EFFECT OF LOAD WITH DYNAMIC CONTRACTIONS ON CONTRALATERAL

HOMOLOGOUS MUSCLE PERFORMANCE

by

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ABSTRACT

Fatigue is defined as a decrease in force and power production and is normally classified as being central or peripheral in origin. A reduction in neural output either from spinal or supraspinal levels characterizes central fatigue, while physiological changes at or distal to the neuromuscular junction characterizes peripheral fatigue. Additionally, peripheral fatigue induced in a specific muscle can result in the development of central fatigue and create in a non-local response. This non-local response is referred to as crossover fatigue and affects non-fatigued muscles.

Research exploring crossover fatigue is in its infancy and appears to be conflicting. Several studies have not shown significant crossover fatigue effects while others support its existence. Despite all studies claiming that their subjects were brought to temporary exhaustion unilaterally, the presence of crossover fatigue phenomenon is not consistent. The inconsistent findings may be related to the differences in the unilateral fatiguing protocols, which include variations in parameters such as exercise intensity, volume and method of muscular contraction.

Based on the inconsistencies in the literature, the following experiment was conducted. Two different fatiguing protocols consisting of dynamic knee extension contractions were implemented to create localized fatigue in the ipsilateral knee extensors. Two different exercise intensities (40% and 70% MVC) were used and pre- and post-intervention measures (e.g. MVC, F100, EMG, median frequency and submaximal endurance performance) were recorded from the contralateral non-fatigued knee extensors. It was hypothesized that a higher intensity of unilateral

dynamic exercise will lead to greater crossover fatigue effects, demonstrated by detriments in muscle strength and endurance performance.

It was found that both 40% and 70% of MVC dynamic fatiguing protocols caused a decrease in subsequent MVC and instantaneous force with greater detriments from the 70% condition. Additionally, the voluntary force produced during the initial 10 seconds of the submaximal endurance test showed a moderate magnitude of variability in both the 40% and 70% conditions compared with the control condition thus, indicated neuromuscular function was impaired.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ANOVA – Analysis of variance

BF – Biceps Femoris

CMEP – Cerviomedullary Evoked Potential

CMJS – Cervicomedullary Junction Stimulation

EMG – Electromyography

ES – Effect Size

H Reflex – Hoffman Reflex

H Max – Hoffman Reflex Maximum

ITT – Interpolated Twitch Technique

M Wave – Muscle Response Wave

MEP – Motor Evoked Potential

MVC – Maximal Voluntary Contraction

SD – Standard Deviation

SEM – Standard Error of the Mean

TMS – Transcranial Magnetic Stimulation

VL – Vastus Lateralis

LITERATURE REVIEW

1. INTRODUCTION

Fatigue is a complex, multifactorial phenomenon with varying definitions depending on the research field of interest (Enoka & Stuart, 1992; St. Clair Gibson, et al., 2003). In neurophysiology, fatigue is defined as a reduction in the central drive to the active muscle fibers resulting in the decrease of force and power production (Gandevia, 2001) or contractile response (MacIntosh, et al., 2006). Fatigue can be so great that it results in task failure or the cessation of a bout of exercise (Gandevia, 2001). Normally, fatigue results from exercise or physical activity involving repeated or continuous maximal or submaximal muscular contractions (MacIntosh, et al., 2006; Taylor & Gandevia, 2008). It has been considered a regulator to exercise performance (Tucker, 2009) and can exist whether or not the exercise or task can be sustained (Barry & Enoka, 2007). Furthermore, fatigue has also been defined as an emotion (Noakes, 2012; St Clair Gibson, et al., 2003) and is suggested to act as a warning sign, most likely important for maintaining physical integrity (Ament & Verkerke, 2009, p. 391).

A maximal voluntary contraction is "a maximal contraction that a subject accepts as maximal and that is produced with appropriate continuous feedback of achievement" (Gandevia, 2001, p.1733). A task involving the maintenance of a maximal contraction shows a decrease in performance, which parallels the increase in the appearance of fatigue (Enoka & Duchateau, 2008). Normally reversible with rest, (NHLBI, 1990) fatigue is often associated with many sensations during exercise. The emotional and conscious perception (St Clair Gibson, et al., 2003) of

1

changes in bodily functions (e.g. breathlessness, increased heart rate, increased internal body temperature, onset of sweating) (Hampson, et al., 2001) may contribute to the perceived difficulty of the task or exercise (MacIntosh, et al., 2006) and lead to its cessation. The overall sensation of fatigue may be delayed in persons with higher fitness levels, as the onset of fatigue depends on the initial state of the neuromuscular system (e.g. energy reserves, ion concentrations and the arrangement of the contractile proteins) (Boyas & Guevel, 2011). Additional factors can affect the onset of fatigue such as level of motivation at the time of activity, memory of previous experiences performing the task, (Ulmer, 1996) mental fatigue (Boksem & Tops, 2008; Marcora, et al., 2009) and specific details of the task (Gruet, et al., 2012). In addition to task intensity (e.g. maximal vs. submaximal contraction) (Taylor & Gandevia, 2008), changes in corticospinal excitability during fatigue can also be influenced by muscle function type (e.g. extensor vs. flexor) (Gruet, et al., 2012) or the speed and duration of the contraction (Enoka & Stuart, 1992). As a result of the many factors affecting fatigue and its onset, Barry and Enoka (2007) state that it's not possible to answer the question "What causes muscle fatigue?" as even relatively subtle variations in a task can be associated with vast differences in the time to task failure (Hunter, et al., 2004). According to Behm (2004), fatigue may be present during prolonged submaximal contractions without a noticeable reduction in force production; therefore, increasing the difficulty of precisely measuring when fatigue actually occurs. Characterized by the subjective perception of fatigue or a reduction in the electromyograph (EMG) output, several mechanisms are suggested to explain the facilitation in force output such as "augmented motor

unit recruitment, increases and decreases in rate coding, the inclusion of catch-like properties, alteration in motor control and neural postactivation potentiation" (Behm, 2004, p. 275). Neural potentiation may provide facilitation to motoneuron excitation via supraspinal and afferent input during prolonged contractions (Behm, 2004). Catch-like properties, classified as "the insertion of additional neural impulses into the established train of motoneuron impulse activity," (Behm, 2004, p.278) can also mask fatigue and aid in force output. Furthermore, increases in both muscle fiber cross bridging, via augmented calcium release from the sarcoplasmic reticulum, and in muscle stiffness can also help in maintaining force production during fatigue, as can alterations in muscle fiber recruitment (Behm, 2004). Lastly, an additional mechanism that can augment force output during ongoing contractions is postactivation potentiation (Behm, 2004), a mechanism attributed to the phosphorylation of the regulatory light chains on the myosin head (Moore & Stull, 1984) and also to the elevation in cytosolic calcium levels following a voluntary contraction (Allen, et al., 1989).

2. CLASSIFICATION OF FATIGUE

Fatigue can originate at different levels along the motor pathway and is normally divided into central or peripheral components however; it's difficult to show that the sensation of fatigue is localized to a single area (St Clair Gibson, et al., 2003). Since the seminal work of Angelo Mosso (Di Giulio, et al., 2006), researchers have been trying to localize fatigue, either in the working muscles or in the nervous system. This approach is trivial, as confusion exists in the literature because the

boundary between the working muscles and the nervous system is not concrete (Barry & Enoka, 2007). For example, is afferent feedback sent to the brain from the working muscles a peripheral or central mechanism (Barry & Enoka, 2007)? Nybo and Secher (2004) have gone to the extreme and stated that this dichotomy is not particularly useful and should be avoided however, since current research still attempts to localize fatigue, defining central and peripheral fatigue is warranted.

2.1. CENTRAL FATIGUE

Central fatigue is defined as a "progressive failure to voluntarily activate the muscle, [which] can originate at both the spinal and supraspinal levels," (Gruet, et al., 2012, p.4). Supraspinal fatigue is the failure to generate output from the motor cortex characterized by a decrease in the number of recruited motor units and/or their firing rate (Gandevia, 2001). In addition, central fatigue can show alterations in: 1) activation of the primary motor cortex; 2) propagation of the command from the central nervous system (CNS) to the motoneurons (pyramidal pathways); and 3) activation of the motoneurons and muscles (Boyas & Guevel, 2011).

2.2. PERIPHERAL FATIGUE

In contrast, peripheral fatigue is said to result from changes at or distal to the neuromuscular junction, which is demonstrated by a reduction in twitch or tetanic force elicited by peripheral nerve stimulation in a relaxed muscle (Gruet, et al., 2012). Previous fatigue research typically portrayed fatigue during intense exercise as a consequence of phosphocreatine depletion and lactic acidosis, resulting in the

term "muscle fatigue" (McKenna & Hargreaves, 2008). Sites altered by peripheral fatigue include: 1) neuromuscular propagation, including propagation at the neuromuscular junction; 2) excitation-contraction coupling; 3) availability of metabolic substrates; 4) state of the intracellular medium; 5) performance of the contractile apparatus; and 6) blood flow (Boyas & Guevel, 2011). However, mechanisms related to peripheral fatigue are often insufficient when explaining the decrease in maximal force production, therefore; changes in the CNS must explain the rest of the story (Millet & Lepers, 2004; Taylor & Gandevia, 2008).

3. ANALYZING FATIGUE AND ITS ORIGIN

Although useful, the distinction between central and peripheral fatigue excludes the individual subjective assessment of the situation, as "the subjective sense a person attributes to an event or experience, tends to be overlooked in scientific research" (Marino, et al., 2011, p.65). Marino et al. (2011) suggests that perhaps "...bringing feed-forward mechanisms of the brain into fatigue research [...] represents the next phase in the unraveling of the fatigue process." Currently, there are several methods utilized in the research that attempt to quantify, localize and explain fatigue such as the interpolated twitch technique (Merton, 1954), transcranial magnetic stimulation (Ridding & Rothwell, 2007), cervicomedullary junction stimulation (Taylor, 2006) and lastly, the Hoffman reflex (Palmierl, et al., 2004).

3.1. INTERPOLATED TWITCH TECHNIQUE

The interpolated twitch technique (ITT) is a method of assessing fatigue and voluntary activation (Behm, et al., 1996; Behm, et al., 2002; Belanger & McComas, 1981; Gandevia, 2001), which involves an electrical stimulus delivered to the motor nerve during a maximal voluntary contraction (Gruet, et al., 2012; Merton, 1954). This technique determines the central drive (e.g. central fatigue) and the peripheral force-generating capacity of the contracting muscles (Allen, et al., 1998). If all the muscle fibers are being recruited during the maximum voluntary contraction, as when the contraction produces the maximum evocable force (Gandevia, 2001), the stimulated motor volley would not result in a superimposed twitch (Merton, 1954); in contrast, if some muscle fibers are not being recruited or not being recruited fast enough, the electric stimulus will evoke additional force production, referred to as superimposed twitch (Gruet, et al., 2012). "The ratio between superimposed twitch and a potentiated twitch elicited in the relaxed muscle," states Gruet et al., "allows quantification of voluntary activation" (2012, p.6). A reduction in voluntary force production suggests failure to drive the working muscles, however; twitch interpolation does not quantify the descending drive to the motoneurons, nor does it take into account the source of this drive (Gruet, et al., 2012).

3.2. TRANSCRANIAL MAGNETIC STIMULATION

Transcranial magnetic stimulation (TMS) is a method of stimulating the brain, within an intact scalp, to investigate activity in the human motor cortex (Ridding & Rothwell, 2007). More specifically, the cortical cells are stimulated trans-synaptically to show if a site upstream from the motor cortex is declining in its

excitation of the cortex during a maximal voluntary contraction (MacIntosh, et al.,

2006). TMS produces a short-latency motor evoked potential (MEP) and an

interruption in the electromyographic (EMG) activity referred to as the silent period

(McNeil, et al., 2009). As fatigue develops, the MEP increases, which is a reflection of

an increase in cortical excitability (McNeil, et al., 2009); however, there is also an

increase in the silent period (Gandevia, et al., 1996), which indicates "an increase in

cortical inhibition as the latter part of the silent period is thought to be due to

intracortical inhibition of voluntary motor output" (McNeil, et al., 2009, p. 5602).

McNeil et al. (2009) adds "These apparently opposite changes make the role of the

motor cortex during fatiguing contractions unclear" (p.5602). The increase in the

superimposed twitch (Taylor & Gandevia, 2008) indicates that the motor cortical

output is suboptimal and insufficient to fully activate all motor units (Gruet, et al.,

2012). Failure seems to occur at the supraspinal level to generate complete motor

cortical output to drive the motor axons maximally (Taylor & Gandevia, 2008). The

evoked response induced by the TMS depends on the activity of the cortex during

stimulation and the orientation of the TMS coil on the head (Ridding & Rothwell,

2007). The response will be larger if the stimulus is applied to a subject actively

contracting the target muscle than if the muscle was relaxed because the

postsynaptic neurons will be closer to their firing threshold (Ridding & Rothwell,

2007). It should be noted however that changes in the MEP could originate at

different levels of the motor pathway (Gruet, et al., 2012) and that the TMS

technique cannot localize fatigue to cortical or spinal neurons (Gruet, et al., 2012;

Taylor, 2006).

