 volumes comprised of 5 blocks of 32 volumes each. Each block consisted of 16 volumes of task (actual contractions or imagery) and 16 volumes of rest. Slice thickness was 8mm with 2mm separation between slices. Prompting for the experiment was done using a data projector and computer running E-prime



Figure 3.1 Illustration of the MRI setup with the specialized wooden apparatus for isometric ulnar deviation.

software, and a projection screen visible to the subject by a mirror attached to the head coil. E-prime software was used to trigger image acquisition in synchrony with the presentation of visual prompts.

Prior to completing the experimental conditions, T1 weighted spin-echo anatomical images (TR= 400ms, TE= 12ms, 256 x 256 acquisition matrix) were acquired in axial, sagittal, and coronal planes, and used for overlaying functional activation maps. To obtain the full volume of cortex for each participant, the third of fourth inferior-most slice was centered on the posterior commissure, depending on the distance from the posterior commissure to the top of the brain. Slice thickness and position matched the functional images for the axial slices.

As mentioned, activation maps were computed using the BOLDfold technique (Borowsky et al., 2002; Sarty and Borowsky, 2005). BOLDfold is essentially a correlation/general linear model method. BOLDfold requires a sufficient rest interval between stimulus volumes for the hemodynamic response to return to baseline. After correction for baseline drift, the mean BOLD function for each voxel, compared between stimulus and rest volumes, is computed and correlated to the actual data as an indication of the consistency of blood flow response from stimulus repetition to repetition during data acquisition. Squaring this correlation (r^2) represents the goodness-of-fit of the mean BOLD function to the observed BOLD response. The squared correlation is equivalent to eta-squared (η^2) or goodness-of-fit as in a simple one-way analysis of variance (ANOVA) and is computed by the following formula:

$$r^2_{\text{mean BOLD: observed BOLD}} = \eta^2 = \text{SS}_{\text{levels}} / \text{SS}_{\text{total}} \quad (3.1)$$

where $\text{SS}_{\text{levels}}$ is the sum of squared deviations between levels of the mean BOLD function and the grand mean, summed over all observations, and SS_{total} is the sum of squared deviations

between individual observations and the grand mean, summed over all observations. All functional maps were computed using an activation threshold value of $\eta = .60$.

Following the BOLDfold analysis, two maps were computed for each of the four conditions (right and left actual, and right and left imagery), a threshold map $\eta_C(p)$ of η goodness-of-fit values and a visibility or intensity map $V_{Condition}(p)$ representing BOLD amplitude, where p is a voxel coordinate (as described by Borowsky et al., 2005). The activation map for each condition was defined as $M_{Condition}(p) = K_{Condition,\eta}(p) V_{Condition}(p)$ where $K_{Condition,\eta}(p) = 1$ if $\eta_{Condition}(p) > .60$ and zero otherwise. Following these computations, intersection (shared) maps (M_{int}) and unique maps (M_{uni}) were computed for paired conditions pre and post for each subject according to the following equations:

$$M_{int}(p) = K_{pre,\eta}(p) K_{post,\eta}(p) (V_{pre}(p) + V_{post}(p))/2 \quad (3.2)$$

$$M_{uni}(p) = [K_{pre,\eta}(p) V_{pre}(p) - K_{post,\eta}(p) V_{post}(p)] [1 - K_{pre,\eta}(p) K_{post,\eta}(p)] \quad (3.3)$$

The intersection map shows only activated voxels common between conditions pre and post, and the unique map represents a difference and shows task subtraction for activations that are not common to conditions pre and post. The unique map displays activations exclusive to either condition. The maps were averaged across participants within each group (actual, imagery) to compute the final maps. The final maps included intersection and unique maps overlaid together on a standardized image to produce a single map for each stimulus condition (right and left actual, right and left imagery) displaying both shared and unique activations.

Using AFNI (Analysis of Functional NeuroImages) software (Cox, 1996), the maps were generated in accordance with the methods of Borowsky et al. (2005). Voxels separated by 1.1 mm distance were clustered and clusters of volume less than $100\mu L$ were clipped out. The data were then blurred using an isotropic Gaussian blur with a full width at half maximum (FWHM)

of 3.91mm. Averaging of images within groups was done following standard piecewise affine transformation of individual data to a standardized brain atlas (Talairach and Tourounx, 1988). Mean activation maps in Talairach coordinates were determined for each map along with the corresponding one sample t statistic for each voxel. The maps show regions of activations that exceed the consistency threshold and a one-tailed t-test against zero for the group. The maps are binary and are presented without color scaling to show varying intensity, since consistent low intensity BOLD functions are as important as consistent high intensity BOLD functions (Borowsky et al., 2005).

3.2.9 Statistics

Strength and muscle thickness data were analyzed using a Group (left, right, control) × Time (pre, post) × Arm (trained, untrained) multivariate analysis (SPSS version 11.5) appropriate for multiple dependent variables with repeated measures. Percent change for strength and muscle thickness was determined by subtracting the post-training from the pre-training score, dividing by the pre-training score and multiplying by 100. This was analyzed using a Group × Arm multivariate analysis to help simplify the results and to allow comparison of the relative magnitude of cross-education. Univariate ANOVA and relevant one-way ANOVA and paired t-tests followed if multivariate significance was found. EMG activation was analyzed using a Group (left, right, control) × Time (pre, post) × Arm (untrained, trained) × Muscle (agonist, antagonist) ANOVA with repeated measures on the last three factors. EMG was not included in the multivariate analysis because of an additional factor in the design (agonist, antagonist). Tukey's Post hoc test was used where appropriate. Significance was set at $p < 0.05$.

3.3 Results

3.3.1 Strength and Muscle Thickness

Congruent with experiment 1, and as expected with strongly right-handed participants, the left arm was significantly weaker than the right arm for all subjects before and after training, $t(32)=7.323, p<0.01$ and $t(32)=6.661, p<0.01$, respectively. There was a significant Group \times Time \times Arm multivariate interaction for strength and muscle thickness, $\Lambda(4, 58)=0.435, p<0.01$. Univariate ANOVA for strength revealed a significant Group \times Time \times Arm interaction, $F(2,30)=3.412, p<0.05$. There was a significant increase in strength over time for the trained arm of the actual training group $t(11)=-7.218, p<0.01$, and the untrained arm of the actual training group $t(11)=-6.846, p<0.01$. No significant changes over time for strength were observed for any other group. The data for the change in strength over time are presented in Table 3.1.

Univariate ANOVA for muscle thickness revealed a significant Group \times Time \times Arm interaction, $F(2, 30)=19.118, p<0.01$. Only the training arm of the actual training group increased significantly over time for muscle thickness $t(11)=-5.473, p<0.01$. Muscle thickness data is presented in Table 3.1.

The analysis of percent change revealed a significant Group \times Arm multivariate interaction for strength and muscle thickness $\Lambda(4, 58)=0.419, p<0.01$. Univariate ANOVA for strength revealed a significant Group effect $F(2, 30)=27.711, p<0.01$. There was no significant difference for relative strength change between the trained and untrained arm across groups. Tukey's post hoc test revealed the relative change in strength pooled across arms for the actual training group ($46.5\pm 4.8\%$) was significantly greater than the imagery training group ($0.1\pm 5.0\%$; $p<0.05$) and control group ($3.6\pm 5.3\%$; $p<0.05$). The relative magnitude of strength change for both the trained and untrained arms is presented in Figure 3.2.

		Actual training Group (n = 11)		Imagery training Group (n = 12)		Control Group (n = 10)	
		Pre	Post	Pre	Post	Pre	Post
Strength (N·m)	Untrained	15.3±1.1	22.3±1.5*	15.5±1.6	15.8±2.1	15.4±1.1	16.1±1.3
	Trained	19.9±1.3	28.8±2.0*	18.8±1.3	18.8±1.6	18.6±1.3	18.7±1.2
Muscle Thickness (cm)	Untrained	3.10±0.05	3.10±0.06	3.02±0.08	3.01±0.06	3.28±0.08	3.26±0.08
	Trained	3.11±0.06	3.37±0.07*	3.04±0.04	3.03±0.04	3.26±0.10	3.22±0.10

Table 3.1 Maximum isometric strength and muscle thickness as a function of test (pre and post) and arm (trained and untrained) for each group (Mean ± SE). *Significantly different than corresponding pre value (p<0.01).

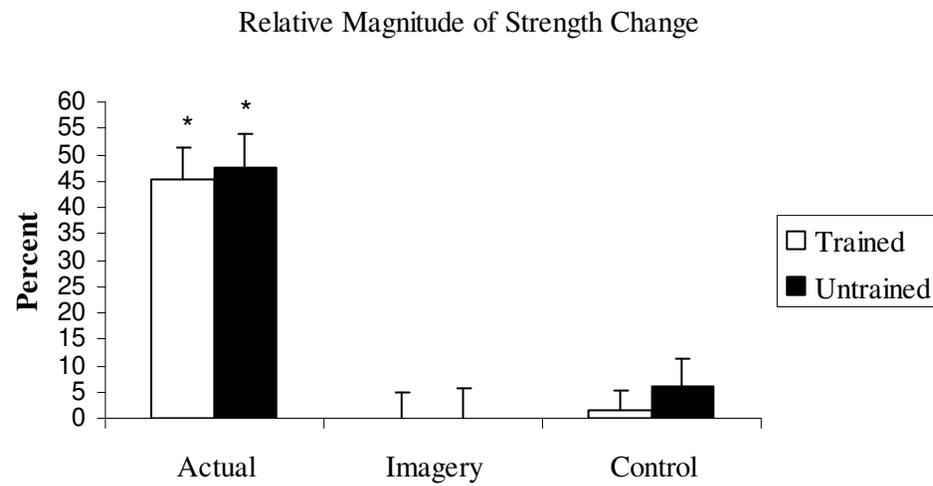


Figure 3.2 Relative magnitude of strength change for the trained and untrained arms for all groups. *Percent change for each arm of the actual training group significantly greater than the corresponding arm from the imagery training and control group ($p < 0.05$).

Univariate ANOVA for muscle thickness revealed a significant Group x Arm interaction, $F(2,30)=19.067, p<0.01$. Tukey's post hoc test revealed that the relative magnitude of muscle thickness gain for the trained arm of the actual training group ($8.4\pm 1.6\%$) was significantly greater than all other arms ($p<0.05$). The magnitude of muscle thickness change for the untrained arm was not significantly different between groups.

3.3.2 Electromyography

The analysis of mean absolute value (MAV) EMG during strength testing was completed on all 33 subjects. There was a significant Group x Time x Muscle interaction, $F(2,30)=5.157, p<0.05$. There was a significant Arm effect, $F(1,30)=11.678, p<0.01$, indicating greater overall activation during contraction with the trained arm. Post hoc analyses of the interaction revealed no significant changes over time for any muscle in any group. Therefore, to better interpret the three-way interaction, change scores were created for each muscle and pooled across arms. One-way ANOVA of the agonist change scores was significant, $F(2,30)=5.354, p<0.05$. Tukey's Post hoc test revealed that the agonist change score for actual training group ($0.086\pm 0.037v$) was significantly different from the imagery training ($-0.041\pm 0.031v; p<0.05$) and control group ($-0.045\pm 0.029v; p<0.05$). Pre and post training MAV muscle activation values are presented in Table 3.2.

Agonist EMG activity (MAV) in both arms during a typical training set was completed on all 23 training subjects. Data from one subject in the actual training group was excluded due to noisy signal acquisition. For the actual training group, agonist EMG activity in the non-training arm and the training arm averaged 17.0% and 92.8% of the corresponding pre training peak isometric EMG activity, respectively. For the imagery training group, agonist EMG activity

		Actual training Group (n = 12)		Imagery training Group (n = 11)		Control Group (n = 10)	
		Pre	Post	Pre	Post	Pre	Post
Agonist (volts)	Untrained	0.215±0.045	0.308±0.046*	0.264±0.036	0.238±0.039	0.244±0.035	0.134±0.046
	Trained	0.336±0.040	0.416±0.174*	0.376±0.030	0.320±0.027	0.225±0.028	0.245±0.021
Antagonist (volts)	Untrained	0.090±0.026	0.062±0.011	0.075±0.018	0.069±0.014	0.062±0.008	0.058±0.011
	Trained	0.090±0.019	0.092±0.025	0.072±0.013	0.055±0.007	0.051±0.008	0.043±0.006

Table 3.2 Maximal isometric MAV muscle activation (EMG) as a function of test (pre and post), arm (trained and untrained) and muscle (agonist and antagonist) for each group (Mean ± SE). *Change score for the agonist muscle pooled across arms significantly greater than imagery training and control groups.

in the non-training arm and training arm averaged 4.0% and 4.9% of the pre training peak isometric EMG activity, respectively.

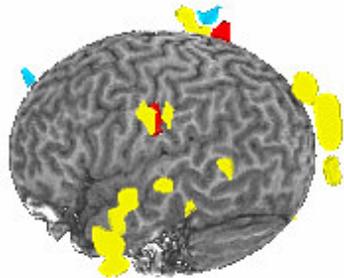
3.3.3 fMRI

As outlined previously, shared and unique activation maps for pre and post training scans are both overlaid on the standardized brain image for ease of comparison. The activation maps are displayed on a 90% underlay (outer 10% is stripped off the brain) for a more inclusive display of 3D rendered activation patterns by showing depth of activation into cortex. Using the 90% underlay was more revealing than the 100% underlay, as activations are sometimes not visible on the surface of the cortex. Separate maps were generated for each condition (right and left actual, right and left imagery) and group (actual, imagery). The 3D brain is displayed in three views: right and left hemisphere, and cerebellum. The cerebellum views are also displayed as 90% brain, and are cut in the coronal plane to isolate the cerebellum. Cerebellum views are also cut inferiorly at $Z=-20$ to allow a full depth view of activation in the cerebellum. To clarify, $Z=0$ in Talairach coordinates is at the level of the anterior and posterior commissure.

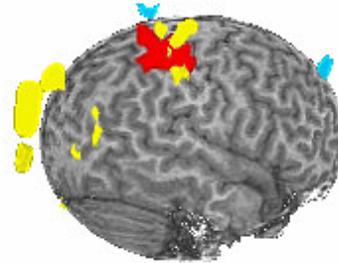
Figure 3.3 displays shared and unique activations for pre and post training for both the right (trained) and left (untrained) actual-contraction conditions for the actual training group, $t(3)=3.537, p<0.001$. The actual left condition showed shared activation in right M1 and S1, and left ventral M1. Regions of activation unique to post training included right M1 and S1, left ventral M1 and S1, left anterior and posterior middle temporal gyrus, left inferior temporal gyrus, medial occipital cortex and posterior medial and left lateral cerebellum. Regions of activation unique to pre training included only dorsal S1 and superior frontal gyrus. The actual right condition exhibited shared activation in left S1, and right superior occipital cortex. Regions

Actual Training Group

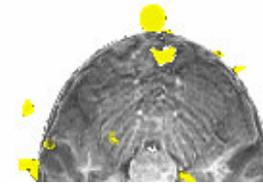
Actual Left (Untrained)



Left Hemisphere

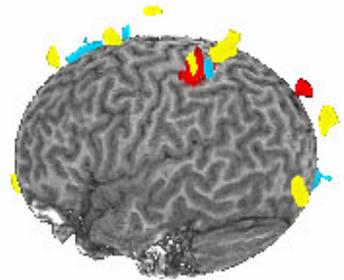


Right Hemisphere

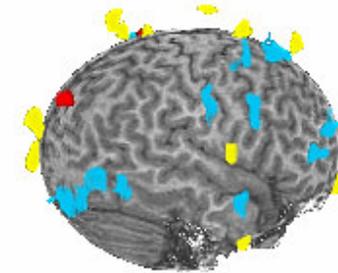


Cerebellum

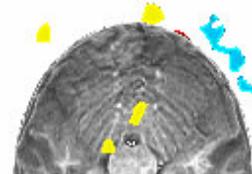
Actual Right (Trained)



Left Hemisphere



Right Hemisphere



Cerebellum

Figure 3.3 Shared and unique activations for pre and post training during actual right and left conditions for the Actual training group. Yellow regions represent activations unique to post training and Blue regions represent activations unique to pre training. Red regions represent activations shared by pre and post training. Therefore, total pre training activation can be inferred by combining red and blue regions, and total post training activation can be inferred by combining red and yellow regions. Note the degree of increased activation after training for both arms.

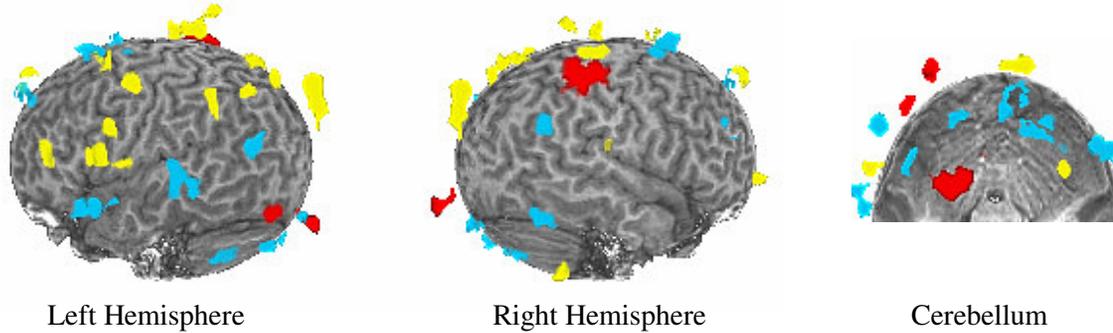
of unique activation for post training included left S1, left dorsal PMC, superior frontal gyrus, medial and left occipital cortex, and anterior cerebellum. Regions of activation unique to pre training included right ventral S1, right PMC, right inferior occipital cortex, right posterior inferior temporal gyrus, right anterior middle temporal gyrus, right prefrontal cortex, and left S1.

Figure 3.4 displays shared and unique activations for pre and post training for both the right (trained) and left (untrained) actual-contraction conditions for the imagery training group, $t(3)=3.537, p<0.001$. The actual left condition showed shared activation in right S1, left inferior occipital cortex, and left anterior cerebellum. Regions of activation unique to post training included left S2, left ventral PMC, medial occipital cortex, left prefrontal cortex, right M1 and S1, and right cerebellum. Regions of activation unique to pre training included bilateral dorsal PMC, left anterior superior temporal gyrus, bilateral superior temporal gyrus/angular gyrus (Wernicke's area), and posterior cerebellum. The actual right condition exhibited shared activation in left S1 cortex, left PMC, bilateral middle and inferior temporal gyrus, medial cerebellum, and superior frontal gyrus. Regions of unique activation for post training included bilateral ventral M1, bilateral prefrontal cortex, right PMC, right superior temporal gyrus, right lateral cerebellum, left dorsal M1 and S1, left SMA, and left inferior occipital lobe. Regions of activation unique to pre training included right inferior temporal gyrus, anterior cerebellum, and superior frontal gyrus.

Figure 3.5 displays shared and unique activations for pre and post training for both the right (trained) and left (untrained) imagery conditions for the actual training group, $t(3)=2.700, p<0.01$. The imagery left condition elicited shared activation in right PMC, left SMA, left prefrontal cortex, and dorsal S2. Regions of activation unique to post training included right

Imagery Training Group

Actual Left (Untrained)



Actual Right (Trained)

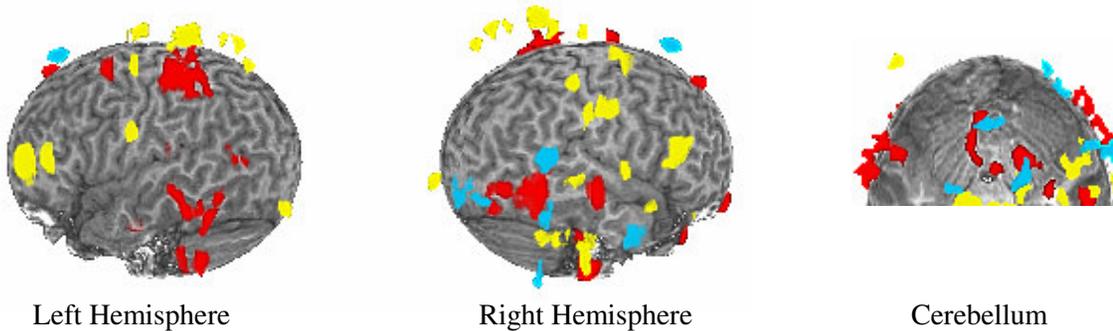
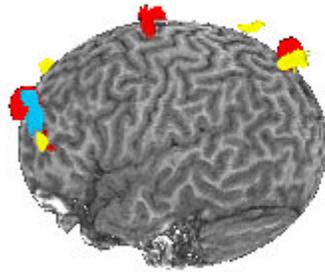


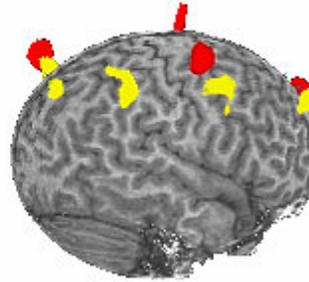
Figure 3.4 Shared and unique activations for pre and post training during actual right and left conditions for the Imagery training group. Yellow regions represent activations unique to post training and Blue regions represent activations unique to pre training. Red regions represent activations shared by pre and post training. Therefore, total pre training activation can be inferred by combining red and blue regions, and total post training activation can be inferred by combining red and yellow regions. Note decreased activation of temporal lobe after training for the untrained arm, and the substantial amount of shared activation (red) between pre and post conditions for the trained arm.