3.3. CERVICOMEDULLARY JUNCTION STIMULATION

Cervicomedullary junction stimulation (CMJS) is another method of assessing fatigue as it targets descending axons in the corticospinal tract, inferior to the motor cortex, at the cervicomedullary junction (Taylor, 2006). Similar to TMS, CMJS activates motoneurons and evokes a short-latency excitatory response, called cervicomeduallary motor evoked potentials (CMEP), which can be recorded from the muscle (Taylor, 2006). CMEPs have a large monosynaptic component and are unaffected by presynaptic inhibition; therefore, their size reflect motoneuron excitability (Petersen, et al., 2002). The comparison of MEPs and CMEPs allows researchers to localize fatigue and changes in excitability to either spinal or cortical sites (McNeil, et al., 2009).

3.4. THE HOFFMAN REFLEX

The Hoffman reflex (H reflex) is an indirect measurement of peripheral fatigue as it is proposed to measure the net excitability and inhibitory influences on alpha-motoneurons at the spinal level (Garland & McComas, 1990; Hortobagyi et al., 1996; Loscher, et al., 1996; Schieppati, 1987); however, Zehr (2002) states the "H reflex is not a direct measure of alpha-motoneuron excitability due to the effect of presynaptic inhibition on reflex amplitude" (p.455). Considered an electrical analogue of the stretch reflex (Palmierl, et al., 2004), the H reflex is created by applying an external electrical stimulation to a mixed peripheral nerve (e.g. both motor and sensory axons) (Zehr, 2002), which is said to bypass the effects of both gamma motoneurons and muscle spindle discharge (Brooke, et al., 1997; Schieppati,

1987). Depending on the amount of electrical current applied to the peripheral nerve, stimulation to evoke the H reflex involves both afferent sensory (Ia-afferent fibers) and efferent motor unit (alpha motoneurons) arcs as well as direct efferent motoneuron activation, which is referred to as the muscle response or the M wave (Palmierl, et al., 2004; Zehr, 2002). Alpha motoneuron activity and subsequent muscle activation is measured via EMG recordings, which can reflect the H reflex without an M wave or an M wave without the H reflex depending on the stimulation intensity (Zehr, 2002).

At relatively lower stimulation intensities, Ia-afferent fibers are preferentially stimulated, due to their intrinsic properties and their larger diameter, (Latash, 1998, as cited by Palmierl, et al., 2004) and send action potentials toward the spinal cord, synapsing on alpha-motoneurons (Palmierl, et al., 2004). If activity of the Ia-afferent is able to depolarize the alpha-motoneuron, action potentials will propagate along the axon and result in muscle contraction, illustrated as an H reflex tracing on the EMG (Palmierl, et al., 2004). Increasing the stimulus intensity eventually results in the H reflex reaching its maximum (H-max), which corresponds with the fullest reflex activation (Palmierl, et al., 2004). The H-max is an estimation of the number of motoneurons a person is capable of activating in a given state (Palmierl, et al., 2004). At higher stimulation intensities, beyond that required to entice an H reflex, results in the depolarization of the motor axons, which send action potentials toward the neuromuscular junction (Palmierl, et al., 2004). If successful in depolarizing the sarcolemma, the action potentials will result in muscle contractions, which create an M wave tracing on the EMG (Palmierl, et al., 2004).

Continuing with progressive increases in the stimulus intensity will eventually result in complete muscle activation, which corresponds to the maximum M wave (Palmierl, et al., 2004; Zehr, 2002).

4. MECHANISMS OF FATIGUE

The inability to produce and maintain the expected or required amount of muscle activation during a task or exercise can result from physiological inadequacies in any of the several locations of the motor command pathway:

"premotor cortex, motor cortex, descending pathways, developing inhibitory pathways, motoneuron activation, neuromuscular junction, muscle fiber membrane, T-tubules, voltages sensors, ryanodine receptors, sarcoplasmic reticulum calcium availability, calcium binding, and finally, actin-myosin interaction" (MacIntosh, et al., 2006, p.227).

These inadequacies are normally divided into central or peripheral components in order to localize their origin.

4.1. CENTRAL FATIGUE

Central fatigue has been said to account for over 25% (Boyas & Guevel, 2011; Taylor & Gandevia, 2008) to as much as 50% (MacIntosh, et al., 2006) in the drop in force production during sustained maximal contractions, which is typically displayed as a drop in the discharge rate and number of motoneurons recruited (Butler, et al., 2003; Gandevia, 2001; Peters & Fuglevand, 1999). This drop in maximal force production starts once the exercise commences and continues to

progressively increase until the task can no longer be performed (Gandevia, 2001).

Taylor and Gandevia (2008) report that three potential actions at the motoneuron

pool can lead to a decline in their firing rate: "1) a decrease in excitatory input; 2) an

increase in inhibitory input; and 3) a decrease in responsiveness of the

motoneurons through a change in their intrinsic properties" (McNeil, et al., 2009;

Taylor & Gandevia, 2008, p.543). Motoneurons of the elbow flexors are suggested to

become less responsive to synaptic input when there is a reduction in the CMEP

during a maximal effort contraction; however, Taylor and Gandevia (2008) state

that this does not reflect disfacilitation (withdrawal of excitatory input); but, McNeil

et al. (2009) propose disfacilitation via decreased muscle spindle discharge as an

explanation for the reduced responsiveness of the motoneurons to descending

input.

In order for a motoneuron to maintain its firing rate and force output, a

greater amount of net excitatory input is required to accommodate for fatiguing

muscle fibers; (Johnson, et al., 2004) however, adjustments can vary among

individuals (Barry & Enoka, 2007). This input will maintain the firing rate of the

previously firing motoneurons, but also recruit additional motoneurons; therefore,

increasing EMG output (Johnson, et al., 2004). However, a phenomenon referred to

as late adaptation describes a decrease in firing rate with sustained, constant

intensity contractions, but is not fatigue in the expected sense, as the firing rate can

be increased if the excitation strength is increased (Gardiner, 2011). Behm (2004)

states the mechanism for this adaptation is attributed to an increase in outward

current, driven by a calcium-activated, potassium conductance. DeLuca et al. (1996)

suggest that late adaptation and potentiation as mechanisms to explain how motor

unit firing rates in human first dorsal interosseus and tibialis anterior muscles

appear to decrease gradually during muscular contractions producing constant

force output, without the recruitment of additional motor units. A property of motor

unit recruitment known as muscle wisdom also describes the decline in motor unit

firing frequency with the maintenance of force production (MacIntosh, et al., 2006).

Muscle wisdom reduces the potential of task failure, while optimizing the motor unit

activation rate to the contractile state of the muscle (Gandevia, 2001; MacIntosh, et

al., 2006). Therefore, an "intrinsic fatigue" mechanism must exist in order to explain

the reduction in motor unit firing rate such as changes in reflex inputs from muscle

afferents, net excitatory descending drive and recurrent inhibition (Johnson, et al.,

2004; Taylor & Gandevia, 2008). Furthermore, McNeil, et al. (2009) found that

spinal mechanisms decrease the motoneuron responsiveness to descending input in

the elbow flexors during the development of central fatigue during maximal

contractions.

4.1.1. GROUP III AND IV MUSCLE AFFERENTS AND THEIR POSSIBLE ROLE IN
CENTRAL FATIGUE

One possible explanation of central fatigue is the activity of group III and IV

muscle afferents, which have been shown to reflexively inhibit spinal motoneurons

(Bigland-Ritchie, et al., 1986; Butler, et al., 2003; Hayes, et al., 2006; Hunter, et al.,

2004; Taylor, et al., 2000). These small diameter afferents are sensitive to both

mechanical and chemical stimuli and increase their firing rate with metabolite

accumulation in a fatigued muscle (Mense, 1977; Sinoway, et al., 1993). Particularly, group III afferents are sensitive to changes in both mechanical and chemical stimuli, whereas group IV afferents are more responsive to changes in chemical stimuli alone (Barry & Enoka, 2007). A research strategy implemented to analyze group III and group IV muscle afferent output is to compare the recovery of muscle function when blood flow is normal and when it is impeded (Barry & Enoka, 2007). Bigland-Ritchie and colleagues (1986) found the reduction in the motor unit discharge rate in the biceps brachii following a sustained maximal voluntary contraction, did not recover when blood flow was occluded for 3-minutes following the contraction, but did recover to control values within 3-minutes, when blood flow was restored. This led to the conclusion that peripheral reflex mediated by group III-IV afferents from the fatigued working muscles contributed to the decrease in the discharge rate seen in the motoneurons supplying the biceps brachii (Bigland-Ritchie, et al., 1986). The theory states that metabolites produced from the muscular contraction remain elevated in the working muscle when blood flow is occluded; therefore, continually stimulating group III and IV afferents, which continues to inhibit spinal motoneurons (Hayes, et al., 2006; Hunter, et al., 2004). Furthermore, group III-IV afferents can reduce excitatory input to the motoneurons via presynaptic inhibition of the group Ia afferents, a process referred to as disfacilitation (Hunter, et al., 2004).

Conversely, Gandevia and colleagues (1996) proposed a decrease in neural drive "upstream" of the motor cortex to explain the genesis of central fatigue after seeing that fatigue-induced changes in EMG responses to magnetic cortical

stimulation recovered rapidly despite maintained ischemia in the elbow flexor

muscles. In addition, Taylor, et al. (2000) showed that "post-contraction ischemia

failed to prolong the depression of responses to corticospinal stimulation" (p.797)

as were responses to motor cortical stimulation. Considering the result from

Bigland-Ritchie et al. (1986), Taylor et al. (2000) were surprised to find that the

continued firing of the small group III-IV afferents via post-contraction ischemia did

not inhibit the motoneuron pool. Taylor et al. (2000) concluded, "neither the

motoneurons nor motor cortical cells are directly inhibited by the firing of

ischemically sensitive group III and IV afferents" (p.799). Furthermore, Butler et al.

(2003) also found despite maintained discharge of group III-IV muscle afferents via

maintained muscle ischemia, CMEPs recovered within 15-second following a

sustained maximal contraction. These findings suggest that group III-IV afferents do

not directly inhibit alpha-motoneurons of the elbow flexors in human subjects; as

well, the reduction in the CMEP during the sustained maximal voluntary contraction

was not a result of the discharge of these afferents (Butler, et al., 2003). Suboptimal

descending output from the motor cortex and diminished spinal motoneuron output

can be possible explanations, but as Butler et al. (2003) state, studying

motoneuronal excitability can be difficult in human subjects. In contrast, CMEPs

evoked in extensor muscles do not recover when the muscles are kept ischemic

following maximal contractions; however, return to control levels when ischemia is

absent (Martin, et al., 2006). These results suggest that group III-IV afferents inhibit

motoneurons of elbow extensors during fatigue, but not elbow flexors (Butler, et al.,

2003; Martin, et al., 2006; Taylor, et al., 2000). Martin et al. (2006) posit the

development of central fatigue during the fatiguing contractions was a result of a decline in motoneuronal excitability or from "activity-dependent changes in corticospinal axons" (p.4800). Paradoxically, Martin et al. (2008) demonstrated that group III-IV afferents activated by hypertonic saline, facilitated elbow flexors and extensors, which is opposite from the predicted pattern previously found in humans (Martin, et al., 2006). Upon comparison of corticospinal and motor cortical stimulation responses, Martin et al. (2008) report, "motor cortical output cells are inhibited by these afferents" (p.1285).

4.1.2. RENSHAW CELLS AND THEIR POSSIBLE ROLE IN CENTRAL FATIGUE

Motoneurons can also receive inhibitory input via recurrent inhibition from Renshaw cells (Hunter, et al., 2004). The recurrent pathway is activated by motoneuron discharge itself (Katz & Pierrot-Deseilligny, 1999), and also includes projections on gamma motoneurons, Ia-inhibitory interneurons and other Renshaw cells (Katz & Pierrot-Deseilligny, 1999). Kukulka et al. (1986) and Rossi et al. (2003) both suggest a combination of recurrent inhibition and motoneuron adaptations might explain a decline in motoneuron excitability during sustained maximal efforts in humans; however, Taylor and Gandevia (2008) report the role of Renshaw cells in fatigue and how they are regulated is uncertain.

4.1.3. ADDITIONAL MECHANISMS ASSOCAITED WITH CENTRAL FATIGUE

Other possible mechanisms have been suggested to contribute to the development of central fatigue; in particular, during prolonged submaximal

contractions (Behm, 2004). Tergau et al. (2000) argue that reduced intracortical facilitation, decreased motor cortex excitability, and the involvement of gama-aminobutyric acid (GABA), as possible explanations for central fatigue following the performance of a maximal number of pull-ups. Newsholme and Blomstrand (1995) state that during aerobic exercise, increasing levels of tryptophan can increase the synthesis of 5-hydroxytryptamine (5-HT), a neurotransmitter associated with sleep promotion and relaxation. Higher levels of tryptophan may potentially result in fatigue and reduced performance during prolonged exercise by increasing mental effort.

Central fatigue is characterized by a reduction in motor output and displayed as a drop in the discharge rate and number of recruited motoneurons (Gandevia, 2001). The ability to produce and maintain force decreases thus, negatively affecting exercise performance. The mechanisms contributing to the development of central fatigue are not clear, as research findings are conflicting. For example, the involvement of group III-IV muscle afferents in central fatigue development is not clearly understood; as are the mechanisms underlying Renshaw cell inhibition. Furthermore, the exercise intensity and duration can have different effects on the development of central fatigue as potentiating mechanisms can mask the presence of fatigue thereby, maintaining performance. Further research needs to be conducted to solidify the neurophysiological mechanisms behind central fatigue and its development in different situations.

4.2 PERIPHERAL FATIGUE

16

Several peripheral sites along the motor pathway can contribute to the generation of fatigue and include impulse conduction along the motor axons, across the neuromuscular junction, and within the muscle fibers, the excitation-contraction coupling mechanism and the actual contractile process (MacIntosh, et al., 2006).

4.2.1. ENERGY SUPPLY AND METABOLITES: BIOCHEMICAL CHANGES IN MUSCLE FIBERS

During high intense exercise, internal stores of adenosine triphosphate (ATP) and the phosphocreatine pathway are utilized to provide immediate sources of energy required for muscle activation but these sources are limited and relatively short acting (Behm, 2004; Sahlin, et al., 1998). Depending on the intensity and duration of the exercise, metabolic byproducts such as adenosine diphosphate (ADP), inorganic phosphate (Pi), creatine and hydrogen ions (H+) are produced and begin to accumulate (Behm, 2004). If more energy is required, it can be supplied via anaerobic glycolysis; however, at the expense of further H+ production and a measurable decrease of intra- and extra-cellular pH (Ament & Verkerke, 2009). The increasing concentration of ADP, Pi and H+ combined with the increase in muscle acidity may negatively influence the ability and efficiency of the cross bridge interactions and contribute to the impairment of ATP generation and the onset of muscle fatigue (Ament & Verkerke, 2009; Fitss, 1994; Sahlin, et al., 1998).

4.2.2. EXCITATION-CONTRACTION COUPLING FAILURE

During the excitation contraction coupling process, calcium is released from the sarcoplasmic reticulum; however, the concentration released is reduced during fatigue, which has been suggested to reduce force production (Ament & Verkerke, 2009; MacIntosh, et al., 2006). In addition, calcium influx back into the sarcoplasmic reticulum is reduced; therefore, calcium begins to accumulate within the myoplasm, which can increase the relaxation time at the end of a contraction (Ament & Verkerke, 2009; MacIntoch, et al., 2006). Increasing sarcoplasm concentrations of Pi during exercise has been suggested to reduce the calcium efflux from the sarcoplasmic reticulum via the precipitation of calcium phosphate in the lumen of the sarcoplasmic reticulum and the phosphorylation of the calcium release channels on the membrane of the sarcoplasmic reticulum (Allen, et al., 2008; Ament & Verkerke, 2009). The decline of the action potential amplitude across the sarcolemma has also been suggested to impair calcium release by the sarcoplasmic reticulum (Ament & Verkerke, 2009).

The differences in fatigue resistance between type I (slow twitch) and type II (fast twitch) muscle fibers are partly associated with differences in the excitation contraction coupling process (Ament & Verkerke, 2009). Slow twitch muscle fibers have lower ATPase turn over and cross bridge cycle rates than fast twitch fibers; in addition, slow twitch fibers have a higher concentration of enzymes catered to oxidative metabolism, which prolongs the onset of fatigue (Ament & Verkerke, 2009).

The relationship between axonal propagation mechanisms and muscle fatigue is still unclear; for example, it is unknown to what extent increasing

18

concentrations of ADP, Pi and H+ have on ion pump activity on the sarcolemma (Ament & Verkerke, 2009). Juel (1988) found that action potential propagation velocity in isolated muscles (in vitro) was dependent on both internal pH and higher potassium concentrations, with minimal effects from changes in the sodium gradient. In addition, MacIntosh et al. (2006) states that action potential propagation may also be hindered by higher potassium concentrations in the transverse tubules. Furthermore, higher myoplasmic concentrations of magnesium and a concomitant break down of ATP may contribute to the reduction in force output seen with fatigue (Westerblad & Allen, 1992). Research examining the generation of peripheral fatigue at the neuromuscular junction show inconsistent findings (Ament & Verkerke, 2009) however; Bigland-Ritchie et al. (1982) concluded that despite intense maximal voluntary contractions, the propagation of the action potential across the motor end plate remained unaffected.

Peripheral fatigue is generalized as occurring beyond the neuromuscular junction. Normally characterized by disturbances in excitation-contraction coupling and the physiological contractile process, the mechanisms behind peripheral fatigue seem to originate from the production of metabolic byproducts during exercise. However, it is still uncertain how metabolic byproducts impact signal propagation in the muscle fiber. In addition should the metabolite accumulation effects on group III-IV muscle afferent activity be considered peripheral or central mechanisms. Research should continue to examine the physiological response to exercise to further the understanding of peripheral fatigue mechanisms and the subsequent negative impact to performance.

Fatigue is a complex phenomenon with global and localized effects that negatively influence motor-task and exercise performance. In particular, the development of central fatigue and its global effects can be further understood by examining unilateral fatigue. A physiological phenomenon known as cross-education shows a positive relationship between homologous and some heterologous muscles thus, indicating global effects from unilateral training. Examining cross-education and its mechanisms may help develop a better understanding for the global effects of fatigue.

5. CROSS EDUCATION

Unilateral interventions have been shown to result in bilateral effects, such as changes in muscle performance (Davis, 1899), alterations in gene expression, inflammation and tissue remodeling (Koltzenburg, et al., 1999). In particular, the contralateral strength training effect (Carroll, et al., 2006) referred to as cross-education, and also cross-exercise, cross-training or cross-transfer (Zhou, 2003), is a "genuine physiological phenomenon" (Lee & Carroll, 2007, p, 4), upon which strength gain appears in the untrained, contralateral limb, following a unilateral resistance training protocol (Lee & Carroll, 2007). First observed in 1894 by Scripture and colleagues, researchers have since been interested in providing physiological explanations for cross-education.

Contradicting the concept of training specificity, unilateral training "normally induces a strength gain of 5-25% in the contralateral, [untrained,] homologous muscle" (Zhou, 2000, p. 180); however, some research has failed to show a

significant cross-education effect (Housh, et al., 1992; Jones & Rutherford, 1987; Krotkiewski, et al., 1979). Regardless, the existence of cross-education has been repeatedly confirmed in the literature (Carroll, et al., 2006). A meta-analysis performed by Munn et al. (2004) found the strength gain in the untrained limb equal to 7.8% with a 35% increase in strength in the trained side, in young healthy individuals. Furthermore, Carroll et al. (2006) updated the meta-analysis by adding three recent studies (Farthing, et al., 2005; Lagerquist, et al., 2006; Munn, et al., 2005) and concluded an average of 7.6% increase in strength in the untrained limb, with a 52% increase in the trained limb. Also, the improvement in contralateral homologous muscle strength following unilateral training appears to be greatest when the testing method is the same as that used to train the ipsilateral limb (Hortobagyi, et al., 1997; Oakman, et al., 1999).

Cross-education appears to occur in various muscle groups and does not appear to depend on relatively direct or indirect corticospinal projections (Lee & Carroll, 2007), as several studies have shown that cross-education can occur in the upper limb (Cannon & Cafarelli, 1987; Shaver, 1975; Shields, et al., 1999; Yue & Cole, 1992) and lower limb muscles (Bezerra, et al., 2009; Carolan & Cafarelli, 1992; Dragert & Zehr, 2011; Evetovich, et al., 2001; Hellebrandt, et al., 1947; Hortobagyi, et al., 1999; Komi, et al., 1978; Ploutz, et al., 1994; Seger, et al., 1998; Shima, et al., 2002; Uh, et al., 2000). The cross-education effect has been said to only occur between homologous muscles (Lee, et al., 2009; Zhou, 2000); however, Sariyildiz et al. (2011) found an improvement in wrist extensor strength in the contralateral limb following ipsilateral wrist flexor training induced with eccentric electrical

muscle stimulation. Strength gains can appear in the non-dominant contralateral limb (Farthing, et al., 2005) and dominant contralateral limb (Adamson, et al., 2008) but is typically greatest in magnitude following dominant limb training (Farthing, 2009). Furthermore, cross-education appears larger in magnitude if the strength task is novel (Farthing, et al., 2007; Farthing, et al., 2005; Hortobagyi, et al., 1997; Lagerquist, et al., 2006) and is proportional to the gains in the trained muscle (Hellebrandt, et al., 1947; Hortobagyi, 2005). Training effects such as power (Kannus, et al., 1992), rate of force development (Adamson, et al., 2008) and endurance (Shields, et al., 1999) can all be transferred to the contralateral limb. Concentric unilateral strength training does not appear to be joint angle specific (Weir, et al., 1997) whereas, eccentric training appears to only transfer strength to the untrained limb at specific joint angles (Weir, et al., 1995). Additionally, cross-education is possible in the elderly (Bemben & Murphy; 2001; Tracy, et al., 1999) and shows merit in a rehabilitative setting (Arai, et al., 2001; Clark & Patten, 2013; Dragert & Zehr, 2013; Farthing, et al., 2009; Farthing, et al., 2011; Kim, et al., 2011; Kofotolis & Kellis, 2007; Magnus, et al., 2010; Magnus, et al., 2013; Mills & Quintana, 1985; Nagel & Rice, 2001; Nelson, et al., 2012; Papandreou, et al., 2009; Papandreou, et al., 2012; Pearce, et al., 2012; Starbuck & Eston, 2012; Stromberg, 1986; Stromberg, 1988; Toca-Herrera, et al., 2008).

5.1. MECHANISMS OF CROSS EDUCATION

The dominant mechanism underlying cross-education has yet to be pinpointed (Zhou, 2003). After analyzing the literature, it appears that peripheral

muscular adaptations are unlikely to contribute substantially to cross-education (Carroll, et al., 2006; Hendy, et al., 2012; Hortobagyi, et al., 1996; Houston, et al., 1983). Therefore the underlying mechanisms have been suggested to be neural (Zhou, 2003). Moreover, Carroll at al. (2006) states, "if hormonally driven adaptations were a major contributor to the contralateral strength training effect, it would be difficult to explain the observation that the effect is specific to the contralateral, homologous muscle" (p. 1516). However Madarame et al. (2008) found cross-transfer of resistance training effects (e.g. hypertrophy and strength) in low intensity trained elbow flexors when combined with leg resistance exercise that involved thigh occlusion. Although this experiment is not a traditional cross-education experiment in that all muscles involved were trained, the results are novel and interesting. The intensity of the upper arm exercise was low (50% of 1-repetition maximum) and not expected to induce hypertrophy; yet, the trained elbow flexors displayed an increase in cross sectional area and isometric torque production following training (Madarame, et al., 2008). The researchers attributed these global effects to systemic hormone production, particularly increases in noradrenaline concentration (Madarame, et al., 2008).

5.1.1. IS CROSS EDUCATION ASSOCIATED WITH MUSCULAR ADAPTATIONS SUCH AS IMPROVEMENTS IN CROSS SECTIONAL AREA?

A number of studies have assessed the occurrence of hypertrophy in untrained knee extensors but have failed to demonstrate significant effects (Hortobagyi, et al., 1996; Houston, et al., 1983; Krotkiewski, et al., 1979; Narici, et al.,

1989; Ploutz, et al., 1994; Wilkinson, et al., 2006). In addition, Housh et al. (1992) found an increase in elbow flexor cross sectional area in the untrained limb following 8-weeks of concentric isokinetic training; however, these results were not statistically significant. In addition, Brown et al. (1990) also failed to show an increase in maximal cross sectional area of the untrained elbow flexors, but found a significant increase in type II fiber area (~10%), accompanied by an increase of the 1-repetition maximum of ~13% in the untrained arm following 12 weeks of unilateral training. Lastly, instead of measuring cross sectional area, Shima et al. (2002) evaluated tetanic and twitch contractions of the plantar flexors, since hypertrophy of a muscle should result in an increase in the force of electrically evoked contractions; however, also failed to show any significant improvements in muscle cross sectional area.