Actual Training Group

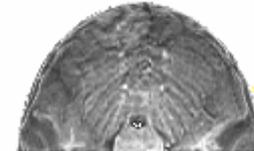
Imagery Left (Untrained)



Left Hemisphere

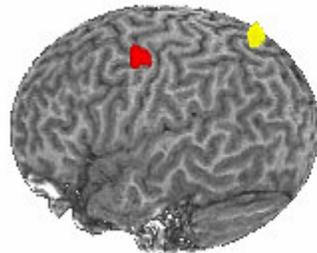


Right Hemisphere

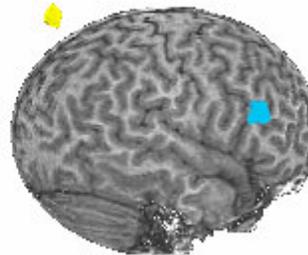


Cerebellum

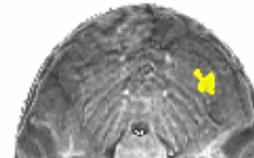
Imagery Right (Trained)



Left Hemisphere



Right Hemisphere



Cerebellum

Figure 3.5 Shared and unique activations for pre and post training during imagery right and left conditions for the Actual training group. Yellow regions represent activations unique to post training and Blue regions represent activations unique to pre training. Red regions represent activations shared by pre and post training. Therefore, total pre training activation can be inferred by combining red and blue regions, and total post training activation can be inferred by combining red and yellow regions. Note the increased activation after training particularly for the untrained arm.

PMC, right prefrontal cortex, and bilateral S2. Regions of activation unique to pre training included only left prefrontal cortex. The imagery right condition exhibited shared activation only in left M1. Regions of unique activation for post training included left S2 and right cerebellum. Regions of activation unique to pre training included only right ventral PMC.

Figure 3.6 displays shared and unique activations for pre and post training for both the right (trained) and left (untrained) imagery conditions for the imagery training group, $t(3)=2.700$, $p<0.01$. The imagery left condition elicited no shared activations between pre and post. Regions of activation unique to post training included left SMA, left middle temporal gyrus, bilateral occipital cortex, and bilateral prefrontal cortex. Regions of activation unique to pre training included only right S2. The imagery right condition exhibited shared activation only in right S2 and right occipital cortex. Regions of unique activation for post training included left SMA, left inferior temporal gyrus, medial occipital cortex, and dorsal S1. Regions of activation unique to pre training included dorsal S2, and right posterior superior temporal gyrus.

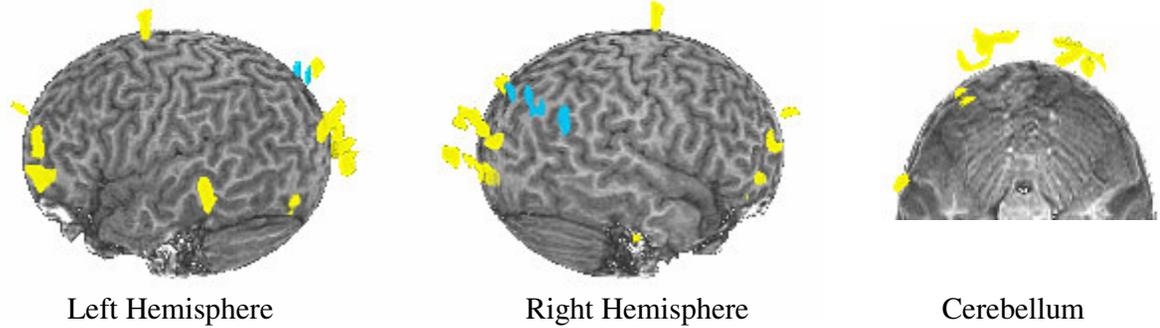
There were no significant regions of activation in sub-cortical structures including basal ganglia, thalamus, and corpus callosum, for any condition in either group, therefore anatomical views of these structures are not shown.

3.4 Discussion

This study was the first to examine both the central and peripheral adaptations with cross-education of strength within the same experiment. Although several functional imaging studies have been able to demonstrate changes in activation in the brain with movement task learning (Karni et al., 1995; Grafton et al., 1995; Jueptner et al., 1997; Grafton et al., 2002; Sakai et al., 2002), this study is the first to show changes in cortical activation associated with strength

Imagery Training Group

Imagery Left (Untrained)



Imagery Right (Trained)

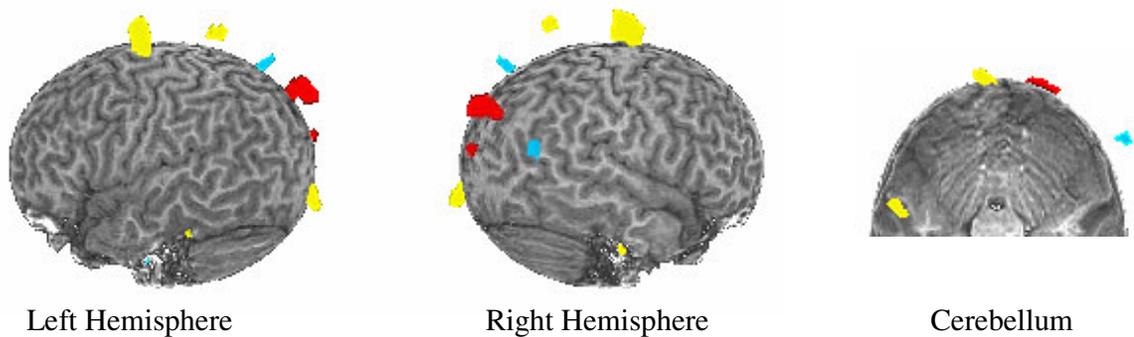


Figure 3.6 Shared and unique activations for pre and post training during imagery right and left conditions for the Imagery training group. Yellow regions represent activations unique to post training and Blue regions represent activations unique to pre training. Red regions represent activations shared by pre and post training. Therefore, total pre training activation can be inferred by combining red and blue regions, and total post training activation can be inferred by combining red and yellow regions. Note the increased activation after training for both arms.

training. This study was also the first to investigate central and peripheral neural adaptation in both limbs in response to imagery training. Previous fMRI studies have determined that motor imagery produces cortical activation similar to actual movement (Leonardo et al., 1995; Cunnington et al., 1996; Porro et al., 1996; Schnitzler et al., 1997; Lotze et al., 1999; Binkofski et al., 2000; Romero et al., 2000; Thobois et al., 2000; Naito et al., 2002), but no study has determined whether imagery training results in CNS adaptation similar to strength training. The major finding of this study is that unilateral actual strength training and unilateral imagery training are both accompanied by changes in cortical activation reflective of motor learning, but only actual training was effective for strength increase in the trained and untrained limb.

Consistent with the results from Experiment 1 after right hand strength training, the magnitude of cross-education of strength (47.7%) in this study was similar to the magnitude of strength gain in the trained arm (45.3%) (Figure 3.2). The magnitude of cross-education in the present study was at least 100% of the strength increase in the trained arm- much larger than the typical magnitude of cross-education relative to the trained limb (35-60%) reported in recent reviews (Zhou, 2000; Munn et al., 2004). Also consistent with previous studies (Garfinkel and Cafarelli, 1992; Farthing and Chilibeck, 2003), cross-education of strength was not accompanied by changes in muscle size, indicating involvement of neural adaptation. Regions of cortical activation associated with the untrained arm seem to isolate motor learning as the mechanism of cross-education of strength. The major regions of increased activation associated with cross-education of strength after actual training included the contralateral sensorimotor strip (M1 and S1), left temporal lobe, and posterior medial cerebellum. Increased activation in M1 with cross-education of strength is consistent with previous studies associating M1 plasticity with motor learning (Karni et al., 1995; Pascual-Leone et al., 1994; Pascual-Leone et al., 1995; Grafton et

al., 1995). For the present study, the region of activation in sensorimotor cortex for the untrained arm associated with post training was enlarged (Figure 3.3). This is consistent with previous studies where motor learning was associated with enlarged M1 activation (Pascual-Leone et al., 1994; Karni et al., 1995; Pascual-Leone et al., 1995). Further, there was evidence of functional reorganization (Pearce et al., 2000) where dorsal regions of sensorimotor cortex were activated before training, but not after training (Figure 3.3). Functional reorganization in the motor strip including new activations, and suppression of previously activated regions has been reported previously with motor learning (Shadmehr and Holcomb, 1997; Van Mier et al., 1998; Pearce et al., 2000; Staines et al., 2002), and may suggest the occurrence of LTP and LTD. Changes in activation in contralateral sensorimotor cortex for the untrained arm were similar to the trained arm, but the total region of activation in sensorimotor cortex for the untrained arm was visibly larger. This is congruent with similar relative strength changes in both the trained and untrained arm (Figure 3.1), with muscle size increases contributing to strength only in the trained arm (Table 3.1). Similar change in activation in contralateral motor strip with both arms also suggests communication between hemispheres regarding an improved motor plan for producing strength. Interestingly, dorsal PMC activation was observed only for the trained limb (Figure 3.3). This might suggest a 'priming' effect for the untrained limb. One hypothesis of this study was that an altered motor plan would be reflected by changes in agonist-antagonist muscle recruitment. This is partially supported in that the change in agonist muscle activation for both arms with actual training was greater than the imagery training and control groups (Table 3.2). Together these results support the cross-activation model reported previously with skill transfer (Parlow and Kinsbourne, 1989), where motor engrams are stored in both hemispheres with unilateral acquisition. As proposed by the model, task acquisition with the more proficient system such as

in the present study (dominant limb), would theoretically provide a better stored engram for the opposite limb. The findings of this study also partially support the theory proposed by Imamizu and Shimojo (1995), where if the task level (brain) is primarily involved in transfer of learning, perfect transfer should occur. Cortical adaptation in conjunction with perfect transfer was indeed observed in the present study. However, peripheral adaptation (manipulator level) was shown in conjunction with central adaptation (brain) in the present study, and Imamizu and Shimojo (1995) theorized that if transfer involved contribution from both the brain and the periphery than intermediate transfer would occur. Notably, the theory of Imamizu and Shimojo (1995) is based on transfer of skills not strength, where changes in muscle size do not contribute to performance improvement. In this study, one could argue that neural adaptation was much greater in the untrained arm than the trained arm, since muscle hypertrophy contributed to strength gain in the trained arm. Muscle hypertrophy was responsible for a portion of the 45.3% increase in strength of the trained arm, whereas the 47.7% increase in strength of the untrained arm was entirely from neural adaptation.

In addition to increased activation in contralateral sensorimotor cortex, post training activation patterns with the untrained arm appear to reflect more overall bilateral activation compared to the trained arm, where there was an apparent shift of activation towards the contralateral hemisphere (Figure 3.3). Bilateral activation with unilateral movement has been shown previously in M1, PMC, and SMA (Kristeva et al., 1991; Toma et al., 1999; Ehrsson et al., 2000; Liu et al., 2000; Gerardin et al., 2000; Binkofski et al., 2000; Nirikko et al., 2001), but no study has determined the effects of unilateral training on cortical lateralization with unilateral movement. More activation in ipsilateral cortex with the untrained arm in combination with similar patterns of adaptation in the contralateral motor strip in both arms provides evidence for

information retrieval from cortex relevant for the trained arm during movement with the untrained arm. Interestingly, new activation in the ipsilateral cortex included substantial left temporal lobe activation (mainly left middle temporal gyrus). Left middle temporal gyrus has been targeted as the region for retrieval of motion knowledge (Martin et al., 1995). Activation of this region with cross-education of strength could reflect retrieval of semantic knowledge of movement acquired through training. Reasonably, stored information about movement from ipsilateral cortex relevant for the trained arm is accessible during movement with the opposite untrained arm. Temporal lobe activation with left-hand learning has been shown previously with right-handers (Grafton et al., 2002). New activation was also shown in occipital cortex for the untrained arm (Figure 3.3), which could reflect some visualization of performing the movement during training. Activation in ventral occipito-temporal cortex has also been linked to semantic memory (Martin and Chao, 2001). Occipital cortex activation unique to post training for the untrained arm could reflect visualization of performing the task with the opposite arm, or a connection between seeing the word 'contract' in the MRI and memories of performing the movement with the opposite arm. A connection between memory of the movement and seeing the word 'contract' in the MRI was likely not present before training, since a strong memory of the movement was not yet present.

Similar ipsilateral activation in temporal lobe was not observed for the trained right arm after actual training, conceivably because the movement is well mastered with the trained arm and retrieval of stored information about the task requirements is not necessary (performing the movement has become automatic). Regions of activation unique to pre training included right temporal lobe, right PMC, and right ventral occipito-temporal cortex; all apparently deactivated with training (Figure 3.3). Activation of these regions before training reflects storage of

information about the movement for future movement with the opposite limb. However, this cannot be confirmed by previous studies, and the same adaptation was not shown for the untrained left limb prior to training. This could be a processing effect unique to the right limb, and might explain why transfer studies historically show preferential transfer from right to left (Parlow and Kinsbourne, 1989; Gordon et al., 1994; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996; Latash, 1999; Teixeira, 2000-experiment 1; Criscimagna-Hemminger et al., 2003; Teixeira and Caminha, 2003), or it could be related to the idea of right-hand advantage with more difficult tasks (Roy and Elliott, 1986; Elliott et al., 1993; Roy et al., 1994). Right temporal lobe has been previously associated with decreased regional CBF with motor sequence learning (Grafton et al., 1995). Motor learning occurring with resistance training may be associated with decreased activation of right temporal lobe as shown in the present study. The apparent decrease in activation of the ipsilateral temporal lobe may also indicate increased lateralization to the contralateral left hemisphere during right-hand contractions after a period right-hand unilateral training.

New activations were also apparent in the cerebellum for both arms after actual training (Figure 3.3). Activation in cerebellum shown after training could reflect LTP with cross-education of strength, both of which are thought to occur with motor learning (Ito, 2000; Sanes, 2003). Another major function of the cerebellum is to compare actual movement with intended in order to shape ongoing movement and improve accuracy (Ghez, 1991). Increased activation in the cerebellum may reflect more precise timing of agonist, antagonist, or synergist muscle activation resulting in improved coordination. This study was able to confirm significant changes in agonist muscle activation (Table 3.2), but no measures of synergist muscle activation were taken.

As discussed earlier, there is conflicting evidence as to the effectiveness of imagery training for increasing strength. Unilateral imagery training as prescribed in this study was not effective for increasing strength in either limb. The present results are consistent with Herbert et al. (1998) who found no effect of imagery training with right arm training (elbow flexors). On the other hand, imagery training has been effective for strength increase with left hand training (fifth digit abduction) (Yue and Cole, 1992) and bilateral lower limb training (plantar-flexion) (Zijdewind et al., 2003). There appears to be no clear relationship to training duration. The present study and the study by Herbert et al. (1998) report training for 6 weeks and 7 weeks, respectively, with no effect. The studies showing imagery training to be effective had training durations of 4 weeks (Yue and Cole, 1992) and 7 weeks (Zijdewind et al., 2003). The exact method of instruction for imagery that is best for eliciting strength gain is also unclear. Similar method of imagery preparation and encouragement was used across studies with the exception of the study by Zijdewind et al. (2003), who presented subjects with a video of the task prior to training to facilitate imagery. Another exception is that the present study used shorter contraction duration (2 seconds) in comparison to the other studies (10-15 seconds). Shorter contraction duration was used to be consistent with actual training and to accommodate the MRI environment, but may have compromised the ability of the subjects to enter into the kind of imagery effective for strength. However, the 2-second contraction duration was highly effective for strength gain with actual training (Figure 3.2). Further, Herbert et al. (1998) found no effect with right arm training using 10-second contractions. The precise imagery training protocol that elicits an increase in strength may be very specific, and even minor deviations from the protocol could lead to no effect. Further research into the effectiveness of imagery training for strength is warranted.

The potential influence of handedness and task familiarity with imagery training should also be considered. As shown in Experiment 1 in strongly right-handed individuals, the limb designated as the training limb can influence the magnitude of strength increase (Figure 2.2). Arguably, imagery training with the weaker left hand in right-handed individuals (Steenhuis and Bryden, 1999) may indicate a rehearsal of the more effective motor program (right hand) for the left hand during training, leading to motor learning and strength increase. This could explain the effectiveness of left hand imagery training for the trained hand shown by Yue and Cole (1992), but does not explain the cross-education effect shown for the untrained right hand in the same study (hand dominance not reported). Yue and Cole (1992) arguably used the most unfamiliar training protocol (isometric fifth digit abduction) leading to 14% cross-education with actual training, and a 22% strength increase in the trained limb along with 10% cross-education with imagery training. The present study produced far more adaptation with actual training, showing 47.7% cross-education with isometric ulnar deviation training, but still found no effect of imagery training for either arm.

Despite showing no effect for strength, imagery training resulted in changes in activation in regions consistent with actual training, providing evidence of motor learning. However, there were also some important differences in activation patterns (temporal lobe). For both arms, adaptations included new activations in contralateral sensorimotor cortex, ipsilateral PMC, contralateral sensory cortex, contralateral prefrontal cortex, and cerebellum, and decreased activation in ipsilateral temporal lobe, cerebellum and prefrontal cortex (Figure 3.4). As compared to actual training, much larger regions of shared activation for both arms were shown for imagery training (Figures 3.4), perhaps indicating less functional reorganization. Interestingly, with imagery training, left temporal lobe activation was evident before training for

the untrained arm, whereas with actual training, left temporal lobe was part of new activation with post training for the untrained arm. This could represent an inability to retrieve semantic memory of the task for the untrained arm after imagery training. Changes in activation associated with the trained arm after imagery training was indicative of functional reorganization in temporal lobe- where decreased activation, shared activations, and new activations were shown (Figure 3.4). New activation in ipsilateral (right) temporal lobe with the training arm may represent retrieval of semantic memory of imagery training, or comparisons between stored information from imagery training and new information associated with actually performing the contractions during post-testing. However, semantic representations have previously been associated with regions of left temporal lobe (Martin, 2001).

Similar evidence of functional reorganization can be seen in cerebellum with imagery training. There appears to be a shift of activations from more posterior activation to anterior-lateral activation in cerebellum when using the untrained arm (Figure 3.4). Lateral activation in cerebellum unique to motor imagery has previously been noted when compared to actual movement (Lotze et al., 1999). Lateral ipsilateral activation for both arms likely reflects an influx of sensory feedback associated with actually performing the contractions. Activation changes in cerebellum could also reflect comparisons between actual movement and what was intended by imagery- especially if movement imagery was not accurate compared to reality. As noted for actual training, functional reorganization in cerebellum with training might reflect LTP and LTD, both of which are thought to occur with motor learning (Ito, 2000; Sanes, 2003). Deactivation in cerebellum with imagery training might suggest LTD of synapses associated with actual contraction.