Several studies have measured EMG activity of the contralateral unexercised limb during ipsilateral homologous muscle contractions and found nil to almost 24% EMG activity (Devine, et al., 1981; Farthing & Chilibeck, 2003; Hortobagyi, et al., 1999; Hortobagyi, 2005; Panin, et al., 1961). However, in order to induce hypertrophic adaptations, a muscle must contract greater than 60% of its maximal force producing capabilities (Hortobagyi, 2005). These low activation intensities combined with the fact that there is no measurable increase in muscle cross sectional area in the untrained arm, cannot explain the improvements in strength seen in the contralateral limb; therefore, neural mechanisms must be predominantly involved (Hortobagyi, 2005). In addition, Panin et al. (1961) found significant EMG recordings from muscles stabilizing the body during unilateral contractions.

24

Perhaps the recruitment of these stabilizing muscles during ipsilateral muscle contractions can contribute to cross-education by creating body stability during contralateral limb contractions.

5.1.2. IS CROSS EDUCATION ASSOCIATED WITH AN INCREASED BLOOD FLOW TO THE UNTRAINED LIMB?

Increased blood flow has been suggested as a potential mechanism related to cross-education (Yasuda & Miyamura, 1983; Yuza, et al., 2000). For example, unilateral rhythmic handgrip training for 6-weeks induced a systemic blood flow adaptation, which was thought to be the primary cause of improved handgrip endurance in the untrained limb (Yasuda & Miyamura, 1983). On the contrary, Shields et al. (1999) states the cross-transfer of endurance may have occurred via bilateral skill transfer instead of being related to the increase in peak blood flow. Moreover, Lee and Carroll, (2007) report that vascular changes during unilateral training are unlikely to directly improve contralateral limb strength and state that the crossover mechanism is more likely to involve the nervous system.

5.2. NEURAL ADAPTATIONS AND THEIR SUGGESTED ROLE IN CROSS EDUCATION

According to Lee & Carroll, (2007) improvements in strength "in the absence of direct training and without concomitant adaptive changes in muscle morphology strongly suggest alterations in neural control" (p. 4). Articles from Zhou (Zhou, 2000; 2003) propose potential neural mechanisms for cross-education: 1) coactivation via bilateral corticospinal pathways (Carr, et al., 1994); 2) diffusion of

impulses between cerebral hemispheres (Cernacek, 1961; Kristeva, et al., 1991; Yue

& Cole, 1992); 3) postural stabilization or learning in coordination (Carolan &

Cafarelli, 1992; Devine, 1981); and 4) afferent modulation (Hortobagyi, et al., 1999).

More recently, Farthing (2009) describes a three level theoretical model of cross-

education of strength transfer in the upper limbs, which is similar to the bilateral

transfer of skills in that it incorporates ideas from the proficiency model and the

cross-activation model (Parlow & Kinsbourne, 1989). Farthing (2009) describes

that the cross-activation model "states that motor programs for a skill or task are

stored in both hemispheres with unilateral acquisition," (p. 183) and that the

proficiency model suggests that task acquisition with the dominant limb, "provides a

better stored motor program for the opposite limb" (p. 183).

5.2.1. INPUT TO THE PRIMARY MOTOR CORTEX

Following unilateral training, changes in higher order inputs to the primary

motor cortex (e.g. visual cortex, parietal cortex, prefrontal cortex, premotor cortex,

supplementary motor area and temporal lobe) occur bilaterally and can modulate

ipsilateral primary motor cortex excitability; therefore, serving as a potential

mechanism in cross-education (Carroll, et al., 2006; Farthing, 2009).

5.2.2. COACTIVATION VIA BILATERAL CORTICOSPINAL PATHWAYS

Approximately 10% of the corticospinal fibers enter the lateral and anterior

corticospinal tract of the ipsilateral side, innervating the upper arm and trunk

muscles but not the muscles of the lower extremities, while the remaining

corticospinal fibers decussate to the contralateral side (Brinkman & Kuypers, 1973; Nyberg-Hansen & Rinvik, 1963). It is hypothesized unilateral muscle contractions can alter the excitability and contribute to motor irradiation of the nondecussated descending pathways (Hellebrandt, 1951; Hendy et al., 2012); thus, potentially contributing to training effects in the untrained muscle (Hortobagyi, 2005). This hypothesis implies involvement of the ipsilateral primary motor cortex; however, Hortobagyi, (2005) states that this is "not tenable for neuroanatomical reasons" (p. 24). Carr et al. (1994) used evoked-EMG to show that common drive to homologous muscles is observed in axial and trunk muscle pairs that are normally coactivated (e.g. left and right diaphragm, rectus abdominus and masseter), but not in muscle pairs that typically act independently (e.g. first dorsal interosseous, forearm extensor muscles, biceps and deltoids). Moreover, the average magnitude of the cross-education effect is on average ~60% of the strength gain in the ipsilateral trained limb, which is not proportional to ~10% of uncrossed descending fibers (Zhou, 2000). "For these uncrossed fibers to have such an effect, they would need to have a unique influence on the ipsilateral motor units either directly or via interneurons in the spinal cord," states Zhou (2000, p. 182).

5.2.3. DIFFUSION OF IMPULSES BETWEEN CEREBRAL HEMISPHERES

Interhemispheric connections exist between most cortical motor areas via the corpus callosum (Carson, 2005) and it has been suggested that the neuroanatomical mechanism explaining cross-education is more related to these connections, rather than to the nondecussated descending motor pathways (Carroll,

et al., 2006; Hortobagyi, 2005). Unilateral motor activity has been proposed to activate homotopic excitatory paths interconnecting the ipsilateral and contralateral primary motor cortex, referred to as motor irradiation, (Cernacek, 1961), the Bilateral Activation Theory (Addamo, et al., 2007) or neural spill-over (Carroll, et al., 2006); thus, producing cortical adaptations bilaterally (Hortobagyi, 2005; Lee & Carroll, 2007). The cortical adaptations are suggested to enhance neural processing and increase neural drive to both the trained and untrained limb (Farthing, 2009). Hellebrandt et al. (1947) states that the cross-education label is a misnomer as the contralateral untrained limb is not actually unexercised since it plays a reflexive role during unilateral training. Nonetheless, support for the enhanced neural processing hypothesis comes from research using imaging techniques (Cramer, et al., 1999; Foltys, et al., 2003; Kawashima, et al., 1993) and neural-magnetic fields, (Kristeva, et al., 1991) which indicate motor centers in both cerebral hemispheres are active during unilateral muscle contraction. Moreover, TMS studies show that ipsilateral motor cortex excitability is suppressed by weak unilateral contractions (Leocani, et al., 2000; Liepert, et al., 2001; Sohn, et al., 2003) and facilitated by higher force and rhythmic contractions (Carson, et al., 2004; Hess, et al., 1986; Hortobagyi, et al., 2003; Lee, et al., 2009; Stedman, et al., 1998). Therefore, it can be extrapolated that cross-education will not occur with weak unilateral contractions and is more likely to occur with higher-level unilateral muscle activation. In the event the corpus callosum has a lesion, these facilitating effects would expect to be absent or altered; however, Meyer et al. (1995) showed unattenuated MEP facilitation in patients with callosal agenesis, suggesting that the interhemisphere effects are not solely

mediated via the corpus callosum. Subcortical networks with connections to both primary motor cortical areas may be responsible in the co-activation of the ipsilateral hemisphere during strong muscular contractions by an ipsilateral muscle (Foltys, et al. 2003; Muellbacher, et al., 2000).

The diffusion of central drive between the hemispheres will also influence intracortical inhibitory and excitatory interneurons via transcallosal fibers (Hortobagyi, 2005). Output from the primary motor cortex during unilateral limb contractions has been shown to increase with reduced interhemispheric inhibition (Farthing, 2009; Hortobagyi, et al., 2011; Latelle, et al., 2012; Muellbacher, et al., 2000); thus, providing another possible cross-education mechanism. Coactivation of the contralateral muscles during unilateral contractions may produce a training effect and learned inhibition of the antagonists; thus, contributing to increased force production in the untrained limb (Zhou, 2003). Goodwill et al. (2012) observed that following 3-weeks of unilateral strength training of the lower limb, there was an increase in bilateral homologous muscle strength, which was accompanied by a decrease in short-latency intracortical inhibition and an increase in corticomotor excitability in the ipsilateral motor cortex. Furthermore, Carolan and Cafarelli, (1992) found following an 8-week isometric, unilateral, maximal voluntary contraction training, that strength improved in both ipsilateral and contralateral knee extensors, which was combined with a decrease in knee flexor coactivation bilaterally.

5.2.4. CAN IMAGINED UNILATERAL CONTRACTIONS LEAD TO CROSS EDUCATION?

Yue and Cole (1992) used imagined maximal voluntary contractions of a small hand muscle to induce ~10% strength gain in the contralateral limb. No changes were seen in twitch force, which suggests a cortical mechanism was responsible for cross-education, possibly associated with motor programming and execution (Yue & Cole, 1992). In contrast, chronic strength training with imagined contractions of the elbow flexors did not result in strength gain in trained muscles (Herbert, et al., 1998). Hortobagyi (2005) suggests since the elbow flexors have a larger cortical involvement compared to the small hand muscle studied by Yue and Cole (1992), imagined contractions were too weak of a training stimulus to modify the cortical area involved in elbow flexion. Furthermore, Farthing et al., (2007) also failed to show strength gain in either trained and untrained forearm muscles following imaginary strength training; however, was able to show strength gain in the untrained contralateral homologous muscle following ipsilateral training. Interestingly, Farthing et al. (2007) used neural imaging techniques to examine the neural mechanisms associated with the cross-education of strength and following unilateral training, found an enlarged region of activation in the contralateral sensorimotor cortex and left temporal lobe during contraction of the left arm muscles, which suggests that adaptations within the sensorimotor cortex and temporal lobe may play important roles in cross-education. This novel discovery of left temporal lobe activation during left-arm contractions, suggests memory retrieval of the strength task previously created from contralateral right limb training and a possible important role in motor planning, execution and cross-education (Farthing, et al., 2007).

5.2.5. IS THERE AN INCREASE IN EMG ACTIVITY IN THE CONTRALATERAL LIMB

DURING IPSILATERAL CONTRACTIONS AND CAN THIS BE A MECHANISM OF CROSS

EDUCATION?

To further investigate changes in motor unit activity of the contralateral limb

and enhanced neural drive following unilateral strength training, researchers have

measured EMG activity in the contralateral limb during maximal contractions post-

training (Cannon & Cafarelli, 1987; Moritani & DeVries, 1979). Moritani and Devries

(1979) found strength gain in the contralateral limb with a concomitant increase in

integrated EMG; however, Cannon and Cafarellli (1987) failed to show changes in

EMG with strength gain in the contralateral limb and concluded neural drive was

not enhanced with unilateral strength training. Nevertheless, Cannon and Cafarelli,

(1987) state that other potential neural mechanisms must have taken place that

resulted in the cross-transfer of strength. Similarly, Carroll et al. (2008) failed to

show that the spillover hypothesis contributes to the cross-transfer of a ballistic

motor skill because comparable increases in corticospinal excitability were also

found for a muscle not even directly involved in the experimental task. Therefore,

the researchers concluded that the performance improvements in the untrained

limb were not correlated with the bilateral increases in corticospinal excitability

(Carroll, et al., 2008). However, TMS response amplitudes following training

increased bilaterally following training, suggesting that unilateral ballistic practice

can result in lasting effects on ipsilateral cortical excitability (Carroll, et al., 2008).

5.3. SUBCORTICAL MECHANISMS

Regarding subcortical mechanisms, Hortobagyi (2005) states that commissural interneurons present in the spinal cord and brain stem may be involved in the transmedian signaling hypothesis involved with cross-education; however, Carroll et al. (2006) report "little is known about the potential for cross-limb neural interaction at subcortical centers involved in movement control, such as the basal ganglia, cerebellum and brain stem nuclei that give rise to nonpyramidal descending tracts" (p. 1519).

5.3.1. SPINAL PATHWAYS

Strong support exists for spinal mechanisms involved in the cross-transfer of strength, as cross-education appears to be greater with electrical muscle stimulation compared to voluntary muscle contractions (Hortobagyi, et al., 1999); however, the exact role of spinal mechanisms involved with the cross-education of strength remains unclear (Farthing, 2009).

5.3.2. AFFERENT MODULATION

Skin and muscle afferents may be activated in the stimulated muscle and have possible excitatory effects on the untrained contralateral homologous muscle (Farthing & Chilibeck, 2003). Research using electrical muscle stimulation has been successful in creating cross-education in the contralateral untrained limb, (Cabric & Appell, 1989; Hortobagyi, et al., 1999; Oakman, et al., 1999; Sariyildiz, et al., 2011; Tachino, et al., 1989; Toca-Herrera, et al., 2008; Zhou, et al., 2002) which suggests

spinal mechanisms are involved. Oakman et al. (1999) and Zhou (2002) found that electrical muscle stimulation and voluntary isometric contraction training had similar effects in strength improvement in the untrained limb whereas Hortobagyi et al. (1999) observed greater cross-education (104% increase in eccentric strength) with electrical muscle stimulation training compared to voluntary training (30% increase in strength). Horotbagyi et al. (1999) suggests Group II muscle afferent involvement with possible changes in the cross-extension reflex (Sherrington, 1910). Toca-Herrera et al. (2008) was able to induce cross-education in the contralateral rectus femoris following only 10-minutes of surface electrical stimulation. The researchers also suggested involvement of the cross-extension reflex and changes in reflex impulses at the medullar level (Toca-Herrera, et al., 2008). Furthermore, in a double-blind control study, Sariyildiz et al. (2011) used electrical stimulation with passive muscle lengthening in the ipsilateral wrist flexors to induce cross-transfer of strength in the contralateral wrist flexors and extensors.

In contrast, Lagerquist et al. (2006) and Fimland et al. (2009) both failed to show changes in H-reflex amplitude in the untrained limb, despite observing bilateral strength gain following unilateral strength training. Furthermore Hortobagyi et al. (2003) found strong left wrist contractions increased MEPs in the right homologous muscle, along with no effect on CMEPs and depression of H-reflex gain. Autogenic stretch reflex circuitry might not play a direct role in cross-education, but alterations in other spinal circuitry involved in reciprocal inhibition (Delwaide, et al., 1988), presynaptic inhibition (Hortobagyi, et al., 2003; Muellbacher, et al., 2000; Delwaide, et al., 1988) or contralateral motoneuron

33

excitability (Carroll, et al., 2006; Farthing & Chilibeck, 2003; Hortobagyi, et al., 2003; Robinson, et al., 1979) are suggested to alter the recruitment of the untrained contralateral homologous limb muscles and contribute to cross-education. Additionally, spinal interneurons that are involved in motor overflow (Post, et al., 2008) and propriospinal paths, may also be involved in cross-education by exerting crossed spinal effects following unilateral training (Hortobagyi, 2005). There are no direct connections between motoneurons on either side of the spine or from group I-IV afferents (Jankowska, 2001; Sherrington, 1906); therefore, strongly suggesting the involvement of spinal interneurons in cross-education (Hortobagyi, 2005).

5.3.3. ECCENTRIC CONTRACTIONS AND CROSS EDUCATION

High intensity unilateral eccentric strength training has shown to result in greater cross-education strength effects to the untrained limb compared to maximal voluntary concentric strength training (Horotbagyi, et al., 1997). Eccentric strength training has also been shown to be joint angle specific (Weir, et al., 1995), and only effective with fast contraction velocities (180°/second compared to 30°/second) (Farthing & Chilibeck, 2003). Cross-education following eccentric strength training most likely involves both afferent and efferent mechanisms, muscle spinal afferent activity and possible modifications to cross-spinal or propriospinal paths (Hortobagyi, et al., 1997; Hortobagyi, 2005).

Cross-education was first described in the literature in 1894 (Scripture, et al., 1894) and dominant neurophysiological mechanisms explaining this phenomenon has still yet to be discovered. Resulting in an average of 7.6% increase of strength in

the untrained limb (Carroll, et al., 2006), unilateral training can be an important aspect of rehabilitation, for example, following stroke (Dragert & Zehr, 2013) or trauma involving immobilization (Farthing, et al., 2009). Evidence appears to support central rather than peripheral mechanisms for cross-education and include neural adaptations that originate at cortical and spinal levels. In addition, global endocrine (Madarame, et al., 2008) effects may also be involved in cross-education and cross-body adaptations. Similarly, negative global effects via neural or endocrine mechanisms following unilateral exercise may be involved in the crossover effect of fatigue thus, reducing performance.

6. CROSSOVER FATIGUE

The existence of cross-education (Carroll, et al., 2006), motor irradiation (Cernacek, 1961) and the suggested existence of command neurons (Rosenbaum, 1977) have prompted researchers to explore the global effects of fatigue (Gandevia, 2001) between homologous and heterologous muscle groups. Examining the impact of unilateral exercise-induced fatigue on uninvolved muscle groups, referred to as crossover fatigue, can further develop the understanding of central fatigue and its influence and role in performance.

Research exploring crossover fatigue appears to be equivocal as results are conflicting, despite subjects being brought to temporary exhaustion or task failure following a unilateral fatigue protocol. Studies have failed to show significant crossover fatigue effects between homologous (Elmer, et al., 2013; Grabiner & Owings, 1999; Regueme, et al., 2007; Todd, et al., 2003; Zijdewind, et al., 1998) and

heterologous muscles (Decorte, et al., 2012; Humphry, et al., 2004; Millet, et al., 2003; Place, et al., 2004; Ross, et al., 2007; Ross, et al., 2010). In contrast, significant crossover fatigue effects have been found in contralateral homologous (Amann, et al., 2013; Doix, et al., 2013; Martin & Rattey, 2007; Rattey, et al., 2006; Triscott, et al., 2008) and heterologous muscle groups (Kennedy, et al., 2013; Takahashi, et al., 2011). Moreover, contralateral postural control during single leg stance has also been negatively affected following ipsilateral lower limb fatigue (McLean & Samorezov, 2009; Paillard, et al., 2010).

  The discrepancy in results may be related to the inconsistency of unilateral fatiguing protocols as several variables differ such as exercise intensities, volumes and types of contraction. Fatiguing protocols have utilized many forms of contractions such as isometric, isotonic and isokinetic with varying contraction intensities to examine crossover fatigue. Isometric fatiguing protocols have been shown to induce (Doix, et al., 2013; Kennedy, et al., 2013; Martin & Rattey, 2007; Paillard, et al., 2010; Rattey, et al., 2006) as well as not induce (Todd, et al., 2003; Zijdewind, et al., 1998) crossover fatigue. For example, a 100 second knee extensor isometric MVC fatigue protocol reduced voluntary activation of the contralateral non-fatigued knee extensors but did not alter MVC force (Rattey, et al., 2006). Conversely, the same fatiguing protocol resulted in a reduction in MVC force output from the contralateral non-fatigued homologous muscles, which was accompanied with larger reductions in voluntary activation (Martin & Rattey, 2007). A different isometric knee extension fatiguing protocol, which was also repeated with tetanic stimulations, was found to disturb postural control during contralateral leg stance

but did not affect MVC (Paillard, et al., 2010). Maximal and submaximal bilateral isometric handgrip exercise held until force was reduced to 80% of pre-fatigue values both resulted in a decrease in ankle plantar flexion MVC and voluntary activation (Kennedy, et al., 2013). Interestingly, the maximal fatiguing protocol was more impactful on reducing ankle plantar flexor MVC and voluntary activation compared to the submaximal fatiguing protocol, indicating that central fatigue to an uninvolved lower limb muscle is intensity-specific (Kennedy, et al., 2013).

Similarly, dynamic contractions show varying crossover fatigue effects as well. Isokinetic knee flexion/extension contractions had no effect on the contralateral hamstrings but actually enhanced contralateral quadriceps MVC force (Strang, et al., 2009). Dynamic free weight lower body exercise induced crossover fatigue in female athletes (McLean & Samorezov, 2009). Furthermore, three 5-minute sets of bilateral leg presses performed with 50% of a dynamic MVC was found to depress motor evoked potentials (MEPs) and short interval intracortical inhibition in non-exercised upper limb muscles (Takahashi, et al., 2011).

Comparing exercise volumes during unilateral fatiguing protocols has not been studied extensively in the literature. However, it appears that the fatiguing protocol volume is an important factor in the development of crossover fatigue (Doix, et al., 2013; Humphy, et al., 2004). Performing only one 100-seconds MVC with the knee extensors was insufficient volume to produce crossover fatigue to the contralateral limb while two bouts of 100-seconds MVC was successful (Doix, et al., 2013). Additionally, unilateral biceps curls performed with 3.5 kg at a frequency of 1 Hz performed to exhaustion resulted in crossover fatigue effects to the contralateral

homologous muscles but failed to do so when only 25% of the volume was performed (Humphry, et al., 2004).

From the limited research, it appears that fatiguing protocols of higher intensity and larger volumes have greater crossover fatigue effects compared to lower intensity and lower volume protocols. Contraction types may also influence the extent of crossover fatigue. More research is necessary to directly compare the effects of varying volume and intensity of a fatiguing resistance protocol on the existence of crossover fatigue.

6.1. SUGGESTED CROSSOVER FATIGUE MECHANISMS

Peripheral muscle fatigue in the contralateral limb can be examined by recording muscle twitch properties (Martin & Rattey, 2007; Rattey, et al., 2006). For example, following a unilateral fatigue protocol, Rattey et al. (2006) found maximal twitch tension remained unchanged in the non-exercise leg, indicating peripheral fatigue did not develop. Additionally, no significant changes were seen in the half-relaxation time or time to peak tension following the fatigue protocol (Rattey, et al., 2006). Lastly, the unchanged M-waves also indicate the contralateral limb was not impacted from an influx of metabolites produced by the ipsilateral fatigued muscle (Rattey, et al., 2006). Rattey et al. (2006) concluded that centrally mediated mechanisms were responsible for the crossover fatigue seen in the contralateral limb, which they suggested was an anticipatory fatigue response to minimize disturbance to cellular homeostasis. Similarly, Martin and Rattey (2007) found that direct electrical stimulation of the contralateral knee extensors revealed no

peripheral muscle fatigue. These results suggest a crossover of central fatigue from a fatigued ipsilateral limb to the rested contralateral homologous muscle group (Martin & Rattey, 2007).

TMS studies have shown MEP amplitude depression in the contralateral muscle (Bonato, et al., 1996; Hess, et al., 1986; Humphry, et al., 2004; Post, et al., 2008; Takahashi, et al., 2009; Triscott, et al., 2008) along with suppression of ipsilateral homologous muscle intracortical facilitation (Baumer, et al., 2002) following unilateral exercise. Furthermore, Takahashi et al. (2009) found that unilateral exhaustive grip exercise decreased corticospinal output excitability of the ipsilateral motor cortex while simultaneously reducing the excitability of short-interval cortical inhibition. Consequently, Takahashi et al. (2009) concluded "the idea that fatigue increases the tonic level of interhemispheric inhibition from the fatigued to the non-fatigued cortex" (p. 198). Muscle fatigue generated in the large lower limb muscle groups has also been shown to reduce corticospinal excitability and short-interval cortical inhibition to heterologous non-exercised upper limb muscles (Takahashi, et al., 2011). Since there are no obvious direct connections in the primary cortex between the motor outputs to the upper and lower limbs, the researchers suggested the interactions must have occurred outside of the primary cortex that led to the changes in MEP amplitude and short-interval cortical inhibition (Takahashi, et al., 2011). Moreover, perhaps the exhausted lower limb muscles resulted in cerebral deoxygenation; thus, influencing motor output to the non-exercised upper limbs (Takahashi, et al., 2011). Similarly, Kennedy et al. (2013) showed upper limb fatigue created in the forearm muscles generated crossover

fatigue and reduced lower limb performance. No peripheral fatigue was discovered in the plantar-flexor muscles as twitch torque and M-wave amplitudes did not change following upper limb fatigue (Kennedy, et al., 2013). After observing a decrease in voluntary activation and maximal voluntary contraction in the plantar-flexors following the upper limb fatigue protocol, the researchers suggested central mechanisms as the primary mechanism (Kennedy, et al., 2013).

Despite showing contralateral homologous muscle MEP depression, Humphry et al. (2004) found no measurable significant functional decrement in the non-exercised muscle. The authors concluded that the reduction in corticospinal excitability had little or no significant impact on the performance parameters measured (Humphry, et al., 2004). In contrast, Samii et al. (1997) failed to show depression or facilitation of MEPs following contralateral homologous exercise. The researchers suggest that the absence of MEP depression may have resulted from a lack of force generation or from co-activation, potentially leading to post-exercise facilitation; thus, masking post-exercise depression in that muscle (Samii, et al., 1997). Strang et al. (2009) also failed to show cross-over fatigue in non-exercised limb and postural muscles following fatiguing unilateral isokinetic knee-extension and flexion contractions but found earlier anticipatory postural adjustment (APA) onset in non-fatigued muscles. This suggests modulation of central motor commands rather than local mechanisms. Therefore, crossover fatigue following a unilateral fatiguing protocol can present with global effects, such as early APA onset in non-fatigued muscles with the absence of performance decrements in postural and contralateral non-fatigued muscles (Strang, et al., 2009).