Synthesizing the fMRI results from the actual conditions leads to an important issue: changes in activation are evident after both actual and imagery training, but only actual training is effective for strength gain. Unfortunately, a disadvantage of fMRI is that it reflects the synaptic activity of populations of neurons including both excitatory and inhibitory input (Arthurs and Boniface, 2002). Therefore, the exact resultant input to the periphery cannot be determined by fMRI. This is why EMG data was important to collect. The EMG analysis in this study was able to detect greater changes in agonist muscle activation in both arms after actual training as compared to the imagery training and control groups (Table 3.2), but no significant changes in activation were observed for any individual muscle over time. Despite this finding, it is likely that the neural input to the untrained limb was changed with actual training. Nonetheless, it should be noted that strength may be increased as a result of an increase in specific tension, or improved force transmission, without any change to muscle activation (Jones and Rutherford, 1987; Enoka, 1988). The present results show that changes in cortical activation are accompanied by changes to neural input to the periphery. However, since the EMG analysis did not include postural and synergist muscle activation, it does not represent the full scope of changes in neural coordination that might be reflected by activation changes in the brain. Further, the EMG analysis could not decipher changes in motor unit properties that may have contributed to strength increase, such as increased conduction velocity, number of active motor-units, and motor-unit discharge rate (Farina et al., 2004). Regardless, the motor pattern associated with the untrained arm was adapted to produce more strength after training. Performance improvement was likely the result of processing sensory feedback to make error corrections, similar to motor learning studies where error reduction and decreased reaction time are noted with performance improvement (Grafton et al., 1995; Jueptner et al., 1997; Van Mier et al., 1998). Presumably, for

strength to improve with imagery training there must also be alterations in the motor program. However, imagery training involves no feedback regarding knowledge of results, limiting the ability to make error corrections. This is a plausible explanation for why imagery training was not effective in the present study, but does not explain why increased activation with imagery training did not coincide with strength improvement. Apparently, the change in cortical activation associated with imagery training did not result in appropriate changes to the motor program necessary to elicit strength increase. For example, new activations in left temporal lobe and the hand region of the contralateral sensorimotor cortex were only shown for the untrained arm after actual training (Figure 3.3). Likewise, activation maps with imagery training appeared to involve much more prefrontal cortex activation suggesting greater involvement of cognitive processing during actual conditions after training. This may reflect more obscurity associated with task performance as compared to actual training. As discussed earlier, these discrepancies could be the determining factor leading to cross-education.

Imagery conditions for both actual and imagery training present much less complicated data. Motor imagery for both actual and imagery training showed activation in PMC and SMA (Figure 3.5 and 3.6). This is consistent with previous studies reporting SMA and PMC with motor imagery (Cunnington et al., 1996; Deiber et al., 1998; Leonardo et al., 1999; Lotze et al., 1999; Binkofski et al., 2000; Romero et al., 2000; Naito et al., 2002). Contrary to the findings of previous studies, the data presented here showed very different activation patterns for motor imagery compared to actual movement. Most studies claim motor imagery elicits similar activation patterns as actual movement (Cunnington et al., 1996; Porro et al., 1996; Schnitzler et al., 1997; Lotze et al., 1999; Leonardo et al., 1995; Binkofski et al., 2000; Romero et al., 2000; Thobois et al., 2000; Naito et al., 2002). Motor imagery has also been shown to include

contralateral M1 (Porro et al., 1996; Schnitzler et al., 1997; Leonardo et al., 1999), superior parietal lobe (Thobois et al., 2000), and cerebellum (Porro et al., 1996; Thobois et al., 2000; Naito et al., 2002), and ipsilateral areas including M1, SMA, and PMC, parietal cortex and prefrontal cortex (Roth et al., 1996; Schnitzler et al., 1997; Binkofski et al., 2000; Gerardin et al., 2000). The findings of this study support superior parietal lobe activation with both arms, but M1 and cerebellum activation was only shown for the right arm after actual training, and ipsilateral SMA was only shown for the untrained left hand with actual training. M1 activation with only right hand imagery in right-handers has also been shown previously (Thobois et al., 2000), supporting the idea that the dominant hand may be more proficient at producing motor imagery. However, in this study, overall activation appeared to be greater with left arm imagery (Figure 3.5 and 3.6).

Although imagery training was not effective for increasing strength, it appeared to be effective for improving motor imagery. Activation patterns after training appear to be more consistent with previous studies (Leonardo et al., 1999; Lotze et al., 1999). Imagery training was associated with very little shared activations between pre and post conditions during motor imagery as compared to actual training, indicating greater functional reorganization. Imagery training was also associated with more activation in occipital cortex, perhaps reflecting an improved ability to visualize movement. New activation in left temporal lobe during imagery was also apparent after imagery training (Figure 3.6) possibly indicating retrieval of semantic memory to produce imagery. Left temporal lobe activation has been shown previously with motor imagery (Gerardin et al., 2000). However, in this study left temporal lobe activation was only shown in the untrained arm. Left temporal lobe activation for the untrained arm may reflect retrieval of semantic knowledge gained by the trained arm, as mentioned in regards to the

untrained arm after actual training. Motor imagery with actual training was associated with more overall activation (shared and new) in premotor areas with imagery, especially with the untrained arm. Premotor activation with motor imagery is consistent with Lotze et al. (1999) who provided some brief training (including imagery and movement) prior to motor imagery assessment. This discrepancy could be related to better knowledge of the complexities of the required movement associated with actual training. Imagery training may only be effective for strength increase after a brief period of actual training.

The major conclusion from this experiment is that changes in cortical activation reflecting motor learning were apparent after unilateral actual and imagery training, but only actual training was effective for improving strength in the trained and untrained arm. These findings allude to the importance of feedback from the periphery in order to induce motor learning in cortex effective for strength increase. Another important finding of this study is that changes in cortical activation uniquely associated with the untrained arm included regions of left temporal lobe, indicating a potential role of memory retrieval of prior movements acquired by the trained arm. Cortical activation associated with cross-education of strength (untrained arm) was also associated with an enlarged region of activation in sensorimotor cortex. This study concludes that the mechanism of cross-education of strength is increased activation in cortex indicative of motor learning in both hemispheres of the brain with unilateral training. Increased activation might indicate that neural plasticity occurred with training. The process of motor learning accompanying unilateral movements likely involves inter-hemispheric communication of an improved motor plan that provides the untrained limb with a reference for preparation and execution of movement in the future.

Chapter 4: General Discussion

4.1 Summary of Major Findings

Cross-education of strength is influenced by strength asymmetries related to handedness, and the preferential direction of transfer is from dominant to non-dominant limb. Further, cross-education of strength is accompanied by changes in activation in both hemispheres of the brain that resemble what has been previously reported with motor learning (Pascual-Leone et al., 1994; Karni et al., 1995; Pearce et al., 2000), which might indicate the occurrence of neural plasticity with training. These results also indicate a relationship between transfer of strength and transfer of skill.

Experiment 1 demonstrated that cross-education of strength was greater in the right to left direction of transfer in right-handed individuals and was not accompanied by increased agonist and/or decreased antagonist activation. Experiment 2 showed that increased activation in contralateral sensorimotor cortex and ipsilateral temporal lobe accompanied contractions of the untrained limb after training. In contrast to Experiment 1, cross-education of strength after right-hand training was accompanied by a significant positive change in agonist activation. Experiment 2 also showed that imagery training resulted in changes in activation in the brain, but was not effective for increasing strength. Changes in activation with imagery training did not include increased activation of temporal lobe. Despite evidence of motor learning after both actual and imagery training, only actual training was effective for improving strength in both the trained and untrained arm, indicating a role of peripheral feedback from the muscle in order to induce motor learning in cortex effective for cross-education of strength.

4.2 Cross-education of Strength and Interlateral Transfer

In addition to highlighting the central and peripheral neural adaptations accompanying cross-education of strength, this project was successful in emphasizing the connection between interlateral transfer of skill and cross-education of strength. Essentially, the only discrepancy between the two types of transfer is the characteristics of the task being transferred and the duration of ‘learning’ or ‘training’. Skill transfer studies usually involve acquisition within minutes or hours, whereas as cross-education of strength studies involve training over the course of many weeks. As will be discussed later, the mechanisms for each type of transfer are related if not the same.

4.2.1 The Direction of Transfer and Strength Asymmetry

The results of Experiment 1 after right arm training are consistent with the majority of interlateral transfer studies where the preferential direction of transfer was from dominant to non-dominant limb (Parlow and Kinsbourne, 1989; Gordon et al., 1994; Imamizu and Shimojo, 1995; Stoddard and Vaid, 1996; Latash, 1999; Teixeira, 2000-experiment 1; Criscimagna-Hemminger et al., 2003; Teixeira and Caminha, 2003). As outlined in Chapter 1, transfer of skill between limbs has been the focus of motor control researchers, whereas exercise physiologists have focused on transfer of strength between limbs with training (cross-education of strength). The skill transfer literature is extensive but is limited mainly to motor tasks involving the hand and arm. Consequently, skill transfer studies always consider the degree of handedness in designing protocol. The tendency for the use of hand and arm movements has made it difficult to apply findings from skill transfer studies to cross-education of strength studies where mostly lower body tasks are used. Regardless of protocol, cross-education of strength studies rarely report limb dominance (Carolan and Cafarelli, 1992; Housh et al., 1992; Weir et al., 1995;

Shields et al., 1999; Ebersole et al., 2002) or have rarely attempted to control for it methodologically (Kannus et al., 1992; Shima et al., 2002; Farthing and Chilibeck, 2003a). As demonstrated by the findings of Experiment 1, the influence of the dominant limb and the direction of transfer are important for cross-education of strength. However, cross-education of strength studies have included a vast range of protocols with varying task complexity, targeting both upper (Moritani and deVries, 1979; Cannon and Cafarelli, 1987; Shields et al., 1999; Ebersole et al., 2002; Farthing and Chilibeck, 2003a) and lower body musculature (Carolan and Cafarelli, 1992; Kannus et al., 1992; Garfinkel and Cafarelli, 1992; Housh et al., 1992; Weir et al., 1995; Hortobágyi et al., 1997; Seger et al., 1998; Hortobágyi et al., 1999; Tracy et al., 1999; Shima et al., 2002). Less is known about transfer asymmetry and the influence of limb dominance on transfer direction for the lower body, so their importance may be underemphasized or assumed to have little impact. Presumably less is known about transfer asymmetry with lower limbs because leggedness may be more difficult to define than handedness and may even differ from footedness (Vanden-Abeelee, 1980). However, more recently, the Waterloo Footedness Questionnaire (WFQ) has been used to reliably determine the degree of footedness (Elias and Bryden, 1998) using a similar scoring system to the Waterloo Handedness Questionnaire (WHQ) used in the present experiment. Elias and Bryden (1998) found that footedness was actually a more reliable predictor of language laterality than handedness. This might indicate that transfer asymmetry with cross-education of strength is more pronounced in the lower limbs than the upper limbs. Cross-education of strength studies that have reported limb dominance with leg training have used kicking preference or take-off in jumping to determine the dominant leg (Housh et al., 1992; Kannus et al., 1992; Weir et al., 1995). However, the dominant limb for kicking and take-off could be opposite for some subjects

(Vanden-Abeelee, 1980). For example, with a strength task such as eccentric training of the knee flexors (Hortobágyi et al., 1997; Seger et al., 1998; Hortobágyi et al., 1999) it could be argued that for dominant right-footed individuals the left leg may be dominant for the task since it is used more for movements related to the protocol, such as the eccentric plant step in kicking or the plyometric one-leg take off step in jumping. The influence of limb dominance on the preferential direction of transfer for the lower body may not be as dramatic as shown for the upper body in Experiment 1.

Another difficulty in comparing cross-education studies using lower body tasks to those using upper body tasks, is that strength asymmetry in untrained individuals appears to be less pronounced for legs than arms. In a recent study by Maupas et al. (2002), left and right leg isokinetic peak torque was similar, where 36 of 40 subjects reported being right-footed. Most likely, this is due to greater contribution of the lower body to normal everyday activities for most people. For the arm training experiments in the present project, there were obvious strength differences between the left and right hands before training. This can be attributed to differences in neural recruitment considering muscle size was similar between arms (Table 2.1 and 3.1). Arguably, task complexity/familiarity could be related to the degree of asymmetry between limbs. Maupas et al. (2002) used very simple movements (isokinetic concentric knee flexion and extension) finding no asymmetry, whereas a much more obscure task was used for the present project (isometric handgrip ulnar deviation) where asymmetry was obvious. By convention, it appears that strength asymmetry between the dominant and non-dominant limb increases with increasing task complexity. Exhaustive left hand practice has been shown to dissipate asymmetry between hands for an aiming task in a right-handed subject (Heath and Roy, 2000) suggesting that becoming more familiar with a task with the left hand reduces asymmetry. Perhaps related to

task familiarity, is that adults show reduced asymmetry between hands as compared to youth (Bryden and Roy, 2005), indicating that experience also reduces asymmetry. Whether or not similar responses are shown for complex or unfamiliar strength tasks is yet to be determined. This knowledge would be beneficial for predicting the influence of handedness or the preferential direction of transfer for future studies of cross-education of strength, or it may enable researchers to predict when cross-education of strength will occur. Interestingly, unilateral training studies not showing cross-education of strength use more conventional and simple tasks such as concentric or isometric elbow flexion and/or knee extension (Garfinkel and Cafarelli, 1992; Housh et al., 1992; Ebersole et al., 2002) as compared to the novel and complex task used in the present experiments. Just as greater task complexity might increase asymmetry between limbs, increasing asymmetry may increase the magnitude of cross-education of strength. Greater task complexity could also explain why the preferential direction of transfer in skill transfer studies is commonly dominant to non-dominant. Most skill transfer studies incorporate complex motor skills, such as mirror writing (Latash, 1999), curl-field reaching paradigm (Criscimagna-Hemminger et al., 2003), inverted-reversed printing (Parlow and Kinsbourne, 1989) and reversed maze learning (Stoddard and Vaid, 1996). Usually in right-handed subjects the right hand is at an advantage when tasks are more difficult or require more accuracy, speed, and timing (Roy and Elliott, 1986; Elliott et al., 1993). Transfer studies that support non-dominant to dominant transfer have used sequence learning tasks that seem to require more cognitive than neuromuscular learning (Grafton et al., 2002).

4.2.2 Cross-education of Strength and Models of Transfer

Recall the models used to explain the findings of transfer studies: the access model (Taylor and Heilman, 1980), the proficiency model (Laszlo et al., 1970) and the cross-activation model (Parlow and Kinsbourne, 1989). The access model suggests motor engrams (motor programs) are stored in the dominant left hemisphere regardless of the hand used. The proficiency model operates on the premise that motor engrams are stored unilaterally in the contralateral brain hemisphere (Thut et al., 1996). Theoretically, the more effective engram will be stored when acquisition is with the more proficient system (left hemisphere of right-handers) and is more beneficial for learning in the opposite side (through commissural fibres). The cross-activation model hypothesizes the storage of dual engrams with right hand acquisition- one in each hemisphere. Therefore the acquisition of a task with the more proficient system would provide a better stored engram for the opposite side. The access model is not supported by the current investigation since the direction of transfer was preferentially right to left, and changes in activation were evident mainly in the contralateral hemisphere for both arms and with no evidence to support the storage of engrams only in the left hemisphere. This seems to refute the idea of a dominant left hemisphere for motor tasks. The proficiency model is supported since sensorimotor cortex activation evident with each arm was mostly contralateral with little ipsilateral activation, and increased activation in sensorimotor cortex was shown in both hemispheres with training. The cross-activation model is also supported in that similar changes in activation were observed in contralateral sensorimotor cortex for both arms, reflecting storage of engrams in both hemispheres with right arm training. Support for the proficiency and cross-activation model from the present investigation suggests a very important role of commissural fibres in communicating motor information between brain hemispheres and therefore between limbs.

The task-manipulator level model presented by Imamizu and Shimojo (1995) suggests greater magnitudes of transfer indicate more involvement at the task level (brain) than the manipulator level (muscles), and if learning is only at the task level, perfect transfer occurs. Perfect transfer implies that the quantified measure of performance was improved to the same degree in both limbs after unilateral acquisition. Perfect transfer was observed in both studies of the present project, suggesting learning with strength transfer is at the task level. This is promising for the potential for cross-education of strength to benefit the recovery of an impaired or injured limb. Further supporting learning at the task level, strength transfer was accompanied by substantial changes in cortical activation. Worth mentioning, is that the present investigation seems to provide evidence for better than perfect transfer with strength training even though relative strength gains were not significantly different between the trained and untrained arms (Figure 2.2 and 3.2). This can be explained by inherent differences between transfer of strength and transfer of skill. With skill transfer, changes in muscle size do not occur, therefore any performance outcomes are strictly neural changes. On the other hand, strength training usually results in muscle hypertrophy for the trained limb, which contributes to the increase in strength in addition to neural adaptation. As evidence of this, after right-hand training in Experiment 1, the trained arm strength increase was approximately 26% with no significant muscle hypertrophy, and cross-education of strength was 39%. In Experiment 2, significant hypertrophy was noted for the trained arm, and the increase in strength (45.3%) was more similar to the magnitude of cross-education (47.7%). Muscle hypertrophy combined with neural adaptation contributed to strength gain in the trained arm, but only neural factors were responsible for strength gain in the untrained limb. Therefore in both studies of the present project, it could be argued that better than perfect transfer of strength was observed. Better than perfect transfer

might also be related to substantial strength asymmetry between limbs at baseline. A weaker left hand has been shown previously with grip strength in right-handers (Steenhuis and Bryden, 1999). The weaker left arm likely reflects poor neuromuscular coordination compared to the right. This is supported by greater overall muscle activation for the trained arm (right) in Experiment 2 (Section 3.3.2).

Unfortunately, the transfer models discussed above do not provide an answer for where motor engrams are stored in cortex, or how learning at the task level is apparently easily transferred between limbs (Imamizu and Shimojo, 1995), because they do not discriminate the specific regions of the brain involved in motor learning or transfer. Thus, they cannot provide support for increased left temporal lobe activation uniquely associated with the untrained arm in Experiment 2 (Figure 3.3). Spatial information such as joint position and rate of change of joint angle (Imamizu and Shimojo, 1995) could be part of what is retrieved from memory during contractions with the untrained arm after training. Presumably, part of the motor engram for the task could be stored in left temporal lobe, or at least in the temporal lobe contralateral to the trained arm, and this information is accessible during future contractions with the opposite arm. As discussed in Experiment 2, motor learning associated with cross-education of strength appears to involve multiple brain regions, suggesting the process of motor learning and transfer is more complex than just passing information from one motor cortex to the other.

4.3 Cross-education of Strength and Imagery Training

Cross-education of strength is not likely to occur if little or no increase in strength is apparent in the trained limb (Zhou, 2000; Munn et al., 2004). In the present project, unilateral imagery training was not effective for increasing strength in either the trained or untrained arm,

but was associated with cortical plasticity during actual contractions (Figure 3.4). Not surprisingly, given substantially greater increases in strength with actual training, cortical plasticity with imagery training was different from actual training, particularly in temporal lobe regions. As discussed previously, temporal lobe activation is likely related to the effectiveness of actual training for cross-education of strength, which implies memory is involved. Further to this, there were larger regions of common activation between pre and post conditions with imagery training (Figures 3.4), perhaps indicating less functional reorganization. Therefore, it could be argued that less drastic changes in cortical output were associated with imagery training as compared to actual training, which could explain why imagery training was not effective for increasing strength in either limb.

The neural output to the agonist and antagonist muscles was unaltered with imagery training, as reflected by non-significant changes in muscle activation and strength. However, there was a decreasing directional trend for muscle activation of both the agonist and antagonist (Table 3.2). Changes in activation evident in cortex with imagery training may have been reflective of alterations in posture and synergist muscle activation that were beneficial for strength, but they were counter-acted by decreased agonist activation resulting in no net change in strength. This cannot be confirmed by the present project, since agonist-antagonist activation changes with imagery training were not significant and postural and synergist muscle activation was not assessed. More than likely, the neural output to the periphery was unaltered with imagery training and therefore no change in strength was observed. In order for imagery training to be effective for increasing strength, an altered motor plan from what was executed at baseline testing must be rehearsed during training and executed during post-testing. Theoretically, this is impossible unless the altered motor plan is drawn from the more proficient limb while training

the less proficient limb. Presumably, since the more proficient limb was used as the training limb in the present investigation, no increase in strength could be observed.

Even though imagery training was not effective for increasing strength, imagery training may still have some benefits. Under the current training strategy, imagery training was obviously not effective for strength gain, but other investigators have demonstrated imagery training protocols effective for increasing strength (Yue and Cole, 1992; Zijdwind et al., 2003; Ranganathan et al., 2004). There is also evidence from the present study that imagery training improved imagery ability (Figure 3.6). Improved imagery ability might be beneficial for future task acquisition, perhaps leading to quicker neuromuscular adaptation. A period of imagery training prior to actual training may facilitate a quicker phase of neuromuscular adaptation for subsequent strength training. This hypothesis warrants future study, and could have important implications for rehabilitation strategies where one has unilateral impairment or dysfunction. Imagery training of the impaired limb prior to physical training may lead to quicker re-learning during subsequent physical training and quicker return to normal function. Motor imagery of movement with the affected limb has been shown to induce cortical responses similar to the uninvolved limb during stroke recovery (Weiss et al., 1994), but whether this impacts the duration or success of recovery remains unknown.