Spinal mechanisms have also been suggested to play a role in crossover fatigue (Paillard, et al., 2010). Paillard et al. (2010) found that fatigue of the ipsilateral quadriceps femoris created with electrical stimulation resulted in crossover fatigue, measured by assessing contralateral leg postural control during single leg stance. Despite failing to show a decrease in maximal voluntary contraction in the contralateral leg following the fatiguing protocol, a reduction in postural control was still observed (Paillard, et al., 2010). With regards to the electrical stimulation resulting in contralateral fatigue, Paillard et al. (2010) suggest activity of group III and IV muscle afferents might alter the gain of the intraspinal neural circuitry; thus, affecting contralateral limb motoneurons via the crossed reflex pathway. Moreover, Amann et al. (2013) found muscle afferent activity resulting from unilateral lower limb fatigue resulted in an inhibitory effect on the output of the spinal motorneurons affecting the contralateral leg.

The existence of crossover fatigue is ambiguous as conflicting results are found within the literature. However, each study used different fatiguing protocols and different methods thus, possibly contributing to the inconsistent findings. Nonetheless, research has yet to examine the effect of unilateral dynamic exercise of different intensities on contralateral homologous muscle performance. It is suggested that central mechanisms contribute to crossover fatigue; therefore, it would be interesting to examine if crossover fatigue is volume and/or load sensitive following unilateral dynamic exercise.

7. CONCLUSIONS

Fatigue is a multifaceted phenomenon normally characterized as having central and peripheral origins. Stressful unilateral exercise has been shown to induce immediate local and global fatigue effects; however, results in the literature are conflicting. Unilateral training has also been shown to lead to positive strength adaptations in both the ipsilateral and contralateral (untrained) limbs. Motor irradiation, bilateral cortical adaptations and afferent modulation are suggested mechanisms underlying cross-education, which also indicate the interconnectedness between the two sides of the body. Nonetheless, conflicts with crossover fatigue research may be related to the fatiguing protocols, in that the load or volume may have been insufficient. Gaps in the literature need to be filled to give a better understanding of the physiology behind the global effects of fatigue. First, the influence of unilateral dynamic isotonic contractions on contralateral limb performance has not been examined. Secondly, the difference between volume and contraction intensity on the appearance of crossover fatigue need to be investigated.

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Effect Of Load With Dynamic Contractions On Contralateral Homologous Muscle

Performance

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ABSTRACT

The purpose of this study was to investigate different intensities of unilateral dynamic quadriceps contractions on non-exercised, contralateral quadriceps muscle performance. In a randomized crossover study design, maximal voluntary contraction force, force developed in the first 100 ms (F100) and electromyography of the non-exercised contralateral knee extensors were measured before and after fatiguing protocols performed by ipsilateral knee extensors. The fatigue protocols consisted of four sets of dynamic knee extensions each to task failure with 40% and 70% MVC on separate days. Endurance performance of the non-exercised knee extensors was also measured post-intervention. Evidence of crossover fatigue of the non-exercised contralateral leg extensors following ipsilateral dynamic contractions was found. Both the 40% ($p = 0.01$, ES = 0.29) and 70% ($p = 0.009$, ES = 0.53) conditions exhibited 4.4% and 7.1% decreases in force from pre- to post-intervention, respectively. In addition, both the 40% ($p = 0.009$, ES = 0.72) and 70% ($p = 0.001$, ES = 2.03) conditions exhibited 23.68% and 34.58% decreases in F100 respectively. The 40% ($p = 0.092$, ES = 0.65) and 70% ($p = 0.078$, ES = 0.79) protocols had a tendency to induce greater contralateral force variation during the initial 10-seconds of the submaximal isometric contraction compared with the control condition. In conclusion, this study highlighted that unilateral lower limb fatigue induced by low intensity, as well as high intensity, dynamic knee extensions leads to crossover fatigue of the contralateral non-exercised limb.

Keywords: central fatigue, peripheral fatigue, maximal voluntary contraction, dynamic contractions, electromyography

INTRODUCTION

Fatigue is a complex, multifactorial phenomenon (Enoka & Stuart, 1992; St. Clair Gibson, et al., 2003) and has been defined as a decrease in force and power production (Gandevia, 2001). Fatigue mechanisms have been classified as being central or peripheral in origin (Gandevia, 2001). Central fatigue is associated with reductions in neural output either from spinal or supraspinal levels that can include decreases in the number of recruited motor units and/or their firing rates (Gandevia, 2001; Gruet, et al., 2012). In contrast, peripheral fatigue is associated with physiological changes at or distal to the neuromuscular junction (Gandevia, 2001). Fatigue induced at a specific muscle can contribute to the development of central fatigue and result in a non-local response (Martin & Rattey, 2007; Rattey, et al., 2006). Non-local responses are evident with crossover fatigue, which in some studies presents as fatigue of a non-exercised muscle following fatiguing contractions of a disparate muscle.

Research exploring crossover fatigue appears to be equivocal. Several studies have not shown significant crossover fatigue effects between homologous (Grabiner & Owings 1999; Regueme, et al., 2007; Todd, et al., 2003; Zijdewind, et al., 1998) and heterologous muscles (Decorte, et al., 2012; Humphry, et al., 2004; Millet, et al., 2003; Place, et al., 2004; Ross, et al., 2007; Ross, et al., 2010). In addition, following exhaustive single leg cycling, Elmer et al. (2013) did not find a reduction in contralateral leg cycling performance. In contrast, significant crossover fatigue effects have been found in contralateral homologous (Doix, et al., 2013; Martin & Rattey 2007; Rattey, et al., 2006; Triscott, et al., 2008) and heterologous muscle

groups (Kennedy, et al., 2013; Takahashi, et al., 2011) following isolated muscular fatigue. Moreover, McLean and Samorezov (2009) found a reduction in single leg landing strategies following fatiguing single leg squats performed on the contralateral limb. Similarly, Paillard et al. (2010) found crossover fatigue affecting postural control during single leg stance in the contralateral limb following ipsilateral quadriceps femoris fatigue generated either by neuromuscular electrical stimulation or by isometric voluntary muscular contractions. Recent research by Amann and colleagues (2013) found that constant load single leg knee-extensor exercise performed to exhaustion resulted in a reduction of endurance time to exhaustion in the consecutively exercised, non-fatigued contralateral leg by ~49%; however, no significant changes were seen in potentiated twitch, MVC force and voluntary muscle activation. Evidently, there is a conflict in the literature regarding the crossover fatigue phenomenon despite studies claiming that subjects were brought to temporary exhaustion. The discrepancy in results may be related to the inconsistency of unilateral fatiguing protocols as several variables differ such as exercise intensities, volumes and types of contraction.

Fatiguing protocols have utilized several contraction types such as isometric, isotonic (dynamic) and isokinetic and varying contraction intensities to examine crossover fatigue. Isometric fatiguing protocols have been shown to induce (Doix, et al., 2013; Kennedy, et al., 2013; Martin & Rattey 2007; Paillard, et al., 2010; Rattey, et al., 2006) as well as not induce (Todd, et al., 2003; Zijdewind, et al., 1998) crossover fatigue. For example, a 100 s knee extensor isometric MVC fatigue protocol reduced voluntary activation of the contralateral non-fatigued knee

82

extensors but did not alter MVC force (Rattey, et al., 2006). Contrarily, Martin and Rattey (2007) used the same fatiguing protocol and found a reduction in MVC force output from the contralateral non-fatigued homologous muscles, which was accompanied with larger reductions in voluntary activation. A different isometric knee extension fatiguing protocol, which was also repeated with tetanic stimulations, was found to disturb postural control during contralateral leg stance but did not affect MVC (Paillard, et al., 2010). Maximal and submaximal bilateral isometric handgrip exercise held until force was reduced to 80% of pre-fatigue values resulted in a decrease in ankle plantar flexion MVC and voluntary activation (Kennedy, et al., 2013). Interestingly, the maximal fatiguing protocol was more impactful on reducing ankle plantar flexor MVC and voluntary activation compared to the submaximal fatiguing protocol indicating that central fatigue to an uninvolved lower limb muscle is intensity-specific (Kennedy, et al., 2013).

Similarly, fatigue protocols using dynamic contractions also have varying crossover fatigue effects. Isokinetic knee flexion/extension contractions had no effect on the contralateral hamstrings but actually enhanced contralateral quadriceps MVC force (Strang, et al., 2009). Dynamic free weight lower body exercise induced crossover fatigue in female athletes (McLean & Samorezov, 2009). Furthermore, three 5-minute sets of bilateral leg presses performed with 50% of a dynamic MVC was found to depress motor evoked potentials (MEPs) and short interval intracortical inhibition in non-exercised upper limb muscles (Takahashi, et al., 2011).

Comparing exercise volumes during unilateral fatiguing protocols has not been studied extensively in the literature. However, it appears that the fatiguing protocol volume is an important factor in the development of crossover fatigue (Doix, et al., 2013; Humphry, et al., 2004). Performing only one 100-seconds MVC with the knee extensors was insufficient volume to produce crossover fatigue to the contralateral limb while two bouts of 100-seconds MVC was successful (Doix, et al., 2013). Additionally, unilateral biceps curls performed with 3.5 kg at a frequency of 1 Hz performed to exhaustion resulted in crossover fatigue effects to the contralateral homologous muscles but failed to do so when only 25% of the volume was performed (Humphry, et al., 2004).

From the limited research, it appears that fatiguing protocols of higher intensity and larger volumes have greater crossover fatigue effects compared to lower intensity and lower volume protocols. Contraction types may also influence the extent of crossover fatigue. More research is necessary to directly compare the effects of varying volume and intensity of a fatiguing resistance protocol on the existence of crossover fatigue.

1. PURPOSE OF STUDY

The purpose of this study was to investigate different intensities of unilateral dynamic quadriceps contractions on non-exercised, contralateral quadriceps muscle performance.

2. RESEARCH HYPOTHESIS

Based on the related literature it was hypothesized that a higher intensity of unilateral dynamic exercise will lead to greater crossover fatigue effects, demonstrated by detriments in muscle strength and endurance performance.

METHODOLOGY

1. SUBJECTS

Twelve (12) recreationally trained (at least 2 training sessions a week for the past 6 months) male (height 177.70 $\pm$ 5.38 cm, weight 84.54 $\pm$ 7.57 kg, age 30 $\pm$ 8.50 yrs.) participants were recruited for this study. Eleven of the participants were determined to be right-leg dominant, while one participant was left-leg dominant (Oldfield, 1971). Prior to testing and after a brief explanation of the procedures of the experiment, each participant completed the Physical Activity Readiness Questionnaire-Plus (Canadian Society for Exercise Physiology, 2011) and read and signed a letter of informed consent. Volunteers who reported neurological complications, surgery or injury to knee structures or cardiovascular conditions such as high blood pressure were not allowed to participate in the experiment. To eliminate confounding variables, participants were instructed not to engage in strenuous physical activity and to abstain from alcohol consumption, caffeine or nicotine for the 24-hour period prior to participation. Testing was performed at similar times during the day to avoid diurnal variations. The Health Research Ethics Authority of the Memorial University of Newfoundland approved this research protocol.

2. EXPERIMENTAL DESIGN

A randomized cross over study design was used to examine the acute effects of localized unilateral knee extensor muscle fatigue on the performance of the contralateral homologous muscle (Fig. 1). The participants were required to attend

the lab on three separate occasions (separated by at least 48 hours) during which

muscle performance (force and electromyography (EMG)) data were collected from

both dominant and non-dominant knee extensors. Experimental sessions consisted

of three testing sessions including control (no intervention), 40% (dominant leg

fatigued by a dynamic knee extension protocol using a load equal to 40% of pretest

MVC) and 70% (dominant leg fatigued by a dynamic knee extension protocol using a

load equal to 70% of pretest MVC). The three experimental protocols were

randomly selected for each experimental session. A series of submaximal and

maximal isometric knee extensions were performed with the non-dominant and

dominant-limb (fatigued limb) before and after the intervention protocols.