Although the contribution the mirror cell system (ventral PMC) to motor imagery or cross-education of strength was not the focus of this project, the potential link to semantic representation of movement warrants discussion. There is evidence of an ‘observation/execution matching system’ active during movement observation (Rizzolatti et al., 1996b; Binkofski et al., 1999; Buccino et al., 2001) that is linked to activation in ventral premotor cortex and S2 (Binkofski et al., 1999). Mirror neurons encoded for a particular task are activated during

observation of the same actions being performed by another (Murata et al., 1997; Rizzolatti et al., 1998; Buccino et al., 2001). In the present project, if motor imagery was effective enough to produce a visual representation of the task, mirror neurons may have been activated. In a sense, subjects could have been observing themselves engaging in the movement. There is some evidence of activation of a mirror system in the present study. Regions of S2 were activated for all subjects during motor imagery, but only actual trained subjects show concurrent ventral premotor cortex activation (left arm imagery; Figure 3.5). Imagery training appeared to be associated with dorsal activation of premotor regions (SMA) along with greater activation of visual cortex (Figure 3.6). The discrepancy between premotor cortex activation with imagery training and actual training could be related to better knowledge of the task. For actual training, new activation in contralateral premotor cortex during motor imagery was in the region appropriate for wrist and hand movements. This is consistent with Buccino et al. (2001), who observed somatotopically organized activation of premotor cortex with different motor observations. However, for the present study premotor cortex activation during imagery was only observed for the untrained left arm. Presumably, this could represent the storage of motor information in the ipsilateral brain hemisphere during unilateral training. In other words, during right arm training the contralateral hemisphere was controlling movement, but the ipsilateral hemisphere might have been encoding information. One brain hemisphere could be observing the activity of the other, and through mirror cells stores information about movement that may become relevant for the opposite limb in the future.

4.4 Mechanisms of Cross-education of Strength

The data presented in this document suggest that cross-education of strength is essentially a form of motor learning originating in higher centers of the CNS. The mechanism of cross-education of strength appears to be revealed; plasticity in cortex reflecting motor learning occurs in both hemispheres with unilateral training. The other candidate mechanisms presented in Chapter 1 should not to be entirely dismissed. One mechanism may be an accessory to the other. For example, adaptations in agonist-antagonist coordination could result from plasticity in the brain. Further, there may be spinal adaptations that contributed to plasticity in the present study that were bypassed since cortical adaptations in the brain were accompanied by assessment of peripheral output at the muscle but not the spinal cord, such as the potential for inter-limb interaction in the spinal cord through interneurons.

4.4.1 Plasticity in the Brain

Plasticity in both hemispheres of the brain with unilateral training is likely the cellular mechanism controlling cross-education of strength. However, cellular adaptations in the brain cannot be proven by fMRI, so cellular mechanisms cannot be confirmed or refuted by the present investigation. To review, neural plasticity reflects lasting or permanent adaptation cortex in response to repetitive stimuli, and involves the formation of new synapses or connections in the brain, and can lead to a larger area of activation in relevant cortex with motor learning (Pascual-Leone et al., 1994; Karni et al., 1995; Pascual-Leone et al., 1995). Increased activation in the brain and a larger area of activation were both observed with cross-education of strength in the present investigation, which could indicate the presence of plasticity with training. Motor learning of skilled tasks and sequences has shown evidence of plasticity in M1 (Karni et al., 1995; for reviews see Sanes and Donoghue, 2000; Sanes, 2003), PMC and SMA (Grafton et al.,

1995; Grafton et al., 2002), basal ganglia (Jueptner et al., 1997) and cerebellum (Jueptner et al., 1997; Sakai et al., 2002). In the current project, cross-education of strength was accompanied by increased activation mainly in sensorimotor cortex, temporal lobe, and cerebellum. Temporal lobe activation could be a unique adaptation to unilateral motor learning. The above mentioned motor learning studies do not report temporal lobe activation, but they focus only on the involved limb and not on the transfer of learning to the opposite limb. The present study provides evidence that temporal lobe was recruited prior to training for the trained limb, but was apparently deactivated with training, whereas the reverse reaction was shown for the untrained limb (Figure 3.3). Brain regions important for retrieval of prior movement knowledge may not be necessary during performance of the task with the trained limb since the task is mastered and probably requires little cognitive effort to execute.

Deactivation of brain regions with learning as shown in several functional imaging studies where cortical reorganization was apparent with motor learning (Jueptner et al., 1997; Shadmehr and Holcomb, 1997; Van Mier et al., 1998; Pearce et al., 2000; Staines et al., 2002; Ward et al., 2003) might also reflect neural plasticity. Plasticity with motor learning likely also involves both LTP and LTD (Sanes and Donoghue, 2000; Sanes, 2003). Substantial strength increases in both limbs in the present project were accompanied by reorganization of activation within the brain. This reflects the importance of both LTP and LTD in order to produce effective and permanent learning. For example, LTP and LTD could enhance motor coordination by increasing activity of neurons associated with agonist or synergist muscles, and decreasing activity of neurons projecting to antagonists or other postural muscles that might detract from optimal execution of movement. The EMG analysis in the present study was able to detect significant changes in agonist but not antagonist output, and unfortunately did not include

synergist and postural muscles. Therefore, precisely how much the increase in cortical activation observed in this project reflects the agonist muscle compared to synergists and postural muscles cannot be confirmed.

Increased activation in cerebellum was also evident with cross-education of strength in the present project. Similar to other cortical structures, the cerebellum is known to reflect LTP and LTD with motor learning (Ito, 2000; Sanes, 2003). Reorganization in cerebellum could reflect diminished activity of climbing fibres reflecting less error (Ito, 2000). Undoubtedly, decreased error would be reflected after a period of strength training. LTD in cerebellum as reflected by diminished climbing fibre activity is also thought to be a memory mechanism (Ito, 2000). This type of adaptation in cerebellum could be linked to semantic memory storage or retrieval. Intuitively, cerebellum could be involved in comparing ongoing movements to stored semantic representations of movement in order to make error corrections, or it could be involved in altering stored information in semantic memory as new adjustments are made to enhance task execution (e.g. slight adjustments in posture during movement).

Change in activation of basal ganglia was not observed in conjunction with cross-education of strength, although it has been reported previously during motor sequence learning (Grafton et al., 1995; Jueptner et al., 1997; Grafton et al., 2002). Recruitment of basal ganglia during sequence learning is appropriate since they contribute to information processing needed for planning and triggering movement (Ghez and Gordon, 1995). Basal ganglia may have been overlooked in the present study because functional imaging was assessed before and after training and not during learning. Further to this, there was no sequence learning involved in the strength task. Interestingly, Jueptner et al. (1997) reported giving reinforcement for correct responses during sequence learning. Basal ganglia activation under these conditions is logical

since they are thought to participate in reinforcement-based learning (Doya, 2000). Since reinforcement was given to the subjects during training in the present study, reward based activity in basal ganglia could be involved in cross-education of strength by contributing to the alteration of stored motor engrams in cortex during training.

The arguments presented above for cross-education of strength being essentially a motor learning adaptation provides evidence that transfer of skill and transfer of strength are controlled by similar mechanisms. Unfortunately, very few studies have used functional imaging to determine cortical activation with skill transfer (Karni et al., 1995; Grafton et al., 2002), and thus the present functional imaging study is difficult to compare with previous findings. Karni et al. (1995) found little or no skill transfer after non-dominant hand sequence learning and therefore do not report functional imaging data for the contralateral hand. Grafton et al. (2002) report significant transfer (reduced reaction time) to the dominant hand after sequence learning with the non-dominant hand, but only report changes in the brain during learning with the non-dominant hand. Functional imaging data reported for the dominant limb only includes difference maps between mirror and original sequences after transfer, but does not include activation maps before transfer occurred. Therefore little can be drawn from this study regarding mechanisms of transfer. An important future study could use functional imaging to determine if similar changes in cortical activation for the contralateral limb are shown with strength transfer and skill transfer. Temporal lobe activation may be important for transfer of motor learning between limbs regardless of the characteristics of the task (e.g. sequence, skill, strength).

4.4.2 Bilateral Cortical Activation

The present investigation (Figure 3.3) provides some support for the theory that cross-education of strength is caused by bilateral cortical activation with unilateral movement. Greater overall bilateral cortical activation was observed for the untrained arm after training. The majority of ipsilateral hemisphere recruitment with the untrained left arm was in left temporal lobe. This provides support for the idea that the untrained limb has access to the information gained by the opposite limb during training. However, in contrast to previous studies, little or no bilateral activation was observed in motor and premotor areas in the present study. Most of the activation in sensorimotor cortex was in the contralateral hemisphere (Figure 3.3). Earlier studies report bilateral activation in motor and premotor areas with unilateral movement (Kristeva et al., 1991; Toma et al., 1999; Ehrsson et al., 2000; Liu et al., 2000; Gerardin et al., 2000; Binkofski et al., 2000; Nirikko et al., 2001), but do not report temporal lobe activation with actual movement. Conceivably, this is because no training took place in these studies, and both limbs were probably similarly exposed to the movement task, so memory retrieval of previous acquisition with the opposite limb was not necessary. Further, the majority of these studies did not compare activation between right and left arms (Toma et al., 1999; Binkofski et al., 2000; Ehrsson et al., 2000; Liu et al., 2000; Gerardin et al., 2000), and most assessed only right-hand movements (Toma et al., 1999; Binkofski et al., 2000; Ehrsson et al., 2000; Liu et al., 2000). In the event that activation was compared between right and left hands, whichever hand was used first in the experiment could influence activation patterns for the opposite hand during subsequent trials. To avoid order effects in the present investigation, the sequence of the experiment for the MRI acquisition was randomized for each subject. As such, temporal lobe activation was probably not linked to the order of the experiment, but rather to adaptations associated with strength training.

Retrieval of motor information from the left temporal lobe for the untrained left limb after training could also be linked to left hemisphere motor dominance. Left motor cortex activation in both right and left-handed subjects with left limb movement has been reported previously (Kim et al., 1993), but more strict contralateral activation with unilateral movement may be the more robust finding (Borowsky et al., 2002). Very little ipsilateral (left) motor cortex activation was noted with left arm movement in the present project, and it was further down the motor strip in the area relevant for the face and head (Figure 3.3). Further to this, ipsilateral (right) M1 activation for the face and head was also noted for the right arm prior to training (Figure 3.3). Activation of this region of motor cortex is puzzling, but it could be due to facial gestures or grimaces that are common when performing muscular contractions. Therefore, ipsilateral activation associated with left arm movement was likely unrelated to the task itself.

Since our subject pool was very strongly right-handed, contralateral hemisphere dominance for language could be expected (Rasmussen and Milner, 1977). Language dominance in the left hemisphere could provide support for the location of semantic memory and movement (left temporal lobe). Interestingly, apraxia (loss or impairment of the ability to execute complex movements or gestures) is commonly associated with aphasia (a slowly progressive language deficit) (Joshi et al., 2003), and the two deficits are often linked together with left hemisphere stroke (Zwinkles et al., 2003). The question remains as to whether the reason for the link between language and motor systems is due to left hemisphere dominance, or close anatomical proximity between premotor regions and Broca's area (Kertesz et al., 1984). Therefore, damage to the cortex in this region would have implications for both functions.

4.4.3 Adaptations in Muscle Activation Patterns

Although transfer of learning between limbs appears to occur in the brain, this does not imply that there is no role of the periphery in cross-education of strength. Adaptations in muscle activation patterns are likely an accessory of plasticity in the brain. In a way, peripheral adaptations validate the meaningfulness of plastic changes in the brain with learning. Meaningful alterations in agonist activation were observed with cross-education in Experiment 2, and there is some evidence from both studies that neural output to the periphery could have been altered since substantial increases in strength were observed in the untrained limb with no change in muscle size. Although, alterations to specific tension and force transmission properties of the muscle could induce an increase in strength without changes to muscle activation patterns (Jones and Rutherford, 1987; Enoka, 1988). Given Bernstein's problem of degrees of freedom or motor redundancy (Latash, 1993), whereby seemingly infinite combinations of muscle activation can produce to same joint torques, two-lead surface EMG as used in the present studies may be an overly crude representation of peripheral nervous system output. Previous studies have been successful in detecting changes in agonist and antagonist activation with cross-education of strength (Carolan and Cafarelli, 1992; Hortobágyi et al., 1997; Hortobágyi et al., 1999; Shima et al., 2002) but no study has measured synergist muscle activation concurrently. A valuable future study could examine peripheral adaptation with cross-education of strength more comprehensively by including synergist and postural muscles in the EMG analysis. For example, assessing muscle activation in the upper arm and shoulder might uncover neural output changes to synergist/stabilizer muscle groups.

Another important reason for assessing synergist and postural muscles with cross-education of strength is related to the complexity and unfamiliarity of the task. The task in the present study was chosen because it is a small hand and wrist movement that could be performed

in the MRI without excessive head motion, and it is a very obscure task that would theoretically involve more substantial neuromuscular adaptation and increase the magnitude of cross-education. Explicitly, the task seems very simple, but it involves multiple muscles of the forearm and hand in order to execute proficiently. Adding further obscurity, the task was also performed in the supine position, implicating stabilizer muscles of the trunk and shoulder. The consequence of using such a complex task is that multiple synergist and postural muscles are involved in the movement. Increasing task complexity will likely increase the degree of asymmetry, which will increase the magnitude of cross-education of strength. If future cross-education of strength studies continue to use very complex or unfamiliar tasks, then the importance of a more detailed EMG assessment of peripheral adaptation will be required.

4.4.4 Increased Excitability of the Contralateral Musculature

Increased motor unit excitability is a neural adaptation associated with resistance training (Aagaard et al., 2002). Hortobágyi et al. (1999) argue that afferent activity from activated muscles during unilateral movement could increase excitability of the contralateral musculature. They found electro-myostimulation (EMS) training more effective for cross-education than voluntary training, proposing that neurons innervating contralateral muscle fibers might be activated through pain receptors and skin sensory afferents during EMS. However, assuming that the brain is not involved in processing peripheral information with artificial muscle activation could be erroneous. Motor learning in the brain could still result from EMS training through feedback. EMS training could also lead to removal of neural inhibition, or activation of previously dormant muscle fibres. These aspects could be transferred to the opposite limb and induce cross-education of strength. Further, if increased muscle excitability is apparent in both

limbs with unilateral training, it would likely be reflected by changes in activation in the brain. Future studies should look at changes in cortical activation associated with EMS training or supra-maximal activation to determine the role of sensory feedback during contraction and its influence on future voluntary contractions. EMS training may serve to educate untrained muscle to maximally activate, and then this new motor program could be encoded in the brain and used for future voluntary contractions of either limb.

In order to determine muscle excitability in conjunction with cross-education the amplitude of the H-reflex would have to be assessed in both limbs before and after training. Unfortunately, the nature of the task used in the present experiment limited the possibility for muscle excitability to be measured using the H-reflex, and whether or not an increase in muscle excitability contributed to cross-education of strength cannot be confirmed. Reliably replicating isometric handgrip ulnar deviation contractions using muscle stimulation would be nearly impossible. Determining how muscle excitability contributes to cross-education of strength warrants future study. However, in order to effectively assess H-reflex, the complexity of the task would have to be reduced and this might compromise the magnitude of cross-education.

4.4.5 Corticospinal Tract Impulses

A disadvantage of the present investigation is that spinal mechanisms that might have been involved in cross-education of strength were not examined. The precise role of corticospinal tracts in motor learning is unclear. Ventral corticospinal tracts descend ipsilaterally and project bilaterally to the medial cell group controlling axial muscles (Martin and Jessell, 1995). The ventral tracts could be involved in neural adaptation associated with postural muscle activation necessary to execute unilateral movement. As discussed in Chapter 1, ventral

corticospinal tracts could also contribute to motor learning in higher levels of the nervous system through the brainstem at the reticular formation. The reticular formation is highly active for integration of various neural inputs and is actively involved in motor learning (Ghez and Gordon, 1995). Relative to inter-limb effects such as cross-education, alterations in neural drive to several involved muscle groups both distally and proximally could be relayed to both cortical hemispheres through the reticular formation as part of the learning process. Even if spinal mechanisms do contribute to cross-education of strength through corticospinal tracts and the reticular formation, the mechanism by which transfer of strength occurs is most likely through communication between cortical hemispheres in the brain. The precise role that the spinal cord plays in relaying relevant information for movement between limbs is unclear, and is likely not able to be determined with human studies.

Chapter 5: Conclusions and Future Research

5.1 Conclusions

The major conclusion of this project is that cross-education of strength is controlled by changes in cortical activation indicative of motor learning in both brain hemispheres after unilateral training. These changes in activation include increased activation of contralateral sensorimotor cortex and ipsilateral temporal lobe, and might reflect the occurrence of cortical plasticity. Cross-education of strength is a motor learning adaptation also reliant on peripheral feedback from muscles during training. Peripheral feedback appears necessary to elicit appropriate changes in neural coordination necessary for cross-education of strength to occur. Cross-education of strength is also influenced by strength asymmetries related to handedness, and the preferential direction of transfer is from dominant to non-dominant limb.

The behavioral similarity between cross-education of strength and interlateral transfer of skill in regards to the preferential direction of transfer leads to the conclusion that they are essentially the same neural adaptation in response to learning or perfecting a motor paradigm (strength or skill). Motor information about a previously novel task having been altered and perfected through strength training, is apparently easily communicated between limbs/brain hemispheres. Cross-education is likely an evolutionary adaptation associated with the existence of bilateral symmetry, whereby knowledge of unilateral movement is necessarily available for both limbs in the event that one limb is temporarily or permanently impaired.

The findings of this project could have practical implications for clinical cases where an injury requires unilateral immobilization (broken bone) or cerebral vascular incident (stroke) results in permanent or temporary functional impairment of one limb or side of the body. These applications will be discussed in further detail in the following sections of the document.

5.2 Limitations

One of the major limitations of this project was that muscle activation and force output could not be measured in the MRI environment. As a result there is no way to determine how the level of muscle activation in the MRI environment compared to that achieved during strength testing or training. Although the subjects were encouraged to aim for approximately 60% of max, the actual intensity of contraction could have varied. A necessary restriction of the MRI environment is that maximal contractions as prescribed in the present study cannot be performed due to the inherent motion artifact yielding unusable data. Therefore, even if force and muscle activation could be measured, maximal activation would not have been achieved. In consolation, previous functional imaging studies have shown that BOLD response does not vary with intensity of contractions corresponding to light and heavy resistance (Ludman et al., 1996). Given this, the activation maps that are displayed in Experiment 2 are likely very similar to what would be shown with maximal or near maximal contractions.

Several limitations associated with EMG acquisition of any kind have been discussed in detail in Experiment 1. One limitation specific to the study design for the present project is that EMG measures were repeated before and after training and compared. This process increases the potential for error associated with comparing the change of muscle activation over time. This is reflected by modest reproducibility of the EMG measures (refer to Section 2.2.5). Another limitation of the present project is that a different type of tape was used to fasten the electrodes in Experiment 2. This resulted in a cleaner signal and less variability, and could be the reason why significant changes in muscle activation were detected in Experiment 2 but not in Experiment 1. Another limitation of this project is that the EMG data only provide an indirect measure of

muscle activation unlike more direct techniques such as twitch interpolation. The task used in the present studies involved multiple muscles due to the required combination of handgrip and ulnar deviation. This made it difficult to effectively use interpolated twitch to gain an estimate of maximal motor unit recruitment.

The generalizability of the present investigation was somewhat limited. The subject pool was restricted to only right-handed females. Although the direction of transfer is unlikely to be affected by gender, previous studies in our lab have shown that females tended to show greater magnitudes of cross-education of strength (Farthing and Chilibeck, 2003a), and there is evidence to suggest females may have a larger and wider corpus callosum (Allen et al., 1991; Salat et al., 1997), which could possibly provide an advantage for task transfer between limbs. Cross-education of strength may also be different with left-handed individuals. Limiting the subject pool was an attempt to control factors that vary the magnitude of cross-education of strength.

Another limitation of the project was that the MRI experiment in Experiment 2 included only a sub-sample of subjects from the two training groups and did not include any control subjects. This was a necessary design repercussion due to the limited availability and high cost of running research projects using MRI at the University of Saskatchewan. The exclusion of control subjects was essentially a feasibility decision, especially since the main focus of the MRI experiment was to determine the change overtime within subjects rather than using between group comparisons.

This project was also limited by the considerable difference between the lab environment where training and testing were conducted and the MRI environment, even though the motor paradigm was very well matched at each location. Again, this was a limitation that can be attributed to limited MRI access. The mock MRI may have been a better environment for

training for the MRI subjects but it was at the hospital at the location of the real MRI. This was quite distant from the training and testing lab, and it was not feasible for the MRI subjects to train at a different location than the other subjects. Further to this, it was very important that the strength training environment was the same as the strength testing environment. This would have been impossible if the subjects had to train using the mock MRI at the hospital. It was also necessary that the training environment was equipped to provide real-time torque measures to provide each subject and the primary researcher with an indication of performance and effort during training. In order for this to be achieved the training had to be done back at the lab using the Biodex.

5.3 Future Research

5.3.1 Strength Asymmetry and Cross-education of Strength

The findings of this project generate a need for further research into the influence of limb dominance and task complexity on strength asymmetry between limbs. For example, future studies should determine the preferential direction of transfer with cross-education of strength in left-handed individuals. Since non-preferred hand proficiency or ambidexterity is common in left-handed individuals (Steenhuis and Bryden, 1999), the preferential direction of transfer may not be the same as with right-handed individuals. Ambidexterity may reduce the amount of strength asymmetry between limbs and may reduce the magnitude of cross-education. Task complexity may also influence the amount of strength asymmetry between limbs. Theoretically, the more complex and unfamiliar the task the more strength asymmetry between limbs. However, this has not been examined with left-handed individuals. The precise contribution of task complexity on strength asymmetry between limbs has yet to be determined even in right-

handed individuals. The present document provides some evidence that greater cross-education is shown with an unfamiliar training paradigm, and previous studies in our lab suggest more complex tasks result in more cross-education of strength (Farthing and Chilibeck, 2003a).

Similar questions arise with regards to cross-education of strength for the lower body. Limb dominance may be less pronounced in the legs, and there seems to be little strength asymmetry between legs in untrained individuals (Maupas et al., 2002). Further, very high magnitudes of cross-education of strength have been reported after left leg training (Hortobágyi et al., 1997; Hortobágyi et al., 1999). The difference in the magnitude of cross-education of strength with right versus left leg training is yet to be determined. Predicting the preferential direction of transfer based on previous studies is difficult, since few studies report leg dominance. A future study replicating the design of Experiment 1 could determine the difference in cross-education of strength when training the right or left leg.

Another very meaningful study could determine the degree of strength asymmetry between the dominant and non-dominant limbs for both the upper and lower body with varying task complexity or familiarity. Hypothetically, with increasing task complexity the degree of unfamiliarity would increase, thereby increasing the amount of strength asymmetry between limbs. Close attention would have to be paid to limb dominance (right or left), since strength asymmetry may only be evident with strong right handedness and may not present itself in the lower body. Follow up studies could compare the magnitude of cross-education of strength after training with a simple task and a complex task, in both the upper and lower body. Theoretically, cross-education of strength would be greater with the complex task for both the upper and lower body. However, if there is little strength asymmetry between lower limbs, task complexity may

only influence the magnitude of cross-education of strength but the direction of transfer would be irrelevant.

5.3.2 Unilateral Immobilization

The potential studies mentioned above could aid researchers in predicting the expression and magnitude of cross-education of strength. They could also have practical implications for rehabilitation strategies in response to unilateral injury (limb immobilization), where training of an uninjured limb may contribute to an increase in strength of an injured or impaired contralateral limb. Preliminary studies could include a period of immobilization of one healthy limb by casting, to induce atrophy and strength loss. Although this would present different neuromuscular adaptations than might be associated with an actual injury that requires immobilization for healing, it could provide a reasonably non-invasive way of determining whether or not unilateral training of the free limb could benefit the impaired limb via cross-education. An important consideration in this case is that if the preferential direction of transfer for cross-education of strength is only from dominant to non-dominant, it may seriously limit the potential for using strength transfer as a method of therapy during unilateral injury or impairment. For example, if an individual has an impaired dominant limb, strength training the non-dominant limb may be of no use. However, another argument is that the preferential direction of transfer for cross-education of strength may be more accurately described as transfer from the more coordinated limb to the uncoordinated limb for the task. In most cases, the dominant limb will show better coordination for a given task, especially if it is unfamiliar or very complex. This might explain why the preferred direction of transfer is usually dominant to non-dominant for skill transfer, and also strength transfer as shown in Experiment 1. But depending

on the demands of the task and previous experience, the dominant limb may not be better coordinated for the task. A perfect example of this is catching with a glove in baseball, where the non-dominant arm is used because the dominant arm is needed to throw. Another prime example is that the dominant leg for take-off is often opposite than kicking preference (Vanden-Abeeel, 1980). In the case of an injured or impaired limb, it could easily be argued that after recovery or during recovery, the more uncoordinated limb for the majority of tasks might become the recently injured or impaired limb, regardless of limb dominance. There is substantial evidence that suggests strength loss with periods of immobilization or unloading is related to neural changes and muscle atrophy (Hortobágyi et al., 2000; Seki et al., 2001a; Seki et al., 2001b; Deschenes et al., 2002; Labarque et al., 2002). Therefore, coordination is likely to be affected with immobilization. The effect of limb immobilization on neural coordination discrepancies or strength asymmetry between the dominant and non-dominant limb is yet to be determined. Theoretically, dominant limb immobilization or injury would reduce strength asymmetry between limbs, and non-dominant limb immobilization might exaggerate it. In addition to using strength and muscle size measures with immobilization, functional imaging would also provide insights into how activation in cortex is reorganized or lateralized with unilateral disuse. Comparing cortical activation maps before and after immobilization might provide evidence of changes in neural coordination and the degree of limb dominance. Handedness questionnaires could also be used to determine how a period of immobilization influences the degree of handedness. Obviously, an immobilized dominant limb would require greater usage of the non-dominant limb for everyday living, but there may be residual effects of using the non-dominant limb that are apparent even after full recovery from immobilization.

5.3.3 Stroke Rehabilitation

The most obvious clinical application of cross-education of strength is to stroke rehabilitation. Unfortunately, strength training of the unaffected limb in an attempt to enhance the acute recovery of the impaired limb after stroke has not been studied. Total body bilateral strength training (moderate intensity) has been effective for improving bench press and leg press strength in stroke survivors (at least 6 months post-stroke), but was not effective for increasing handgrip strength of either the unaffected or affected limb (Rimmer et al., 2000). Most rehabilitation protocols have centered on recovery of functional ability of the impaired limb through constraint-induced movement therapy (CIMT). CIMT involves extensive motor training of the affected limb in conjunction with restriction of the unaffected limb, and has been effective during recovery after mild to moderate stroke (Taub et al., 1993; Kunkel et al., 1999; Miltner et al., 1999; Schaechter et al., 2002). Hallett (2001) suggested recovery from stroke in addition to acute spontaneous recovery is likely the result of plasticity in the brain. Recent studies have used fMRI to assess cortical reorganization after stroke, and report plasticity and functional reorganization with stroke recovery (Liepert et al., 2000; Carey et al., 2002; Schaechter et al., 2002; Ward et al., 2003; Kim et al., 2004). These studies suggest stroke recovery includes a process of motor re-learning involving plasticity of damaged and undamaged brain regions. Given the proposed involvement of plasticity in recovery from stroke, and the evidence of increased activation in both brain hemispheres as a mechanism of transfer of strength between limbs provided in the present project, unilateral training of the unaffected limb might be effective for inducing re-learning and recovery of strength of the affected limb.

The success of therapies such as CIMT for stroke rehabilitation is well-documented (Taub et al., 1993; Kunkel et al., 1999; Miltner et al., 1999; Schaechter et al., 2002), but there

may be room for more intense forms of rehabilitation such as strength training. Typically, CIMT includes typical everyday motor tasks such as grasping and using a spoon or moving objects from one location to another (Taub et al., 1993). While these movement paradigms are important for functional recovery and regaining quality of life, they are likely not sufficient enough to facilitate recovery of strength loss for the affected limb. Immediately post-stroke, where significant hemiparesis and motor dysfunction are apparent, intense strength training of the unaffected side may induce quicker functional recovery through cross-education of strength. Unilateral training may provide an initiation of plasticity in the damaged hemisphere. Exposure to more intense movements requiring maximal or near maximal activation of muscle may be beneficial for re-learning of many functional tasks with the affected limb. Of course, once motor function begins to return existing therapies such as CIMT could be applied, but could be modified to include more strength activities that require maximal or near maximal muscle activation. This may further facilitate the recovery of function of everyday type movements which require much lower intensity muscle contractions.

Therapies for stroke could also include strength training of both limbs in addition to CIMT. Engaging in maximal activation of the unaffected limb might be associated with its own benefits for the affected limb. For example, it may enhance the ability of the affected limb to engage in maximal activation, or it may even result in an increase in strength through cross-education. If the training environment includes a variety of more complex strength tasks that require unique neural recruitment strategies, subsequent performance of everyday activities might be more easily accomplished. Future research should explore the application of cross-education of strength as a strategy to facilitate and quicken the process of recovery from stroke. In conjunction with existing effective rehabilitative strategies such as CIMT, strength training of

both the affected and unaffected may be the missing link on the path to uncovering the protocol that leads to complete recovery from stroke.

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Appendices

Appendix A: Certificate of Approval Experiment 1



Certificate of Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	BMC #
Philip D. Chilibeck	Kinesiology	03-1144

INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT

College of Kinesiology
105 Gymnasium Place
Saskatoon SK S7N 5C2

SPONSORING AGENCIES

UNIVERSITY OF SASKATCHEWAN

TITLE:

Effect of Unilateral Hand Grip Training on Cross-Education

ORIGINAL APPROVAL DATE	CURRENT EXPIRY DATE	APPROVAL OF
26-Aug-2003	01-Aug-2004	Protocol and consent form as submitted

CERTIFICATION

The University of Saskatchewan Biomedical Research Ethics Board has reviewed the above-named research project at a full-board meeting (any research classified as minimal risk is reviewed through the expedited review process). The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to governing law. This approval is valid for the above time period provided there is no change in experimental protocol or in the consent process.

ONGOING REVIEW REQUIREMENTS/REB ATTESTATION

In order to receive annual renewal, a status report must be submitted to the Chair for Committee consideration within one month of the current expiry date each year the study remains open, and upon study completion. Please refer to the following website for further instructions: <http://www.usask.ca/research/ethics.shtml>. In respect to clinical trials, the University of Saskatchewan Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations and carries out its functions in a manner consistent with Good Clinical Practices. This approval and the views of this REB have been documented in writing.

APPROVED:

Barry D. McLennan, Ph.D., Chair
University of Saskatchewan
Biomedical Research Ethics Board

Please send all correspondence to:

Office of Research Services, University of Saskatchewan
Room 3403, 110 Gymnasium Place
Box 5000 RPO University
Saskatoon, SK S7N 4J8
Phone: (306) 966-4053 Fax: (306) 966-2069

Appendix B: Certificate of Approval Experiment 2



Certificate of Approval

PRINCIPAL INVESTIGATOR	DEPARTMENT	BMC #
Philip D. Chilibeck	Kinesiology	03-887

INSTITUTION (S) WHERE RESEARCH WILL BE CARRIED OUT

Royal University Hospital
103 Hospital Drive
Saskatoon SK S7N 0W8

SPONSORING AGENCIES

AMERICAN COLLEGE OF SPORTS MEDICINE FOUNDATION

TITLE:

Motor Cortex Response to Unilateral Training: A Functional Magnetic Resonance Imaging (fMRI) Study

ORIGINAL APPROVAL DATE	CURRENT EXPIRY DATE	APPROVAL OF
21-Mar-2003	01-Mar-2004	Protocol as submitted Revised Patient Information and Consent Form (19 Mar 03)

CERTIFICATION

The University of Saskatchewan Biomedical Research Ethics Board has reviewed the above-named research project at a full-board meeting (any research classified as minimal risk is reviewed through the expedited review process). The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to governing law. This Approval is valid for the above time period provided there is no change in experimental protocol or in the consent process.

ONGOING REVIEW REQUIREMENTS/REB ATTESTATION

In order to receive annual renewal, a status report must be submitted to the Chair for Committee consideration within one month of the current expiry date each year the study remains open, and upon study completion. Please refer to the following website for further instructions: <http://www.usask.ca/research/ethics.shtml>. In respect to clinical trials, the University of Saskatchewan Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations and carries out its functions in a manner consistent with Good Clinical Practices. This approval and the views of this REB have been documented in writing.

APPROVED.

Barry D. McLennan, Ph.D., Chair
University of Saskatchewan
Biomedical Research Ethics Board

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University Advisory Committee on Ethics in Human Experimentation (UACEHE)
 210 Kirk Hall
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 SASKATOON SK S7N 5C8

STATUS REPORT FORM



This form is submitted for the following purpose

Annual status report and re-approval request

The ongoing review requirement stipulated that a status report must be submitted before the one year expiry date.

Notice of study closure

Report Prepared by: _____ Date: March 2/04

1. PRINCIPAL INVESTIGATOR
 Philip Chillbeck
NOTE: An investigator who does not maintain a physical presence at the trial site in proportion to the inherent level of risk that subjects will be exposed to cannot continue to be identified as the principal investigator. The responsibility must be transferred to a new principal investigator.

2. DEPARTMENT/DIVISION Kinesiology 3. UACEHE FILE # 03-887

4. STUDY SITE(S)
College of Kinesiology, and Department of Nuclear Medicine, Royal University Hospital

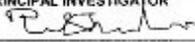
5. TITLE OF PROTOCOL AND PROTOCOL # (where applicable)
Motor Cortex Response to Unilateral Training: A Functional Magnetic Resonance Imaging (fMRI) Study

6. SPONSOR (where applicable)
 None

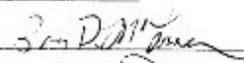
7. BRIEF SUMMARY OF PROGRESS OF STUDY (projected completion date for recruitment and data collection, number of subjects admitted to date, target enrollment, anticipated end date). Are subjects currently receiving study treatment or interventions, or is the study only active for follow-up to endpoints?
 We have only started recruiting subjects for this study. We are planning to recruit 20 healthy female subjects of age 18 or older. We have decided to recruit only female subjects because we require subjects that are not experienced in resistance exercise training. From our experience, male subjects are more likely to be resistance-trained.

8. ARE THERE ANY ASPECTS OF THIS STUDY WHICH SHOULD BE BROUGHT TO THE ATTENTION OF THE UACEHE (i.e., any new information or knowledge bearing on the anticipated risks or anticipated benefits, and therefore possibly affecting subjects' ongoing decision to participate in this study. Clinical trialsists should reflect upon adverse events associated with their protocol).
 No

9. WHAT ARE YOUR CURRENT SAFETY REVIEW PROCEDURES FOR THIS RESEARCH PROJECT (i.e., drug safety monitoring board (DSMB), clinical end-point committee (CEC), hotline, periodic reporting to the ethics board)?
 Phone hotline

10. PRINCIPAL INVESTIGATOR

 Signature
 Date: March 1st 2004

ONGOING REVIEW REQUIREMENT(S): Please note that this form, once signed by the chair or designee, will serve as your official re-approval certificate. This approval is valid for up to one year. The UACEHE will require the submission of an annual status report at least one month prior to the expiration date indicated below.

For Administrative Use Only:
 Approved On: MAR 02 2004 Expiry Date: March 1, 2005
 Signature of Chair or designee: 

February 5, 2001

Appendix C: Consent Forms

Consent form Experiment 1

Title: Effect of dominant vs. non-dominant unilateral forearm training on cross-education

Names of Researchers: Philip D. Chilibeck, Ph.D., Associate Professor, College of Kinesiology (966-1072); Jonathan Farthing, M.Sc., graduate student researcher, College of Kinesiology (373-0946).

Purpose and Objectives of the Study: Cross-education is a term that refers to the increase in strength of an untrained limb when the opposite limb is trained. It is uncertain what causes this effect, but it most likely involves alterations that occur in the way our brains send messages to our muscles during strength training. The increase in strength of the untrained limb may depend on whether the dominant or non-dominant limb is trained. The purpose of this study is to determine whether there is a difference in the level of cross-education between people that train their dominant versus non-dominant limb.

Possible Benefits of the Study: You may increase your forearm strength during this study. Researchers will benefit from this study because they will gain a better understanding of how the brain functions during exercise training. These benefits are not guaranteed.

Procedures: You will initially be given a questionnaire that determines which limb is your dominant limb. You will be randomized (by chance) into one of three groups: 1) A group that will train their dominant hand; 2) A group that will train their non-dominant hand; 3) a control group that will not participate in any exercise training. The exercise training will involve forearm exercise performed three times per week for eight weeks. Each training session will take approximately 10 minutes. The following tests will be done on three separate occasions: Two weeks before the training, one week before the training, and after the eight weeks of training in all subjects:

- 1) Strength testing of your forearm. This will be done by exerting force on a device called a “dynamometer” which records the force you are able to exert with your hand. This test will be done on both hands.
- 2) Activation of your forearm muscles will be measured during the strength testing to determine your ability to fully contract your muscles. This will be done by placing electrodes (stickers) on both sides of your forearms. These stickers are connected by wires that feed into a device that records the electrical activity in your muscles.
- 3) The thickness of your forearm muscles will be measured using ultrasound. This involves application of a gel to your skin surface. A probe is then placed over the gel and sends sound waves through your arm. The reflection of the sound waves allows an image of your muscle to be produced on a computer screen.

These three sets of tests will take approximately 45-60 minutes to complete.

Foreseeable risks and discomfort: There may be some muscle soreness after the strength testing and during the early part of the training. A proper warm up (stretching) will help to minimize this soreness. There are no known risks of the measurements of muscle activation or the ultrasound. There may be unforeseen risks during the project or after it is completed.

Freedom to withdraw from the study: You are free to withdraw from the study at anytime, without your academic status being affected if you are a student.

Precautions that will be taken to protect your anonymity: All data collected will be stored in a locked office in the College of Kinesiology. The results of the study will be published in a student's thesis and a journal article, but only aggregate data will be reported and you will be unidentifiable.

Contact information for questions: If you have questions concerning the study you can contact Dr. Philip Chilibeck at 966-1072 or 343-6577 or Jonathan Farthing, graduate student researcher, at 966-1099 or 373-0946 (home).

If you have any questions about your rights as a research subject, or concerns about your participation in this study, you should contact the Chair of the Biomedical Research Ethics Board, c/o the Office of Research Services, University of Saskatchewan at (306) 966-4053.

During the study we will advise you of any new information that may have a bearing on your decision to continue in the study.

We will advise you of your own results and the overall results of the study at the completion of the study.

Alternatives to the study: You do not have to participate in this study to increase your forearm strength. You could take part in a different training program (i.e. squeezing a tennis ball on a daily basis) to increase your forearm strength.

By signing below, you confirm that the contents of the consent have been explained, that you understand the contents of the consent, and that you have received a copy of the consent form for your own use.

Participant's Signature: _____ Date: _____

Researcher's Signature: _____ Date: _____

Witness' Signature: _____ Date: _____

Consent Form Experiment 2

Title of the Study: Motor cortex response to unilateral training: a functional Magnetic Resonance Imaging (fMRI) study.

Purpose and objectives

The purpose of the present investigation is to determine the motor cortex response in both sides of the brain after a period of resistance training the handgrip of one arm.

Possible benefits

Benefits include strength increases in both arms as a result of resistance training one arm (a phenomenon called cross-education). This effect is not observed in all cases, and is not guaranteed. Subjects will be entitled to a MR (magnetic resonance) image of their brain in action while performing a motor task. This is not guaranteed as sometimes MR images can be affected by artifacts that can destroy a clean picture. Participation in this study will help researchers identify potential mechanisms responsible for the cross-education effect, and could lead to important research for individuals with an injured or immobilized arm or leg (casting situations, stroke sufferers). It will also give insight as to how the sides of the body communicate during a movement task performed on one side of the body.

Procedures

All participants will be exposed to two handgrip strength testing sessions (before and after training), which will include maximal contractions of the forearm muscles (by squeezing and handgrip device). Participants will also be exposed to two MRI sessions (before and after training) at the Royal University Hospital in Saskatoon, Saskatchewan, which will each last approximately 30 minutes in duration. The imaging sessions will include handgrip squeezing of the right and then the left arm. After testing procedures are completed before training subjects will be randomly assigned into one of two groups: actual or imagined (mental) training. The training will consist of 8 weeks of handgrip resistance training of one arm, 3 times per week. Each training session will include 5 sets of 8 repetitions, and will be completed with supervision in the College of Kinesiology exercise physiology lab at the University of Saskatchewan. Testing procedures will then be repeated after training is completed.