2.1 GENERAL PROCEDURES

Participants were seated in the knee extension machine (Modular Leg

Extension, Cybex International, Medway, MA, USA) with the hip and knee were fixed

at 90° and 83° respectively. The knee angle was measured with a goniometer and

was not equal to 90° because of the downward angle of the seat pan. To eliminate

upper body involvement, a strap was placed around the waist and participants were

instructed to cross their hands across their chest. The dominant - and the non-

dominant ankle were then inserted into padded ankle cuffs that were attached to

strain gauges (Omega engineering Inc., LCCA 250, Don Mills, Ontario) via taut non-

extensible straps. The strain gauge and the straps were secured to the isotonic leg

extension machine via a custom-built apparatus (Technical Services Memorial

University of Newfoundland) and were adjusted to form a 90^0 angle with the

87

subject's lower shin (Fig. 2). Differential voltage from the strain gauge, which was sampled at a rate of 2,000-Hz, was amplified, digitally converted (Biopac Systems Inc. DA 100 and analog to digital converter MP100WSW; Holliston, MA) and monitored on a computer. A commercial software program (AcqKnowledge III, Biopac Systems Inc., Holliston, MA) was used to analyze the digitally converted analog data.

After positioning on the knee extension machine, subjects performed a warm-up including two sets of 10 dynamic bilateral knee extensions with a load equivalent to approximately 30% subject`s body mass. In addition, both the left and right legs performed five submaximal unilateral isometric knee extension contractions. Subjects were instructed to contract for five seconds at a force equal to 6-8/10 on a scale of one to ten, where 10/10 equaled maximal effort.

Next, participants performed two unilateral isometric knee extension MVCs with the non-dominant and dominant limb, respectively. Each MVC was performed for 5 s and 2 min rest was given between MVCs. If the difference between the two MVCs was more than 5%, a third MVC was performed. Subjects were instructed to initiate each MVC by contracting their involved muscles as hard and as fast as possible. Subsequently, the intervention protocol (a 7-minute rest period for control session, or the 40% or 70% fatigue protocol) was performed (detail described below). An indication of the extent of dominant limb fatigue was provided with a MVC testing between the third and fourth sets. The last set of the fatigue protocol was then performed after 60-seconds rest. Immediately after (within 10 s) the completion of the dominant leg fatigue protocol, subjects were asked to perform a

MVC (five seconds) with their non-dominant limb followed by a submaximal

endurance test at 70% pretest MVC (knee at 83^0; 0^0 being full extension) for as long

as possible. The knee extension force production was monitored on the screen and

participants were instructed to reach the 70% MVC line marked on the screen.

However, subjects were not able to view the elapsed time.

2.2 FATIGUE PROTOCOL

The two fatigue protocols used in this study consisted of 4 sets of voluntary

dynamic knee extensions ($83°$ to $0°$ and return with $0°$ being full knee extension)

with each set performed to task failure at loads equal to 40% or 70% of the greatest

dominant leg pretest MVC measured at the beginning each testing session (Fortier,

et al., 2010; Schmidtbleicher, 1985). Dynamic knee extensions were performed at a

1-Hz tempo, which was dictated by a metronome. One-minute recovery was allotted

between sets. Schmidtbleicher (1985) reported that isometric MVC force is

approximately 20% higher compared to concentric muscle contractions and 20%

lower compared to eccentric contractions. Therefore, the isometric MVC was

multiplied by a factor of 0.8 before the 40% and 70^0 loads were calculated. To

determine the appropriate loads for each of the two fatiguing protocols, the average

force produced during one isotonic knee extension repetition was measured. The

knee extension machine was plate loaded (4.55-kg plate increments) and adjusted

by changing the location of a pin. One-kilogram weights were used to allow for more

precise adjustments in the load. To ensure full range of motion was obtained for

each repetition, the distal portion of the shin (tibia) had to contact a piece of nylon

tape that was positioned at a height equal to full knee extension. Fatigue was defined as the inability to extend the knee and contact the nylon tape.

Immediately following the third set of the fatigue protocol, an isometric MVC was performed with the dominant knee extensors to determine the extent of dominant knee extensor fatigue. Total repetitions per set were recorded while incomplete repetitions were discounted. The EMG activity was monitored and subjects were instructed to ensure the non-dominant (reference or non-exercised) limb was relaxed during the dominant (fatigued) limb contractions.

2.3. ELECTROMYOGRAPHY

Self-adhesive Ag/AgCl electrodes (MeditraceTM 130 ECG conductive adhesive electrodes) were located parallel to the direction of the vastus lateralis (VL) and biceps femoris (BF) muscle fibres. The electrodes were placed at the mid-point of the anterior superior iliac spine to the patella for the VL and the gluteal fold and popliteal space for the BF. The inter-electrode distance was 2 cm (centre to centre) and electrode locations were recorded to ensure consistent placement for all sessions (Paddock & Behm, 2009). The ground electrode was placed on the lateral femoral epicondyle. Prior to electrode placement, the skin was shaved and abraded to remove dead skin with sandpaper and cleansed with an isopropyl alcohol swab to decrease skin resistance. An inter-electrode impedance of < 5 kOhms was obtained prior to recording to ensure an adequate signal-to-noise ratio. All EMG signals were amplified (Biopac System Inc., DA 100: analog-digital converter MP150WSW; Holliston, Massachusetts) and recorded with sampling rate of 2000 Hz using a

commercially designed software program (AcqKnowledge III, Biopac System Inc.).

EMG activity was filtered with a Blackman -61 dB band-pass filter between 10-500

Hz, amplified (bi-polar differential amplifier, input impedance = 2MΩ, common

mode rejection ratio > 110 dB min (50/60 Hz), gain x 1000, noise > 5 μV), and

analog-to-digitally converted (12 bit) and stored on personal computer for further

analysis.

3. MEASUREMENTS AND DATA ANALYSIS

　　　　MVC and submaximal voluntary contraction (at 70% pretest MVC). Peak

force production and instantaneous force output (force developed in the first 100

ms of the MVC) were calculated from the MVC trials (Hearn, et al., 2009). In addition,

to determine if there were any fatigue-related changes in the ability to maintain

70% MVC during the endurance test (i.e. motor control; co-ordination,

synchronization), the average force output and the standard deviation of the force

output were measured during the first 10-seconds. That start of the submaximal

contraction was considered the point at which the force output exceeded the 70%

value of the isometric MVC.

　　　　The EMG activity of the VL and BF was quantified during pre- and post-test

knee extension MVCs before and after the interventions. A finite infinite response

high pass filter was used (frequency cutoff fixed at 20 Hz) on all EMG data. The EMG

data was rectified and the root mean square EMG (average of 20 data points) of each

muscle was calculated across 1-second window that included the peak force output

(0.5 s before and 0.5 s after peak force). In addition, power spectral analysis was

conducted to compute the median frequency with an epoch equal 3-second window that included the peak force output.

For the submaximal endurance test (70% MVC) the root mean square of the EMG signal was measured during the first 10-seconds to determine the EMG output. A power spectrum analysis was then conducted to determine the median frequency. Neuromuscular efficiency during the first 10-seconds of the submaximal contraction was calculated by dividing the integral of the EMG signal by the average force.

4. STATISTICAL ANALYSIS

Statistical analyses were calculated using SPSS software (Version 16.0, SPSS, Inc, Chicago, IL). Intraclass correlation coefficient (ICC) was computed for MVC force, F100, EMG VL and EMG BF in both dominant and nondominant leg. In order to determine the effect of three exercise protocols (control, 40% and 70% of MVC) on pre- and post-test measurements, a two way analysis of variance (ANOVA) with repeated measure (3 conditions × 2 times) was performed for each variable (e.g. MVC or EMG measures) with the fatigued and non-fatigued leg. If significant results were obtained from main effects, a series of paired t-tests were used to compare different conditions and times. Significance was defined as $p < .05$. In addition, to determine the effect of three exercise protocols (control, 40% and 70% of MVC) on endurance test (submaximal isometric knee extension at 70% MVC) measures, a one way analysis of variance (AVOVA) with repeated measure (3 conditions) was performed followed by a series of paired t-tests to compare different conditions if the ANOVA showed any significant main effect. Significance was defined as $p < .05$.

Cohen effect size statistics (ES) were conducted to evaluate the magnitude of the

changes following various exercise protocols to the criterion of >0.70 large; 0.40-

0.70 medium and <0.40 small (Table 1) (Cohen, 1988).

RESULTS

1. FATIGUE PROTOCOL

The average number of repetitions performed to task failure was approximately 6 ± 2 (~12 s of work; 70% MVC) and 13 ± 5 (~26 s of work; 40% MVC).

2. MVC FORCE

Statistical analysis revealed a significant main effect for time ($F_{(1, 11)}$ = 44.16, *p = 0.000*) and condition ($F_{(2,22)}$ = 15.56, *p = 0.000*) for MVC force production by the fatigued leg (Table 2). In addition, a significant interaction effect (condition * time) was found for this parameter ($F_{(2,22)}$ = 48.04, *p = 0.000*). Furthermore, paired sampled t-test showed that MVC force decreased significantly from pre- to post-test by 32.10% and 21.60% in the 40% (*p = 0.000*, ES = 2.13) and 70% conditions (*p = 0.000*, ES = 1.27), respectively. No significant change was observed in the control condition (Fig. 3a).

Statistical analysis revealed a significant main effect for time ($F_{(1, 11)}$ = 15.38, *p = 0.002*) for MVC force production by the non-exercised leg. Bonferroni post hoc test demonstrated that post-test was significantly less than pre-test (*p = 0.002*). There was no significant (*p = 0.199*) main effect for condition (Fig. 3b). Contralateral force deficits were modest ranging from 4-7%.

3. F100

There was a significant main effect for time for the fatigued leg for instantaneous force production ($F_{(1,11)}$ = 76.14, *p = 0.000*). Both the 40% (*p = 0.000*, ES = 2.13) and 70% (*p = 0.000*, ES = 1.19) conditions showed 45.9% and 31.9% reductions in F100 from pre- to post-intervention, respectively (Fig. 4a).

The analysis showed a significant main effect for time for the non-dominant leg for instantaneous force production ($F_{(1,11)}$ = 27.59, *p = 0.01*). In addition, a significant interaction effect (condition * time) was found for this parameter ($F_{(2,22)}$ = 5.08, *p = 0.018*). Both the 40% (*p = 0.009*, ES = 0.72) and 70% (*p = 0.001*, ES = 2.03) conditions exhibited 23.7% and 34.6% decreases in F100 from pre- to post-intervention, respectively (Fig. 4b). There was no significant (*p = 0.40*) main effect for condition.

4. EMG

4.1. VASTUS LATERALIS

A significant main effect for time was recorded for the dominant fatigued leg for VL EMG ($F_{1,9}$ = 8.07, *p = 0.019*). In addition, a significant interaction effect (condition * time) was found for this parameter ($F_{(2,22)}$ = 8.54, *p = 0.002*). Both the 40% (*p = 0.005*, ES = 0.61) and 70% (*p = 0.008*, ES = 0.37) conditions showed 22.8% and 11.7% reductions in VL EMG from pre- to post-intervention, respectively. No significant results were found regarding VL EMG (all *p > 0.492*) in the contralateral non-exercised leg.

4.2. BICEPS FEMORIS

No significant changes were found regarding BF EMG in both the dominant and non-dominant sides.

5. MEDIAN FREQUENCY

5.1. VASTUS LATERALIS

Statistical analysis revealed a significant main effect for time for the dominant fatigued leg with for VL median frequency ($F_{(1,11)}$ = 7.34, *p = 0.024*). Both the 40% (*p = 0.026*, ES = 0.90) and 70% (*p = 0.009*, ES = 0.63) conditions showed 12.9% and 10.1% reductions in VL median frequency from pre- to post-intervention, respectively. Bonferroni post hoc test demonstrated that post-test was significantly less than pre-test (*p = 0.024*).

No significant results were found regarding VL median frequency (all *p > 0.141*) in the contralateral, non-exercised leg.

5.2. BICEPS FEMORIS

No significant changes were found regarding BF median frequency in both the dominant and non-dominant sides.

6. SUBMAXIMAL ENDURANCE TEST

There was no significant effect of crossover fatigue on the duration of the endurance test (control: 36.21 $\pm$ 11.46; 40%: 35.26 $\pm$ 10.02; 70%: 33.00 $\pm$ 9.49); average force maintained in first 10-seconds, VL and BF EMG, VL and BF median frequency and neuromuscular efficiency. However, the variability of the voluntary

96

force output during the maintenance of 70% MVC of the non-exercised limb exhibited a tendency for a main effect for conditions ($F_{(2,22)}$ = 3.012, *p = 0.078*). Paired sample t-test revealed that 40% (t = -1.912, *p = 0.092*, ES = 0.65) and 70% (t = -2.024, *p = 0.078*, ES = 0.79) protocols induced greater contralateral force output variation compared with the control condition.