A researcher will thoroughly discuss the details of the task you will perform both before you go into the MRI and while you are in the MRI. Magnetic resonance imaging is a non-invasive technique that generates radio signals from the nuclei of hydrogen atoms in the water molecules in your body. The functional magnetic resonance imaging (fMRI) procedure we will be using works on a principle known as Blood Oxygenation Level Dependence (BOLD). BOLD fMRI uses signals that are shaped by the blood circulating in your body and is completely non-invasive (i.e., neither foreign substances nor ionizing radiation are used or needed). Hemoglobin is the substance in your blood that carries oxygen to your cells. When it is carrying oxygen it is known as oxyhemoglobin and is the substance that makes blood in your arteries bright red. BOLD imaging works because deoxyhemoglobin is paramagnetic and oxyhemoglobin is not. The difference affects the ability of the surrounding water to generate an MRI signal in the following manner. When the oxygen is used by cells, as in specific areas of nerve cells in the brain when you engage in a motor task like handgrip contractions, the remaining deoxyhemoglobin will, at

first, reduce the MRI signal. Increased blood flow to the active regions in your brain will then quickly offset the reduced deoxyhemoglobin with an excess of oxyhemoglobin, which increases the MRI signal. The final result is that we measure an increase in MRI signal in the part of your brain activated by the assigned task. The signal increase is, however, very subtle. Therefore repeated tests and statistical data processing are required before we can precisely identify the regions in your brain that were activated by the assigned tasks.

Because the fMRI signal is sensitive to motion artifacts, we will be using some sort of head restraint to keep your head from moving during the study. Various methods of restraint are available including ordinary pillows, vacuum pillows and/or, for very sensitive tests, a proprietary molding compound. All methods of restraint are safe and the particular method to be used for this study will be discussed in detail with you by the investigators.

Side effects and foreseeable risks

Some discomfort can be experienced during and up to 48 hours after a resistance training session. Muscle injuries can occur with training but are very rare with handgrip movements.

Claustrophobia can be a problem associated with the cramped interior space of the MRI. MRI itself is the latest innovation in diagnostic imaging. It is exciting because it provides a detailed view of the inside of the body without using radiation. MRI uses a large magnet and radiowaves to give a clear picture of various body organs and tissues. An illustration of the MRI setup is given below along with a map showing the location of the Royal University Hospital MRI suite where the study will be performed. You will be given the opportunity to view the MRI equipment before the study.

In the magnet scan room, a technician will help you onto a padded table and after being properly positioned, you will be secured with soft pads to ensure that you are as still as possible during the scan if the study does not involve large head motion. After you are comfortable, the padded table will be moved smoothly into the magnet opening. During the scan you will notice a loud “pinging” sound – that is the sound caused by rapid electrical current reversal in the MRI’s electromagnets. There is an intercom system so that the MRI researchers can hear you and if you become uncomfortable at any point just say so and a technician will be right there to help you.

Your study will take approximately 30 minutes. Your study could be delayed because of emergency use of the MRI by physicians for patients so please plan for a possible stay of 2 or 3 hours.

You cannot participate in the study if you answer YES to ANY of the following questions.

DO YOU HAVE:	YES	NO
Cardiac pacemaker	___	___
Brain surgical clips	___	___
Aneurysm clips	___	___
Heart valve	___	___
Insulin pump	___	___
Shrapnel	___	___
Metal fragments in eye	___	___
Cochlear implant	___	___
Aortic or carotid clips	___	___
IUD	___	___
Shunts	___	___
Harrington rod	___	___
Permanent eye liner	___	___
Tattoos near the head	___	___
Surgical pins, plates, nails, screws	___	___
Stainless steel wire	___	___
Prostheses, i.e. artificial hips, joints, penile implants, magnetic sphincters	___	___
Any metal anywhere inside or outside your body or head which cannot be easily removed	___	___
Are you pregnant	___	___
Are you claustrophobic	___	___

Some subjects experience a closure of space around the body once they are in the magnet, but keep in mind that the magnet is open at both ends. You are never totally closed in and you will be able to see out with a mirror.

You cannot be scanned if you have a heart pacemaker or have had brain aneurysm surgery.

PLEASE DO NOT: · wear any make-up; · wear a bra or girdle; · wear jewelry of any kind; · have anything in your pockets

Wear clothes without zippers, metal buttons, etc. (e.g. track suit) if possible. If this is not possible, the technician will direct you to a change room where you will be given a hospital gown/robe to wear for the test and a locker provided for your purse/wallet/valuables.

FINAL CHECKLIST: The following items must not be take into the magnet room. Severe personal injury and/or damage to the equipment could result. Your pockets must be empty. Do not enter the magnet room with any of the following items:

- glasses * removable dental work * hearing aid * jewelry * watch * wallet/money-clip * keys * pen/pencils * coins * pocket knife * belt buckle * zippers/buttons/rivets/fasteners * hairpins/barrettes * shoes * metal bra hooks * bra and girdle under-wire support * sanitary belt * safety pins * ID or medical alert bracelets * magnetic strip cards (e.g. credit cards, bank cards, hotel security cards, parking garage cards, etc)

Withdrawal from the study: You, the participant, are free to withdraw from the study at anytime without affecting your level of clinical care. When a participant withdraws, his/her data will be deleted from the study and destroyed. If appropriate, the researcher may choose to discontinue a participant's involvement in the study in which case his/her data will be deleted and destroyed (e.g., if you are unable to perform the assigned task in which case the data will not be useful).

Confidentiality and Anonymity: Your confidentiality and anonymity, including your data and any storage medium, will be protected at all times in secured computers (by participant number, not by name), which are behind locked doors when unattended. The researcher will safeguard and store the data, results, and associated material for a minimum of five years.

Debriefing and Feedback: Your data will be shown to you and discussed in terms of the experimental hypothesis when you are finished. Please feel free to ask any questions.

Consent:

I, (print) _____, understand that participation in this research is entirely voluntary and that if I have any questions about the study, or my rights as a participant in this research, I may submit them to the Advisory Committee on Ethics in Human Experimentation through the Office of Research Services (966-4053). I have read the above protocol. I understand the conditions and risks associated with the resistance training sessions. I understand that no metal objects are to be worn near or in the MRI, and I am indicating that I have no metal objects on or in my body prior to entering the MRI room. The procedure and possible risks have been explained to me, I understand them and I agree to participate. I also understand that I am free to withdraw from the study at any time, and the researcher will advise me if there is any new information that could affect my decision to continue. I have been offered a copy of this form for my own records.

Participant:

(Parent or Guardian if participant is under 18 years of age.)

Researcher:

Date: _____

Appendix D: Raw Data Experiment 1

Strength, Muscle Thickness, Training Experience, Handedness, Height, Weight

Sub#	group	Ht	Wt	Training Exp	Hand Score	UNpreS	UNpostS	%chng	TRpreS	TRpostS	%chng	UNpreMT	UNpostMT	%chng	TRpreMT	TRpostMT	%chng
7	L	166.6	70.0	10	15	25	20	-20.0	14	11	-21.4	3.05	2.81	-7.9	3.10	3.24	4.5
2	L	175.4	62.6	5	16	18	19	5.6	13	17	30.8	3.28	2.95	-10.1	3.16	3.14	-0.6
9	L	171.2	68.5	8	20	21	26	23.8	17	21	23.5	3.02	2.89	-4.3	3.15	3.16	0.3
29	L	169.4	61.5	0	16	24	25	4.2	11	21	90.9	3.35	2.98	-11.0	3.10	3.25	4.8
10	L	168.3	61.5	0	17	18	22	22.2	14	23	64.3	2.95	2.61	-11.5	2.90	2.90	0.0
38	L	167.5	74.9	0	12	13	15	15.4	8	10	25.0	3.50	3.33	-4.9	3.59	3.83	6.7
23	L	160.2	54.0	3	19	14	21	50.0	7	19	171.4	3.10	2.96	-4.5	2.53	2.95	16.6
19	L	163.9	62.5	12	19	18	16	-11.1	13	14	7.7	2.73	2.81	2.9	2.73	3.33	22.0
43	L	172.1	63.5	3	18	23	22	-4.3	12	18	50.0	2.97	2.95	-0.7	3.20	3.29	2.8
39	L	173.0	78.0	0	18	16	17	6.3	9	12	33.3	3.34	3.21	-3.9	3.06	3.03	-1.0
20	L	152.0	48.3	0	20	18	21	16.7	12	14	16.7	2.58	2.54	-1.6	2.70	2.80	3.7
35	L	174.5	75.0	0	20	21	21	0.0	16	19	18.8	3.13	2.98	-4.8	2.98	3.21	7.7
33	L	163.0	64.9	3	18	17	19	11.8	9	12	33.3	2.93	2.89	-1.4	2.84	3.01	6.0
12	R	156.4	55.8	0	18	10	19	90.0	14	20	42.9	2.28	2.17	-4.8	2.64	2.62	-0.8
22	R	168.5	63.2	2	18	14	22	57.1	21	27	28.6	2.88	2.89	0.3	3.00	3.08	2.7
37	R	165.1	64.5	4	19	16	24	50.0	19	33	73.7	2.95	2.88	-2.4	3.24	3.23	-0.3
42	R	175.6	59.0	12	19	11	15	36.4	17	15	-11.8	2.87	2.65	-7.7	2.87	2.85	-0.7
1	R	170.3	72.9	0	19	13	18	38.5	21	27	28.6	3.22	3.01	-6.5	3.09	3.36	8.7
27	R	163.6	68.4	3	9	10	18	80.0	18	21	16.7	2.92	3.02	3.4	3.21	2.91	-9.3
36	R	166.3	75.8	4	15	10	14	40.0	15	17	13.3	3.04	3.10	2.0	3.06	3.07	0.3
21	R	159.8	51.0	0	19	10	10	0.0	17	14	-17.6	2.23	2.25	0.9	2.02	2.43	20.3
25	R	171.7	63.4	0	19	13	14	7.7	19	20	5.3	2.96	3.06	3.4	2.93	2.82	-3.8
24	R	185.2	78.4	0	18	13	16	23.1	19	25	31.6	2.97	2.95	-0.7	3.03	3.09	2.0
4	R	170.9	102.2	0	18	16	21	31.3	20	28	40.0	3.13	3.21	2.6	3.34	3.50	4.8
34	R	165.9	61.2	12	20	12	14	16.7	15	24	60.0	2.92	2.79	-4.5	2.71	2.87	5.9
14	con	167.5	63.0	12	19	17	22	29.4	14	19	35.7	2.61	2.65	1.5	2.83	2.84	0.4
5	con	177.4	72.2	2	18	27	30	11.1	18	19	5.6	3.21	2.91	-9.3	3.35	2.98	-11.0
8	con	172.3	66.0	0	16	16	17	6.3	21	23	9.5	3.05	2.96	-3.0	3.07	2.95	-3.9
3	con	169.8	60.5	0	19	12	11	-8.3	19	18	-5.3	2.63	2.64	0.4	2.88	2.75	-4.5
6	con	166.5	73.0	8	18	25	27	8.0	18	21	16.7	3.17	2.92	-7.9	3.25	2.93	-9.8
13	con	165.2	65.9	0	17	7	8	14.3	7	11	57.1	2.40	2.55	6.3	2.61	2.50	-4.2
16	con	160.5	53.9	5	19	10	15	50.0	18	23	27.8	2.39	2.50	4.6	2.70	2.47	-8.5
31	con	162.5	55.9	2	13	14	12	-14.3	10	10	0.0	3.27	3.09	-5.5	3.03	2.88	-5.0
40	con	170.4	67.4	1.5	17	22	25	13.6	26	30	15.4	3.17	3.10	-2.2	3.01	2.93	-2.7
30	con	161.0	56.0	0	16	14	17	21.4	22	22	0.0	3.30	3.15	-4.5	3.19	2.78	-12.9
17	con	155.9	60.3	0	19	18	20	11.1	10	10	0.0	2.64	2.71	2.7	2.63	2.50	-4.9
28	con	168.7	61.2	6	17	15	11	-26.7	17	18	5.9	3.58	3.23	-9.8	3.43	2.89	-15.7
15	con	152.7	65.8	0	16	15	17	13.3	20	22	10.0	3.49	3.51	0.6	3.44	3.38	-1.7
11	con	164.3	54.1	0	16	18	21	16.7	14	13	-7.1	2.66	2.70	1.5	2.42	2.38	-1.7

EMG Mean Absolute Value

Sub#	group	UN-PRE-Ag	UN-POST-Ag	UN-PRE-Ant	UN-POST-Ant	TR-PRE-Ag	TR-POST-Ag	TR-PRE-Ant	TR-POST-Ant
7	L	0.320	0.190	0.035	0.025	0.330	0.410	0.099	0.030
2	L	0.270	0.200			0.230	0.360	0.100	0.071
9	L	0.210	0.180			0.310	0.370		
29	L	0.360	0.210			0.390	0.380	0.031	0.120
10	L	0.200	0.240	0.025	0.023	0.280	0.360	0.034	0.043
38	L	0.084	0.080	0.014	0.025	0.170	0.160	0.039	0.037
23	L	0.240	0.220	0.080	0.120	0.270	0.420	0.027	0.063
19	L	0.260	0.130	0.024	0.016	0.260	0.260	0.018	0.057
43	L	0.320	0.510	0.030	0.036	0.180	0.330	0.030	0.033
39	L	0.250	0.230	0.033	0.042	0.250	0.330	0.035	0.035
20	L	0.390	0.230	0.047	0.110	0.350	0.220	0.036	0.046
35	L	0.240	0.160	0.025	0.030	0.350	0.350		
33	L	0.170	0.300	0.110	0.045	0.330	0.310	0.028	0.034
12	R	0.250	0.230	0.022	0.022	0.180	0.460	0.028	0.021
22	R	0.540	0.280	0.063	0.310	0.310	0.420	0.036	0.064
37	R	0.440	0.380	0.028	0.048	0.180	0.260	0.032	0.041
42	R	0.200	0.320	0.033	0.036	0.150	0.400	0.036	0.046
1	R	0.430	0.270	0.022	0.024	0.430	0.180	0.056	0.033
27	R	0.320	0.240	0.020	0.019	0.270	0.340	0.020	0.025
36	R	0.220	0.210	0.031	0.029	0.190	0.280	0.020	0.059
21	R	0.490	0.290	0.183	0.035	0.290	0.220		
25	R	0.350	0.310	0.033	0.031	0.260	0.260	0.039	0.026
24	R	0.270	0.200	0.017	0.015	0.260	0.570	0.024	0.035
4	R	0.190	0.150	0.045	0.035	0.360	0.220	0.025	0.025
34	R	0.290	0.210	0.021	0.050	0.300	0.350	0.025	0.150
14	con	0.150	0.150	0.024	0.024	0.300	0.280	0.035	0.032
5	con	0.310	0.400	0.028	0.014	0.390	0.290	0.025	0.025
8	con					0.330	0.280	0.058	0.014
3	con	0.500	0.380	0.026	0.033	0.440	0.240	0.032	0.030
6	con	0.210	0.200	0.028	0.093	0.250	0.300	0.026	0.033
13	con	0.310	0.350	0.023	0.028	0.220	0.200	0.025	0.028
16	con	0.390	0.320	0.030	0.033	0.290	0.220	0.023	0.036
31	con	0.260	0.230	0.033	0.027	0.230	0.330	0.015	0.024
40	con	0.580	0.370	0.138	0.063	0.300	0.310	0.020	0.042
30	con	0.340	0.310						
17	con	0.360	0.370	0.020	0.033	0.310	0.270	0.015	0.015
28	con					0.240	0.230	0.020	0.039
15	con	0.150	0.210	0.044	0.037	0.180	0.140	0.110	0.087
11	con	0.330	0.200	0.024	0.032	0.260	0.290	0.015	0.022

Appendix E: Raw Data Experiment 2

Strength, Muscle Thickness, Training Experience, Handedness, VMIQ, Height, Weight

Sub#	group	Ht	Wt	Training Exp	VMIQ-EX	VMIQ-IN	Hand Score	RpreS	RpostS	%chng	LpreS	LpostS	%chng	RpreMT	RpostMT	%chng	LpreMT	LpostMT	%chng
1-MRI	Act	172.9	57.0	6	54	33	19	21	29	38.10	14	22	57.14	2.94	3.21	9.2	3.05	3.10	1.6
2-MRI	Act	167.4	73.0	5	40	35	16	23	32	39.13	18	26	44.44	3.04	3.64	19.7	3.02	3.23	7.0
3-MRI	Act	156.4	63.5	0	49	53	20	15	20	33.33	11	14	27.27	3.07	3.47	13.0	3.15	3.15	0.0
7	Act	181.8	67.0	0	26	60	19	22	30	36.36	14	23	64.29	3.33	3.57	7.2	3.24	3.24	0.0
8	Act	168.3	71.5	0	43	34	20	12	16	33.33	9	13	44.44	3.47	3.70	6.6	3.04	3.08	1.3
13	Act	167.5	63.0	3	50	46	16	29	38	31.03	23	26	13.04	3.09	3.58	15.9	3.17	3.04	-4.1
20	Act	162.8	70.0	3	43	34	17	16	30	87.50	13	23	76.92	3.33	3.42	2.7	3.43	3.39	-1.2
19	Act	171.3	79.5	4	62	44	18	22	41	86.36	18	33	83.33	3.27	3.36	2.8	3.23	3.26	0.9
12	Act	157.2	66.0	7	45	48	16	17	27	58.82	16	22	37.50	2.98	3.10	4.0	3.03	3.00	-1.0
28	Act	160.6	53.5	3	24	24	20	17	24	41.18	16	24	50.00	2.83	3.04	7.4	2.87	2.83	-1.4
30	Act	165.7	54.0	0	35	31	20	22	31	40.91	19	22	15.79	2.81	3.05	8.5	2.77	2.71	-2.2
32-MRI	Act	172.7	64.0	6	49	32	14	23	27	17.39	12	19	58.33	3.18	3.29	3.5	3.23	3.26	0.9
24-MRI	Imag	170.2	64.0	1	24	24	16	25	27	8.00	25	27	8.00	3.05	3.08	1.0	3.08	3.04	-1.3
25-MRI	Imag	175.4	67.0	8	24	24	20	22	25	13.64	20	23	15.00	3.21	3.12	-2.8	3.41	3.24	-5.0
31-MRI	Imag	157.3	57.5	2	58	55	18	20	20	0.00	17	13	-23.53	2.78	2.81	1.1	2.75	2.78	1.1
33-MRI	Imag	154.4	53.5	8	24	27	20	17	16	-5.88	9	7	-22.22	2.93	2.89	-1.4	2.91	2.96	1.7
4	Imag	178.3	67.0	2	34	29	20	21	25	19.05	21	26	23.81	2.92	2.86	-2.1	2.69	2.80	4.1
11	Imag	157.0	54.5	1	36	29	20	11	12	9.09	10	10	0.00	3.21	3.20	-0.3	3.52	3.49	-0.9
22	Imag	161.8	49.5	0	30	36	15	14	12	-14.29	10	9	-10.00	3.08	3.06	-0.6	3.05	3.00	-1.6
18	Imag	166.6	64.5	10	51	46	15	14	17	21.43	11	15	36.36	2.91	2.97	2.1	2.96	2.96	0.0
16	Imag	168.4	62.5	3	55	55	15	23	22	-4.35	17	17	0.00	3.17	3.19	0.6	2.95	2.86	-3.1
14	Imag	166.3	63.0	9	53	57	14	19	14	-26.32	12	10	-16.67	3.04	2.98	-2.0	2.98	2.99	0.3
15	Imag	168.2	50.0	0	31	27	6	21	17	-19.05	19	17	-10.53	3.18	3.19	0.3	2.91	2.95	1.4
29	Con	163.7	54.5	4	45	45	19	18	17	-5.56	13	10	-23.08	3.37	3.22	-4.5	3.47	3.39	-2.3
27	Con	176.7	61.5	2	47	54	18	12	11	-8.33	13	15	15.38	3.03	3.03	0.0	2.97	2.97	0.0
5	Con	164.2	77.0	0	86	58	17	22	23	4.55	14	15	7.14	3.60	3.69	2.5	3.73	3.74	0.3
6	Con	163.2	71.5	0	48	48	15	12	15	25.00	8	11	37.50	3.24	3.23	-0.3	3.29	3.28	-0.3
9	Con	163.0	56.5	2	40	51	16	20	18	-10.00	16	16	0.00	3.23	3.00	-7.1	3.09	3.00	-2.9
10	Con	163.0	80.0	2	24	32	13	21	20	-4.76	15	16	6.67	3.83	3.84	0.3	3.52	3.53	0.3
17	Con	172.1	68.5	4	32	29	15	17	20	17.65	19	21	10.53	2.78	2.85	2.5	3.10	3.13	1.0
21	Con	166.0	79.0	7	98	46	20	23	21	-8.70	18	20	11.11	3.30	3.18	-3.6	3.30	3.34	1.2
26	Con	167.2	68.5	2	24	28	20	23	24	4.35	20	22	10.00	3.35	3.25	-3.0	3.39	3.20	-5.6
34	Con	169.9	66.0	5	82	74	18	18	18	0.00	18	15	-16.67	2.89	2.91	0.7	2.96	3.01	1.7

EMG Mean Absolute Value

Sub#	group	R-PRE-Ag	R-POST-Ag	Diff	R-PRE-Ant	R-POST-Ant	Diff	L-PRE-Ag	L-POST-Ag	Diff	L-PRE-Ant	L-POST-Ant	Diff
1-MRI	Act	0.337	0.678	0.341	0.105	0.027	-0.078	0.052	0.328	0.276	0.121	0.046	-0.075
2-MRI	Act	0.321	0.455	0.134	0.042	0.037	-0.005	0.043	0.394	0.352	0.045	0.031	-0.014
3-MRI	Act	0.381	0.495	0.114	0.025	0.030	0.005	0.045	0.124	0.079	0.018	0.019	0.001
7	Act	0.185	0.486	0.301	0.117	0.033	-0.084	0.244	0.215	-0.029	0.069	0.052	-0.017
8	Act	0.533	0.294	-0.239	0.147	0.082	-0.065	0.130	0.317	0.187	0.085	0.055	-0.030
13	Act	0.246	0.184	-0.062	0.046	0.036	-0.010	0.178	0.069	-0.109	0.362	0.109	-0.253
20	Act	0.230	0.298	0.068	0.060	0.102	0.042	0.205	0.266	0.061	0.035	0.031	-0.004
19	Act	0.656	0.710	0.054	0.041	0.077	0.036	0.525	0.451	-0.074	0.030	0.029	-0.001
12	Act	0.298	0.211	-0.087	0.108	0.074	-0.034	0.119	0.230	0.111	0.079	0.042	-0.037
28	Act	0.341	0.301	-0.040	0.261	0.278	0.017	0.292	0.287	-0.005	0.037	0.096	0.059
30	Act	0.320	0.550	0.230	0.065	0.256	0.191	0.466	0.326	-0.140	0.097	0.142	0.045
32-MRI	Act	0.185	0.325	0.140	0.063	0.075	0.012	0.277	0.687	0.410	0.097	0.092	-0.005
24-MRI	Imag	0.361	0.262	-0.099	0.057	0.077	0.020	0.315	0.271	-0.044	0.035	0.045	0.010
25-MRI	Imag	0.522	0.288	-0.234	0.140	0.050	-0.090	0.285	0.173	-0.112	0.038	0.058	0.020
31-MRI	Imag	0.254	0.237	-0.017	0.030	0.036	0.006	0.194	0.181	-0.013	0.056	0.032	-0.024
33-MRI	Imag	0.452	0.348	-0.104	0.100	0.109	0.009	0.205	0.011	-0.194	0.097	0.086	-0.011
4	Imag	0.372	0.516	0.144	0.044	0.057	0.013	0.576	0.446	-0.130	0.055	0.136	0.081
11	Imag	0.397	0.253	-0.144	0.154	0.042	-0.112	0.170	0.151	-0.019	0.063	0.026	-0.037
22	Imag	0.448	0.322	-0.126	0.059	0.080	0.021	0.277	0.308	0.031	0.113	0.135	0.022
18	Imag	0.329	0.247	-0.082	0.041	0.043	0.002	0.268	0.168	-0.100	0.045	0.031	-0.014
16	Imag	0.472	0.449	-0.023	0.038	0.039	0.001	0.189	0.429	0.240	0.034	0.038	0.004
14	Imag	0.353	0.284	-0.069	0.067	0.038	-0.029	0.293	0.160	-0.133	0.240	0.143	-0.097
15	Imag	0.177	0.310	0.133	0.057	0.039	-0.018	0.134	0.319	0.185	0.047	0.030	-0.017
29	con	0.363	0.203	-0.160	0.042	0.035	-0.007	0.430	0.469	0.039	0.087	0.037	-0.050
27	con	0.226	0.252	0.026	0.029	0.031	0.002	0.227	0.007	-0.220	0.030	0.032	0.002
5	con	0.113	0.301	0.188	0.042	0.038	-0.004	0.201	0.153	-0.048	0.042	0.056	0.014
6	con	0.058	0.186	0.128	0.073	0.043	-0.030	0.080	0.253	0.173	0.097	0.133	0.036
9	con	0.270	0.326	0.056	0.037	0.049	0.012	0.353	0.129	-0.224	0.075	0.103	0.028
10	con	0.268	0.199	-0.069	0.033	0.030	-0.003	0.184	0.119	-0.065	0.031	0.023	-0.008
17	con	0.234	0.181	-0.053	0.041	0.027	-0.014	0.148	0.020	-0.128	0.051	0.049	-0.002
21	con	0.307	0.262	-0.045	0.079	0.100	0.021	0.242	0.005	-0.237	0.048	0.048	0.000
26	con	0.191	0.173	-0.018	0.085	0.043	-0.042	0.194	0.175	-0.019	0.072	0.041	-0.031
34	con	0.219	0.368	0.149	0.052	0.035	-0.017	0.385	0.007	-0.378	0.084	0.062	-0.022

Appendix F: Statistical Tables Experiment 1

Strength and Muscle Thickness Doubly Multivariate Analysis: Multivariate Table

Multivariate Tests(d)

Effect			Value	F	Hypothesis df	Error df	Sig.
Between Subjects	Intercept	Pillai's Trace	.992	2162.981(b)	2.000	35.000	.000
		Wilks' Lambda	.008	2162.981(b)	2.000	35.000	.000
		Hotelling's Trace	123.599	2162.981(b)	2.000	35.000	.000
		Roy's Largest Root	123.599	2162.981(b)	2.000	35.000	.000
	GROUP	Pillai's Trace	.077	.724	4.000	72.000	.578
		Wilks' Lambda	.923	.719(b)	4.000	70.000	.582
		Hotelling's Trace	.084	.713	4.000	68.000	.586
		Roy's Largest Root	.084	1.509(c)	2.000	36.000	.235
Within Subjects	TIME	Pillai's Trace	.561	22.352(b)	2.000	35.000	.000
		Wilks' Lambda	.439	22.352(b)	2.000	35.000	.000
		Hotelling's Trace	1.277	22.352(b)	2.000	35.000	.000
		Roy's Largest Root	1.277	22.352(b)	2.000	35.000	.000
	TIME * GROUP	Pillai's Trace	.342	3.718	4.000	72.000	.008
		Wilks' Lambda	.669	3.899(b)	4.000	70.000	.006
		Hotelling's Trace	.479	4.068	4.000	68.000	.005
		Roy's Largest Root	.441	7.935(c)	2.000	36.000	.001
	ARM	Pillai's Trace	.091	1.760(b)	2.000	35.000	.187
		Wilks' Lambda	.909	1.760(b)	2.000	35.000	.187
		Hotelling's Trace	.101	1.760(b)	2.000	35.000	.187
		Roy's Largest Root	.101	1.760(b)	2.000	35.000	.187
	ARM * GROUP	Pillai's Trace	.696	9.598	4.000	72.000	.000
		Wilks' Lambda	.384	10.736(b)	4.000	70.000	.000
		Hotelling's Trace	1.396	11.866	4.000	68.000	.000
		Roy's Largest Root	1.227	22.084(c)	2.000	36.000	.000
TIME * ARM	Pillai's Trace	.255	5.979(b)	2.000	35.000	.006	
	Wilks' Lambda	.745	5.979(b)	2.000	35.000	.006	

TIME * ARM * GROUP	Hotelling's Trace	.342	5.979(b)	2.000	35.000	.006
	Roy's Largest Root	.342	5.979(b)	2.000	35.000	.006
	Pillai's Trace	.595	7.624	4.000	72.000	.000
	Wilks' Lambda	.435	9.036(b)	4.000	70.000	.000
	Hotelling's Trace	1.230	10.458	4.000	68.000	.000
	Roy's Largest Root	1.172	21.087(c)	2.000	36.000	.000

a Computed using alpha = .05

b Exact statistic

c The statistic is an upper bound on F that yields a lower bound on the significance level.

d Design: Intercept+GROUP

Within Subjects Design: TIME+ARM+TIME*ARM

Strength and Muscle Thickness Doubly Multivariate Analysis: Univariate Table

Univariate Tests

Source	Measure		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME	STENGTH	Sphericity Assumed	370.806	1	370.806	43.302	.000
		Greenhouse-Geisser	370.806	1.000	370.806	43.302	.000
		Huynh-Feldt	370.806	1.000	370.806	43.302	.000
		Lower-bound	370.806	1.000	370.806	43.302	.000
	MTHICK	Sphericity Assumed	.056	1	.056	3.314	.077
		Greenhouse-Geisser	.056	1.000	.056	3.314	.077
		Huynh-Feldt	.056	1.000	.056	3.314	.077
		Lower-bound	.056	1.000	.056	3.314	.077
TIME * GROUP	STENGTH	Sphericity Assumed	58.465	2	29.232	3.414	.044
		Greenhouse-Geisser	58.465	2.000	29.232	3.414	.044
		Huynh-Feldt	58.465	2.000	29.232	3.414	.044
		Lower-bound	58.465	2.000	29.232	3.414	.044
	MTHICK	Sphericity Assumed	.170	2	.085	5.003	.012
		Greenhouse-Geisser	.170	2.000	.085	5.003	.012
		Huynh-Feldt	.170	2.000	.085	5.003	.012
		Lower-bound	.170	2.000	.085	5.003	.012
Error(TIME)	STENGTH	Sphericity Assumed	308.279	36	8.563		
		Greenhouse-Geisser	308.279	36.000	8.563		
		Huynh-Feldt	308.279	36.000	8.563		
		Lower-bound	308.279	36.000	8.563		
	MTHICK	Sphericity Assumed	.610	36	.017		
		Greenhouse-Geisser	.610	36.000	.017		
		Huynh-Feldt	.610	36.000	.017		
		Lower-bound	.610	36.000	.017		
ARM	STENGTH	Sphericity Assumed	.560	1	.560	.032	.859
		Greenhouse-Geisser	.560	1.000	.560	.032	.859
		Huynh-Feldt	.560	1.000	.560	.032	.859
		Lower-bound	.560	1.000	.560	.032	.859

ARM * GROUP	MTHICK	Sphericity Assumed	.106	1	.106	3.551	.068	
		Greenhouse-Geisser	.106	1.000	.106	3.551	.068	
		Huynh-Feldt	.106	1.000	.106	3.551	.068	
		Lower-bound	.106	1.000	.106	3.551	.068	
	STENGTH	Sphericity Assumed	769.069	2	384.535	21.985	.000	
		Greenhouse-Geisser	769.069	2.000	384.535	21.985	.000	
		Huynh-Feldt	769.069	2.000	384.535	21.985	.000	
		Lower-bound	769.069	2.000	384.535	21.985	.000	
	Error(ARM)	MTHICK	Sphericity Assumed	.182	2	.091	3.059	.059
			Greenhouse-Geisser	.182	2.000	.091	3.059	.059
			Huynh-Feldt	.182	2.000	.091	3.059	.059
			Lower-bound	.182	2.000	.091	3.059	.059
		STENGTH	Sphericity Assumed	629.674	36	17.491		
			Greenhouse-Geisser	629.674	36.000	17.491		
			Huynh-Feldt	629.674	36.000	17.491		
			Lower-bound	629.674	36.000	17.491		
TIME * ARM		MTHICK	Sphericity Assumed	1.074	36	.030		
			Greenhouse-Geisser	1.074	36.000	.030		
			Huynh-Feldt	1.074	36.000	.030		
			Lower-bound	1.074	36.000	.030		
		STENGTH	Sphericity Assumed	9.599	1	9.599	3.720	.062
			Greenhouse-Geisser	9.599	1.000	9.599	3.720	.062
			Huynh-Feldt	9.599	1.000	9.599	3.720	.062
			Lower-bound	9.599	1.000	9.599	3.720	.062
	TIME * ARM * GROUP	MTHICK	Sphericity Assumed	.087	1	.087	11.077	.002
			Greenhouse-Geisser	.087	1.000	.087	11.077	.002
			Huynh-Feldt	.087	1.000	.087	11.077	.002
			Lower-bound	.087	1.000	.087	11.077	.002
		STENGTH	Sphericity Assumed	18.111	2	9.056	3.510	.041
			Greenhouse-Geisser	18.111	2.000	9.056	3.510	.041
			Huynh-Feldt	18.111	2.000	9.056	3.510	.041
			Lower-bound	18.111	2.000	9.056	3.510	.041
MTHICK		Sphericity Assumed	.327	2	.163	20.905	.000	
		Greenhouse-Geisser	.327	2.000	.163	20.905	.000	

Error(TIME*ARM)	STENGTH	Huynh-Feldt	.327	2.000	.163	20.905	.000
		Lower-bound	.327	2.000	.163	20.905	.000
		Sphericity Assumed	92.889	36	2.580		
		Greenhouse-Geisser	92.889	36.000	2.580		
		Huynh-Feldt	92.889	36.000	2.580		
		Lower-bound	92.889	36.000	2.580		
	MTHICK	Sphericity Assumed	.282	36	.008		
		Greenhouse-Geisser	.282	36.000	.008		
		Huynh-Feldt	.282	36.000	.008		
		Lower-bound	.282	36.000	.008		

a Computed using alpha = .05

Strength and Muscle Thickness (Percent Change Data) Doubly Multivariate Analysis: Multivariate Table

Multivariate Tests(d)

Effect			Value	F	Hypothesis df	Error df	Sig.
Between Subjects	Intercept	Pillai's Trace	.527	19.464(b)	2.000	35.000	.000
		Wilks' Lambda	.473	19.464(b)	2.000	35.000	.000
		Hotelling's Trace	1.112	19.464(b)	2.000	35.000	.000
		Roy's Largest Root	1.112	19.464(b)	2.000	35.000	.000
	GROUP	Pillai's Trace	.293	3.095	4.000	72.000	.021
		Wilks' Lambda	.709	3.290(b)	4.000	70.000	.016
		Hotelling's Trace	.408	3.472	4.000	68.000	.012
		Roy's Largest Root	.402	7.227(c)	2.000	36.000	.002
Within Subjects	ARM	Pillai's Trace	.222	4.991(b)	2.000	35.000	.012
		Wilks' Lambda	.778	4.991(b)	2.000	35.000	.012
		Hotelling's Trace	.285	4.991(b)	2.000	35.000	.012
		Roy's Largest Root	.285	4.991(b)	2.000	35.000	.012
	ARM * GROUP	Pillai's Trace	.733	10.415	4.000	72.000	.000
		Wilks' Lambda	.382	10.831(b)	4.000	70.000	.000
		Hotelling's Trace	1.320	11.223	4.000	68.000	.000
		Roy's Largest Root	1.028	18.505(c)	2.000	36.000	.000

a Computed using alpha = .05

b Exact statistic

c The statistic is an upper bound on F that yields a lower bound on the significance level.

d Design: Intercept+GROUP

Within Subjects Design: ARM

Strength and Muscle Thickness (Percent Change Data) Doubly Multivariate Analysis: Univariate Table

Univariate Tests

Source	Measure		Type III Sum of Squares	df	Mean Square	F	Sig.
ARM	STENGTH	Sphericity Assumed	962.169	1	962.169	2.191	.148
		Greenhouse-Geisser	962.169	1.000	962.169	2.191	.148
		Huynh-Feldt	962.169	1.000	962.169	2.191	.148
		Lower-bound	962.169	1.000	962.169	2.191	.148
	MTHICK	Sphericity Assumed	207.729	1	207.729	10.066	.003
		Greenhouse-Geisser	207.729	1.000	207.729	10.066	.003
		Huynh-Feldt	207.729	1.000	207.729	10.066	.003
		Lower-bound	207.729	1.000	207.729	10.066	.003
ARM * GROUP	STENGTH	Sphericity Assumed	6912.499	2	3456.250	7.871	.001
		Greenhouse-Geisser	6912.499	2.000	3456.250	7.871	.001
		Huynh-Feldt	6912.499	2.000	3456.250	7.871	.001
		Lower-bound	6912.499	2.000	3456.250	7.871	.001
	MTHICK	Sphericity Assumed	755.929	2	377.965	18.316	.000
		Greenhouse-Geisser	755.929	2.000	377.965	18.316	.000
		Huynh-Feldt	755.929	2.000	377.965	18.316	.000
		Lower-bound	755.929	2.000	377.965	18.316	.000
Error(ARM)	STENGTH	Sphericity Assumed	15808.968	36	439.138		
		Greenhouse-Geisser	15808.968	36.000	439.138		
		Huynh-Feldt	15808.968	36.000	439.138		
		Lower-bound	15808.968	36.000	439.138		
	MTHICK	Sphericity Assumed	742.906	36	20.636		
		Greenhouse-Geisser	742.906	36.000	20.636		
		Huynh-Feldt	742.906	36.000	20.636		
		Lower-bound	742.906	36.000	20.636		

a Computed using alpha = .05

EMG Univariate Analysis of Variance

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
ARM	Sphericity Assumed	.000	1	.000	.067	.797
	Greenhouse-Geisser	.000	1.000	.000	.067	.797
	Huynh-Feldt	.000	1.000	.000	.067	.797
	Lower-bound	.000	1.000	.000	.067	.797
	Upper-bound	.000	1.000	.000	.067	.797
ARM * GROUP	Sphericity Assumed	.016	2	.008	1.316	.284
	Greenhouse-Geisser	.016	2.000	.008	1.316	.284
	Huynh-Feldt	.016	2.000	.008	1.316	.284
	Lower-bound	.016	2.000	.008	1.316	.284
	Upper-bound	.016	2.000	.008	1.316	.284
Error(ARM)	Sphericity Assumed	.166	28	.006		
	Greenhouse-Geisser	.166	28.000	.006		
	Huynh-Feldt	.166	28.000	.006		
	Lower-bound	.166	28.000	.006		
	Upper-bound	.166	28.000	.006		
TIME	Sphericity Assumed	.001	1	.001	.143	.708
	Greenhouse-Geisser	.001	1.000	.001	.143	.708
	Huynh-Feldt	.001	1.000	.001	.143	.708
	Lower-bound	.001	1.000	.001	.143	.708
	Upper-bound	.001	1.000	.001	.143	.708
TIME * GROUP	Sphericity Assumed	.010	2	.005	1.238	.305
	Greenhouse-Geisser	.010	2.000	.005	1.238	.305
	Huynh-Feldt	.010	2.000	.005	1.238	.305
	Lower-bound	.010	2.000	.005	1.238	.305
	Upper-bound	.010	2.000	.005	1.238	.305
Error(TIME)	Sphericity Assumed	.116	28	.004		
	Greenhouse-Geisser	.116	28.000	.004		
	Huynh-Feldt	.116	28.000	.004		

	Geisser					
	Huynh-Feldt	.116	28.000	.004		
	Lower-bound	.116	28.000	.004		
MUSCLE	Sphericity Assumed	3.641	1	3.641	535.920	.000
	Greenhouse-Geisser	3.641	1.000	3.641	535.920	.000
	Huynh-Feldt	3.641	1.000	3.641	535.920	.000
	Lower-bound	3.641	1.000	3.641	535.920	.000
MUSCLE * GROUP	Sphericity Assumed	.012	2	.006	.907	.415
	Greenhouse-Geisser	.012	2.000	.006	.907	.415
	Huynh-Feldt	.012	2.000	.006	.907	.415
	Lower-bound	.012	2.000	.006	.907	.415
Error(MUSCLE)	Sphericity Assumed	.190	28	.007		
	Greenhouse-Geisser	.190	28.000	.007		
	Huynh-Feldt	.190	28.000	.007		
	Lower-bound	.190	28.000	.007		
ARM * TIME	Sphericity Assumed	.016	1	.016	7.058	.013
	Greenhouse-Geisser	.016	1.000	.016	7.058	.013
	Huynh-Feldt	.016	1.000	.016	7.058	.013
	Lower-bound	.016	1.000	.016	7.058	.013
ARM * TIME * GROUP	Sphericity Assumed	.011	2	.005	2.327	.116
	Greenhouse-Geisser	.011	2.000	.005	2.327	.116
	Huynh-Feldt	.011	2.000	.005	2.327	.116
	Lower-bound	.011	2.000	.005	2.327	.116
Error(ARM*TIME)	Sphericity Assumed	.064	28	.002		
	Greenhouse-Geisser	.064	28.000	.002		
	Huynh-Feldt	.064	28.000	.002		
	Lower-bound	.064	28.000	.002		
ARM *	Sphericity	.004	1	.004	.854	.363

MUSCLE	Assumed					
	Greenhouse-Geisser	.004	1.000	.004	.854	.363
	Huynh-Feldt	.004	1.000	.004	.854	.363
	Lower-bound	.004	1.000	.004	.854	.363
ARM * MUSCLE * GROUP	Sphericity Assumed	.016	2	.008	1.816	.181
	Greenhouse-Geisser	.016	2.000	.008	1.816	.181
	Huynh-Feldt	.016	2.000	.008	1.816	.181
	Lower-bound	.016	2.000	.008	1.816	.181
Error(ARM*MUSCLE)	Sphericity Assumed	.124	28	.004		
	Greenhouse-Geisser	.124	28.000	.004		
	Huynh-Feldt	.124	28.000	.004		
	Lower-bound	.124	28.000	.004		
TIME * MUSCLE	Sphericity Assumed	.002	1	.002	.439	.513
	Greenhouse-Geisser	.002	1.000	.002	.439	.513
	Huynh-Feldt	.002	1.000	.002	.439	.513
	Lower-bound	.002	1.000	.002	.439	.513
TIME * MUSCLE * GROUP	Sphericity Assumed	.005	2	.002	.476	.626
	Greenhouse-Geisser	.005	2.000	.002	.476	.626
	Huynh-Feldt	.005	2.000	.002	.476	.626
	Lower-bound	.005	2.000	.002	.476	.626
Error(TIME*MUSCLE)	Sphericity Assumed	.135	28	.005		
	Greenhouse-Geisser	.135	28.000	.005		
	Huynh-Feldt	.135	28.000	.005		
	Lower-bound	.135	28.000	.005		
ARM * TIME * MUSCLE	Sphericity Assumed	.019	1	.019	6.019	.021
	Greenhouse-Geisser	.019	1.000	.019	6.019	.021

ARM * TIME * MUSCLE * GROUP	Huynh-Feldt	.019	1.000	.019	6.019	.021
	Lower-bound	.019	1.000	.019	6.019	.021
	Sphericity Assumed	.015	2	.008	2.464	.103
	Greenhouse- Geisser	.015	2.000	.008	2.464	.103
	Huynh-Feldt	.015	2.000	.008	2.464	.103
Error(ARM*TIM E*MUSCLE)	Lower-bound	.015	2.000	.008	2.464	.103
	Sphericity Assumed	.086	28	.003		
	Greenhouse- Geisser	.086	28.000	.003		
	Huynh-Feldt	.086	28.000	.003		
	Lower-bound	.086	28.000	.003		

Appendix G: Statistical Tables Experiment 2

Strength and Muscle Thickness Doubly Multivariate Analysis: Multivariate Table

Multivariate Tests(c)

Effect			Value	F	Hypothesis df	Error df	Sig.
Between Subjects	Intercept	Pillai's Trace	.996	3966.678(a)	2.000	29.000	.000
		Wilks' Lambda	.004	3966.678(a)	2.000	29.000	.000
		Hotelling's Trace	273.564	3966.678(a)	2.000	29.000	.000
		Roy's Largest Root	273.564	3966.678(a)	2.000	29.000	.000
	GROUP	Pillai's Trace	.368	3.379	4.000	60.000	.015
		Wilks' Lambda	.665	3.279(a)	4.000	58.000	.017
		Hotelling's Trace	.454	3.178	4.000	56.000	.020
		Roy's Largest Root	.272	4.087(b)	2.000	30.000	.027
Within Subjects	TIME	Pillai's Trace	.569	19.169(a)	2.000	29.000	.000
		Wilks' Lambda	.431	19.169(a)	2.000	29.000	.000
		Hotelling's Trace	1.322	19.169(a)	2.000	29.000	.000
		Roy's Largest Root	1.322	19.169(a)	2.000	29.000	.000
	TIME * GROUP	Pillai's Trace	.768	9.345	4.000	60.000	.000
		Wilks' Lambda	.240	15.090(a)	4.000	58.000	.000
		Hotelling's Trace	3.132	21.921	4.000	56.000	.000
		Roy's Largest Root	3.121	46.815(b)	2.000	30.000	.000
	ARM	Pillai's Trace	.678	30.550(a)	2.000	29.000	.000
		Wilks' Lambda	.322	30.550(a)	2.000	29.000	.000

	Hotelling's Trace	2.107	30.550(a)	2.000	29.000	.000
	Roy's Largest Root	2.107	30.550(a)	2.000	29.000	.000
ARM * GROUP	Pillai's Trace	.290	2.547	4.000	60.000	.048
	Wilks' Lambda	.711	2.690(a)	4.000	58.000	.040
	Hotelling's Trace	.403	2.821	4.000	56.000	.033
	Roy's Largest Root	.397	5.950(b)	2.000	30.000	.007
TIME * ARM	Pillai's Trace	.330	7.156(a)	2.000	29.000	.003
	Wilks' Lambda	.670	7.156(a)	2.000	29.000	.003
	Hotelling's Trace	.494	7.156(a)	2.000	29.000	.003
	Roy's Largest Root	.494	7.156(a)	2.000	29.000	.003
TIME * ARM * GROUP	Pillai's Trace	.565	5.913	4.000	60.000	.000
	Wilks' Lambda	.435	7.486(a)	4.000	58.000	.000
	Hotelling's Trace	1.298	9.087	4.000	56.000	.000
	Roy's Largest Root	1.297	19.460(b)	2.000	30.000	.000

a Exact statistic

b The statistic is an upper bound on F that yields a lower bound on the significance level.

c Design: Intercept+GROUP

Within Subjects Design: TIME+ARM+TIME*ARM

Strength and Muscle Thickness Doubly Multivariate Analysis: Univariate Table

Univariate Tests

Source	Measure		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME	MTHICK	Sphericity Assumed	.027	1	.027	4.227	.049
		Greenhouse-Geisser	.027	1.000	.027	4.227	.049
		Huynh-Feldt	.027	1.000	.027	4.227	.049
		Lower-bound	.027	1.000	.027	4.227	.049
	STRENGTH	Sphericity Assumed	260.549	1	260.549	32.053	.000
		Greenhouse-Geisser	260.549	1.000	260.549	32.053	.000
		Huynh-Feldt	260.549	1.000	260.549	32.053	.000
		Lower-bound	260.549	1.000	260.549	32.053	.000
TIME * GROUP	MTHICK	Sphericity Assumed	.181	2	.091	14.049	.000
		Greenhouse-Geisser	.181	2.000	.091	14.049	.000
		Huynh-Feldt	.181	2.000	.091	14.049	.000
		Lower-bound	.181	2.000	.091	14.049	.000
	STRENGTH	Sphericity Assumed	447.820	2	223.910	27.545	.000
		Greenhouse-Geisser	447.820	2.000	223.910	27.545	.000
		Huynh-Feldt	447.820	2.000	223.910	27.545	.000
		Lower-bound	447.820	2.000	223.910	27.545	.000
Error(TIME)	MTHICK	Sphericity Assumed	.194	30	.006		
		Greenhouse-Geisser	.194	30.000	.006		

		Huynh-Feldt	.194	30.000	.006		
		Lower-bound	.194	30.000	.006		
	STRENGTH	Sphericity Assumed	243.862	30	8.129		
		Greenhouse-Geisser	243.862	30.000	8.129		
		Huynh-Feldt	243.862	30.000	8.129		
		Lower-bound	243.862	30.000	8.129		
ARM	MTHICK	Sphericity Assumed	.062	1	.062	2.445	.128
		Greenhouse-Geisser	.062	1.000	.062	2.445	.128
		Huynh-Feldt	.062	1.000	.062	2.445	.128
		Lower-bound	.062	1.000	.062	2.445	.128
	STRENGTH	Sphericity Assumed	492.328	1	492.328	61.448	.000
		Greenhouse-Geisser	492.328	1.000	492.328	61.448	.000
		Huynh-Feldt	492.328	1.000	492.328	61.448	.000
		Lower-bound	492.328	1.000	492.328	61.448	.000
ARM * GROUP	MTHICK	Sphericity Assumed	.158	2	.079	3.083	.061
		Greenhouse-Geisser	.158	2.000	.079	3.083	.061
		Huynh-Feldt	.158	2.000	.079	3.083	.061
		Lower-bound	.158	2.000	.079	3.083	.061
	STRENGTH	Sphericity Assumed	50.320	2	25.160	3.140	.058
		Greenhouse-Geisser	50.320	2.000	25.160	3.140	.058
		Huynh-Feldt	50.320	2.000	25.160	3.140	.058
		Lower-bound	50.320	2.000	25.160	3.140	.058

Error(ARM)	MTHICK	Sphericity Assumed	.767	30	.026		
		Greenhouse-Geisser	.767	30.000	.026		
		Huynh-Feldt	.767	30.000	.026		
		Lower-bound	.767	30.000	.026		
	STRENGTH	Sphericity Assumed	240.362	30	8.012		
		Greenhouse-Geisser	240.362	30.000	8.012		
		Huynh-Feldt	240.362	30.000	8.012		
		Lower-bound	240.362	30.000	8.012		
TIME * ARM	MTHICK	Sphericity Assumed	.050	1	.050	14.660	.001
		Greenhouse-Geisser	.050	1.000	.050	14.660	.001
		Huynh-Feldt	.050	1.000	.050	14.660	.001
		Lower-bound	.050	1.000	.050	14.660	.001
	STRENGTH	Sphericity Assumed	.841	1	.841	.579	.453
		Greenhouse-Geisser	.841	1.000	.841	.579	.453
		Huynh-Feldt	.841	1.000	.841	.579	.453
		Lower-bound	.841	1.000	.841	.579	.453
TIME * ARM * GROUP	MTHICK	Sphericity Assumed	.131	2	.065	19.118	.000
		Greenhouse-Geisser	.131	2.000	.065	19.118	.000
		Huynh-Feldt	.131	2.000	.065	19.118	.000
		Lower-bound	.131	2.000	.065	19.118	.000
	STRENGTH	Sphericity Assumed	9.908	2	4.954	3.412	.046
		Greenhouse-Geisser	9.908	2.000	4.954	3.412	.046

		Huynh-Feldt	9.908	2.000	4.954	3.412	.046
		Lower-bound	9.908	2.000	4.954	3.412	.046
Error(TIME* ARM)	MTHICK	Sphericity Assumed	.103	30	.003		
		Greenhouse- Geisser	.103	30.000	.003		
		Huynh-Feldt	.103	30.000	.003		
		Lower-bound	.103	30.000	.003		
	STRENGTH	Sphericity Assumed	43.562	30	1.452		
		Greenhouse- Geisser	43.562	30.000	1.452		
		Huynh-Feldt	43.562	30.000	1.452		
		Lower-bound	43.562	30.000	1.452		

Strength and Muscle Thickness (Percent Change Data) Doubly Multivariate Analysis: Multivariate Table

Multivariate Tests(c)

Effect			Value	F	Hypothesis df	Error df	Sig.
Between Subjects	Intercept	Pillai's Trace	.591	20.946(a)	2.000	29.000	.000
		Wilks' Lambda	.409	20.946(a)	2.000	29.000	.000
		Hotelling's Trace	1.445	20.946(a)	2.000	29.000	.000
		Roy's Largest Root	1.445	20.946(a)	2.000	29.000	.000
	GROUP	Pillai's Trace	.781	9.603	4.000	60.000	.000
		Wilks' Lambda	.231	15.671(a)	4.000	58.000	.000
		Hotelling's Trace	3.279	22.955	4.000	56.000	.000
		Roy's Largest Root	3.264	48.958(b)	2.000	30.000	.000
Within Subjects	ARM	Pillai's Trace	.367	8.413(a)	2.000	29.000	.001
		Wilks' Lambda	.633	8.413(a)	2.000	29.000	.001
		Hotelling's Trace	.580	8.413(a)	2.000	29.000	.001
		Roy's Largest Root	.580	8.413(a)	2.000	29.000	.001
	ARM * GROUP	Pillai's Trace	.589	6.268	4.000	60.000	.000
		Wilks' Lambda	.419	7.914(a)	4.000	58.000	.000
		Hotelling's Trace	1.370	9.592	4.000	56.000	.000
		Roy's Largest Root	1.356	20.345(b)	2.000	30.000	.000

a Exact statistic

b The statistic is an upper bound on F that yields a lower bound on the significance level.

c Design: Intercept+GROUP

Within Subjects Design: ARM

Strength and Muscle Thickness (Percent Change Data) Doubly Multivariate Analysis: Univariate Table

Univariate Tests

Source	Measure		Type III Sum of Squares	df	Mean Square	F	Sig.
ARM	MTHICK	Sphericity Assumed	104.265	1	104.265	14.229	.001
		Greenhouse-Geisser	104.265	1.000	104.265	14.229	.001
		Huynh-Feldt	104.265	1.000	104.265	14.229	.001
		Lower-bound	104.265	1.000	104.265	14.229	.001
	STRENGTH	Sphericity Assumed	83.287	1	83.287	.648	.427
		Greenhouse-Geisser	83.287	1.000	83.287	.648	.427
		Huynh-Feldt	83.287	1.000	83.287	.648	.427
		Lower-bound	83.287	1.000	83.287	.648	.427
ARM * GROUP	MTHICK	Sphericity Assumed	279.431	2	139.715	19.067	.000
		Greenhouse-Geisser	279.431	2.000	139.715	19.067	.000
		Huynh-Feldt	279.431	2.000	139.715	19.067	.000
		Lower-bound	279.431	2.000	139.715	19.067	.000
	STRENGTH	Sphericity Assumed	54.430	2	27.215	.212	.810
		Greenhouse-Geisser	54.430	2.000	27.215	.212	.810
		Huynh-Feldt	54.430	2.000	27.215	.212	.810
		Lower-bound	54.430	2.000	27.215	.212	.810
Error(ARM)	MTHICK	Sphericity Assumed	219.827	30	7.328		
		Greenhouse-Geisser	219.827	30.000	7.328		
		Huynh-Feldt	219.827	30.000	7.328		
		Lower-bound	219.827	30.000	7.328		
	STRENGTH	Sphericity Assumed	3858.575	30	128.619		
		Greenhouse-Geisser	3858.575	30.000	128.619		
		Huynh-Feldt	3858.575	30.000	128.619		
		Lower-bound	3858.575	30.000	128.619		

EMG Univariate Analysis of Variance

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
ARM	Sphericity Assumed	.115	1	.115	11.678	.002
	Greenhouse-Geisser	.115	1.000	.115	11.678	.002
	Huynh-Feldt	.115	1.000	.115	11.678	.002
	Lower-bound	.115	1.000	.115	11.678	.002
ARM * GROUP	Sphericity Assumed	.026	2	.013	1.297	.288
	Greenhouse-Geisser	.026	2.000	.013	1.297	.288
	Huynh-Feldt	.026	2.000	.013	1.297	.288
	Lower-bound	.026	2.000	.013	1.297	.288
Error(ARM)	Sphericity Assumed	.296	30	.010		
	Greenhouse-Geisser	.296	30.000	.010		
	Huynh-Feldt	.296	30.000	.010		
	Lower-bound	.296	30.000	.010		
TIME	Sphericity Assumed	.002	1	.002	.219	.643
	Greenhouse-Geisser	.002	1.000	.002	.219	.643
	Huynh-Feldt	.002	1.000	.002	.219	.643
	Lower-bound	.002	1.000	.002	.219	.643
TIME * GROUP	Sphericity Assumed	.060	2	.030	4.109	.026
	Greenhouse-Geisser	.060	2.000	.030	4.109	.026
	Huynh-Feldt	.060	2.000	.030	4.109	.026
	Lower-bound	.060	2.000	.030	4.109	.026
Error(TIME)	Sphericity Assumed	.219	30	.007		
	Greenhouse-Geisser	.219	30.000	.007		
	Huynh-Feldt	.219	30.000	.007		
	Lower-bound	.219	30.000	.007		
MUSCLE	Sphericity Assumed	2.851	1	2.851	157.974	.000
	Greenhouse-Geisser	2.851	1.000	2.851	157.974	.000

	Huynh-Feldt	2.851	1.000	2.851	157.974	.000
	Lower-bound	2.851	1.000	2.851	157.974	.000
MUSCLE * GROUP	Sphericity Assumed	.079	2	.039	2.181	.131
	Greenhouse-Geisser	.079	2.000	.039	2.181	.131
	Huynh-Feldt	.079	2.000	.039	2.181	.131
	Lower-bound	.079	2.000	.039	2.181	.131
Error(MUSCLE)	Sphericity Assumed	.541	30	.018		
	Greenhouse-Geisser	.541	30.000	.018		
	Huynh-Feldt	.541	30.000	.018		
	Lower-bound	.541	30.000	.018		
ARM * TIME	Sphericity Assumed	.005	1	.005	.777	.385
	Greenhouse-Geisser	.005	1.000	.005	.777	.385
	Huynh-Feldt	.005	1.000	.005	.777	.385
	Lower-bound	.005	1.000	.005	.777	.385
ARM * TIME * GROUP	Sphericity Assumed	.019	2	.009	1.539	.231
	Greenhouse-Geisser	.019	2.000	.009	1.539	.231
	Huynh-Feldt	.019	2.000	.009	1.539	.231
	Lower-bound	.019	2.000	.009	1.539	.231
Error(ARM*TIME)	Sphericity Assumed	.182	30	.006		
	Greenhouse-Geisser	.182	30.000	.006		
	Huynh-Feldt	.182	30.000	.006		
	Lower-bound	.182	30.000	.006		
ARM * MUSCLE	Sphericity Assumed	.126	1	.126	14.770	.001
	Greenhouse-Geisser	.126	1.000	.126	14.770	.001
	Huynh-Feldt	.126	1.000	.126	14.770	.001
	Lower-bound	.126	1.000	.126	14.770	.001
ARM * MUSCLE * GROUP	Sphericity Assumed	.007	2	.003	.388	.682
	Greenhouse-Geisser	.007	2.000	.003	.388	.682
	Huynh-Feldt	.007	2.000	.003	.388	.682
	Lower-bound	.007	2.000	.003	.388	.682
Error(ARM*MUSCLE)	Sphericity Assumed	.257	30	.009		
	Greenhouse-Geisser	.257	30.000	.009		
	Huynh-Feldt	.257	30.000	.009		
	Lower-bound	.257	30.000	.009		

TIME * MUSCLE	Sphericity Assumed	.002	1	.002	.232	.634
	Greenhouse-Geisser	.002	1.000	.002	.232	.634
	Huynh-Feldt	.002	1.000	.002	.232	.634
	Lower-bound	.002	1.000	.002	.232	.634
TIME * MUSCLE * GROUP	Sphericity Assumed	.069	2	.034	5.157	.012
	Greenhouse-Geisser	.069	2.000	.034	5.157	.012
	Huynh-Feldt	.069	2.000	.034	5.157	.012
	Lower-bound	.069	2.000	.034	5.157	.012
Error(TIME*MUSCLE)	Sphericity Assumed	.199	30	.007		
	Greenhouse-Geisser	.199	30.000	.007		
	Huynh-Feldt	.199	30.000	.007		
	Lower-bound	.199	30.000	.007		
ARM * TIME * MUSCLE	Sphericity Assumed	.002	1	.002	.486	.491
	Greenhouse-Geisser	.002	1.000	.002	.486	.491
	Huynh-Feldt	.002	1.000	.002	.486	.491
	Lower-bound	.002	1.000	.002	.486	.491
ARM * TIME * MUSCLE * GROUP	Sphericity Assumed	.025	2	.012	2.535	.096
	Greenhouse-Geisser	.025	2.000	.012	2.535	.096
	Huynh-Feldt	.025	2.000	.012	2.535	.096
	Lower-bound	.025	2.000	.012	2.535	.096
Error(ARM*TIME*MUSCLE)	Sphericity Assumed	.148	30	.005		
	Greenhouse-Geisser	.148	30.000	.005		
	Huynh-Feldt	.148	30.000	.005		
	Lower-bound	.148	30.000	.005		