DISCUSSION

The most important finding of the present study was ipsilateral dynamic contractions induced crossover fatigue of the non-exercised contralateral leg extensors. Two major specific findings were that with the non-exercised contralateral knee extensors 1) both 40% and 70% of MVC dynamic fatiguing protocols caused a decrease in subsequent MVC and instantaneous force, and 2) voluntary force during the initial 10 s of the submaximal endurance test exhibited a moderate magnitude of variability in both the 40% and 70% conditions compared with the control condition.

The present evidence for crossover fatigue is in accordance with previous research where MVC force decrements were seen in both the ipsilateral and contralateral lower limbs following a unilateral fatiguing protocol (Amann, et al., 2013; Doix, et al., 2013; Martin & Rattey, 2007; Takahashi, et al., 2011). The frequency of force decrements occurring in the non-dominant, non-exercised leg with 40% and 70% fatiguing protocols in the present study was 10/12 and 11/12 subjects respectively. The present findings contradict the lack of crossover fatigue impairments found with a 100 s duration isometric quadriceps fatiguing protocol (Rattey, et al., 2006). Furthermore, Todd et al. (2003) had subjects alternate between 60-second MVCs performed with the elbow flexors twice and found that voluntary drive from the motor cortex measured with transcranial magnetic stimulation (TMS) was slightly less able to produce maximal force by the contralateral muscles implying that the crossover fatigue effect is small and has a minor functional effect. Isometric contractions of the smaller upper limb muscles

such as the first dorsal interosseus (Zijdewind, et al., 1998) and extensor carpi radialis (Samii, et al., 1997) have also failed to create crossover fatigue effects. Hence muscle size may not be the most distinguishing factor for crossover fatigue as the lack of crossover fatigue has been reported with such disparate muscles as the quadriceps, elbow flexors, forearm and hand muscles. The unique aspect of this study however was that the fatiguing protocol consisted of dynamic leg extensions involving both concentric and eccentric contractions.

There are few studies that demonstrate crossover fatigue performance deficits with dynamic contractions (Amann, et al., 2013; Triscott, et al., 2008). Amann et al. (2013) found that constant load single leg knee-extensor exercise performed to exhaustion (> 9 min) resulted in a reduction of time to exhaustion in the non-fatigued contralateral leg; however, no significant changes were seen in potentiated twitch, MVC force and voluntary muscle activation. Dynamic biceps curls performed to exhaustion have resulted in reduced biceps curl endurance performance and a reduction in MEPs in the contralateral non-fatigued elbow flexors (Humphry, et al., 2004; Triscott, et al., 2008). Additionally, bilateral leg presses performed with 50% of a dynamic MVC were found to depress cortical excitability of non-exercised upper limb muscles (Takahashi, et al., 2011). H-reflex (afferent excitability of the motoneuron) activity decreases with higher velocity contractions (Duclay, et al., 2009; Larsen, et al., 2004) and hence dynamic contractions may induce greater motoneuron inhibition than isometric contractions. Furthermore, crossover fatigue effects following lengthening and shortening (eccentric / concentric) contractions may arise from the greater afferent feedback

99

from the muscle spindle afferents (Ribot-Ciscar, et al., 2003) than with isometric or concentric only (isokinetic) contractions. Furthermore, Doix et al. (2013) suggested the body compensates for a fatigued lower limb by reducing the performance of the non-exercised leg to maintain lower limb homeostasis or symmetry. On the contrary, isokinetic exercise consisting of concentric/concentric knee flexion/extension contractions (7 sets of 20 repetitions) had no effect on the contralateral hamstrings but actually enhanced contralateral quadriceps MVC force (Strang, et al., 2009). Grabiner and Owings (1999) used unilateral isokinetic concentric- and eccentric-only MVCs (3 sets of 25 repetitions) and found no crossover fatigue effects following the concentric fatigue protocol but found an enhanced eccentric MVC following the eccentric fatigue protocol. Furthermore, both unilateral submaximal plyometric exercise (432 ± 178 rebounds) performed until exhaustion on a sledge ergometer (Regueme, et al., 2007) and 10-minutes of maximal unilateral cycling (Elmer, et al., 2013) failed to result in crossover fatigue effects.

Differences in volume and intensity are variables that may confound the crossover fatigue evidence. The present study demonstrated that although both contraction intensities resulted in crossover fatigue, the higher (70%) intensity manifested a moderate magnitude effect compared to a small magnitude effect for the 40% condition (no statistical significant difference between conditions). While not well elucidated in the literature, there is some corroborating evidence for a more substantial crossover fatigue effect with higher intensity contractions. Kennedy et al. (2013) compared maximal and submaximal (30% MVC) bilateral

isometric handgrip exercise performed to exhaustion and examined if any fatigue effects would be seen in the ankle plantar flexors. Interestingly, the maximal fatiguing protocol was more impactful on reducing ankle plantar flexor MVC and voluntary activation, compared to the submaximal fatiguing protocol (Kennedy, et al., 2013). The average number of repetitions to failure in the present study was approximately 6 (~12 s of work; 70% MVC) and 13 (~26 s of work; 40% MVC). Other lower body crossover fatigue studies have implemented higher volume, lower intensity activities such as 3-7 sets of 20-25 knee extension/flexion repetitions (Grabiner & Owings, 1999; Strang, et al., 2009), 432 rebound actions (Regueme, et al., 2007), 9-10 minutes of knee extensions (Amann, et al., 2013) or cycling (Elmer, et al., 2013). Thus higher intensity dynamic contractions may accentuate the crossover fatigue effect.

However, contrary to Martin and Rattey (2007), contralateral force deficits in the non-exercised leg of the present study were seen with no significant change in VL EMG activity or median frequency. The frequency of VL EMG decrements occurring in the non-exercised leg with the 40% and 70% fatiguing protocols was 5/11 and 6/12 subjects, respectively. Also, the frequency of VL median frequency increases occurring in the non-exercised leg with the 40% and 70% fatiguing protocols was 6/12 and 8/12 subjects, respectively. Perhaps this non-significant response can be explained by the non-linear force-EMG relationship (Madeleine, et al., 2001; Solomonow, et al., 1986). The earliest studies on the force-EMG relationship reported a linear relationship (Bigland & Lippold, 1954; Lippold, 1952) however; contemporary studies have illustrated a non-linear or curvilinear force-

EMG relationships with the quadriceps during isometric (Alkner, et al., 2000) and dynamic (Fujita, et al., 2011) contractions. A non-linear force-EMG relationship indicates that the EMG is not sensitive to all changes in force output. As the contralateral force deficits were modest ranging from 4-7%, the non-linear force-EMG relationship may not have portrayed possible changes in activation.

Additionally, force impairments without reductions in EMG activity have also been reported with instability resistance exercise studies (Anderson & Behm, 2004; Behm, et al., 2010; Behm & Colados, 2012). Described as a stiffening strategy, the body utilizes a greater component of a muscular contraction to protect the joints in novel, threatening or fatiguing situations, which results in less force available to exert against an external resistance (Behm, et al., 2010; Carpenter, et al., 2001).

In the present study, crossover fatigue not only affected non-exercised contralateral muscle force output but motor control as well. There was a tendency for greater variability in the maintenance of submaximal forces (70% MVC). Other studies have also demonstrated non-local fatigue-induced motor control deficits such as alterations in single leg landing strategies (McLean & Samorezov, 2009), center of pressure during bilateral stance (Berger, et al., 2010) and postural control during single leg stance (Paillard, et al., 2010). Muscle fatigue can affect joint position sense by affecting the afferent feedback, therefore affecting proprioceptive and kinesthetic feedback (Gribble & Hertel, 2004; Macefield, et al., 1990). The change in perception and movement execution strategies seen in the contralateral limb have been attributed to altered supraspinal and spinal control pathways,

(McLean & Samorezov, 2009) likely modified via the inhibitory action of the fatigued muscles in the ipsilateral limb (Paillard, et al., 2010).

Although not directly measured in the present study, there are a number of mechanisms that could contribute to the crossover fatigue effect. Previous crossover fatigue research attributes performance decrements in the non-fatigued limb to centrally derived mechanisms (Bonato, et al., 1996; Doix, et al., 2013; Martin & Rattey 2007; Rattey, et al., 2006) that could occur at both the spinal and supraspinal levels (Gruet, et al., 2012; Taylor & Gandevia, 2008). Proposed mechanisms related to cross education (Carroll, et al., 2006; Lee & Carroll, 2007; Zhou, 2000; Zhou, 2003) where strength gains appear in the untrained contralateral limb following unilateral resistance training might help explain crossover fatigue mechanisms. Following unilateral training, changes in higher order inputs to the primary motor cortex occur bilaterally and can modulate ipsilateral primary motor cortex excitability (Carroll, et al., 2006; Farthing, 2009). Furthermore, inhibitory and excitatory interneurons via interhemispheric connections exist between most cortical motor areas via the corpus callosum (Carson, 2005) and transcallosal fibers (Hortobagyi, 2005). It has been suggested that the neuroanatomical mechanism explaining cross-education is more related to these connections, rather than to the nondecussated descending motor pathways (Carroll, et al., 2006; Hortobagyi, 2005). Unilateral motor activity has been proposed to activate homotopic excitatory paths via command neurons (Rosenbaum, 1977), thus interconnecting the ipsilateral and contralateral primary motor cortex. This bilateral activation is referred to as motor irradiation (Cernacek, 1961, Doix, et al., 2013), the Bilateral Activation Theory

(Addamo, et al., 2007) or neural spill-over (Carroll, et al., 2006). Moreover, strong support also exists for spinal mechanisms, as cross-education appears with electrical muscle stimulation (Hortobagyi, et al., 1999); however, the exact role of spinal mechanisms (Farthing, 2009) involved with crossover fatigue remains unclear. Group III and IV afferent activity from the accumulation of metabolites in the ipsilateral limb may result in spinal inhibition (Bigland-Ritchie, et al., 1986) and alter motorneuron excitation to the contralateral uninvolved limb (Amann, et al., 2013; Doix, et al., 2013). Furthermore, group III and IV afferents can reduce excitatory input to the motoneurons via presynaptic inhibition of the group Ia afferents; a process referred to as disfacilitation (Hunter, et al., 2004).

CONCLUSION

In conclusion, this study highlighted that unilateral lower limb fatigue induced by low intensity, high volume as well as high intensity, low volume dynamic knee extensions leads to crossover fatigue to the contralateral, non-exercised limb. Further research should investigate the neural mechanism(s) responsible for the affected performance of the contralateral limb.

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TABLES

Table 1. Intraclass Correlation Coefficients

Leg	Variable	ICC Cronbach's Alpha
Dominant	MVC Force	0.952
Dominant	F100	0.647
Dominant	EMG VL	0.949
Dominant	EMG BF	0.887
Non-Dominant	MVC Force	0.977
Non-Dominant	F100	0.878
Non-Dominant	EMG VL	0.908
Non-Dominant	EMG BF	0.791

Table 2. Absolute Values of the Dominant Leg

Condition	Time	Mean (SD)	Significance	Effect Size
VL EMG (millivolts)				
Control	Pre	0.5 (0.19)		
	Post	0.54 (0.22)	0.146	0.10
40%	Pre	0.57 (0.26)		
	Post	0.44 (0.15)	0.005	0.61
70%	Pre	0.51 (0.18)		
	Post	0.45 (0.14)	0.008	0.37
BF EMG (millivolts)				
Control	Pre	0.037 (0.010)		
	Post	0.036 (0.008)	0.504	0.06
40%	Pre	0.035 (0.007)		
	Post	0.030 (0.014)	0.504	0.22
70%	Pre	0.037 (0.012)		
	Post	0.033 (0.013)	0.504	0.16
VL Median Frequency (Hertz)				
Control	Pre	35.81 (4.75)		
	Post	37.39 (6.47)	0.666	0.14
40%	Pre	35.74 (3.90)		
	Post	31.11 (6.09)	0.026	0.90
70%	Pre	37.27 (5.06)		
	Post	33.49 (6.69)	0.009	063
BF Median Frequency (Hertz)				
Control	Pre	37.62 (5.92)		
	Post	39.24 (8.79)	0.429	0.11
40%	Pre	39.17 (5.60)		
	Post	37.41 (4.52)	0.429	0.17
70%	Pre	40.53 (2.89)		
	Post	41.0 (1.28)	0.429	0.10

Figure 1. Experimental Design

Warm Up
Submaximal dynamic knee extensions (bilaterally) and isometric knee extensor contractions (unilaterally).

⬇

INDEPENDENT VARIABLES

Condition 1 **Control** 7-min rest	**Condition 2** **Fatigue Protocol** 4 sets of dynamic knee extensions with 40% MVC, performed to task failure. 60-sec rest between sets.	**Condition 3** **Fatigue Protocol** 4 sets of dynamic knee extensions with 70% MVC, performed to task failure. 60-sec rest between sets.

⬇

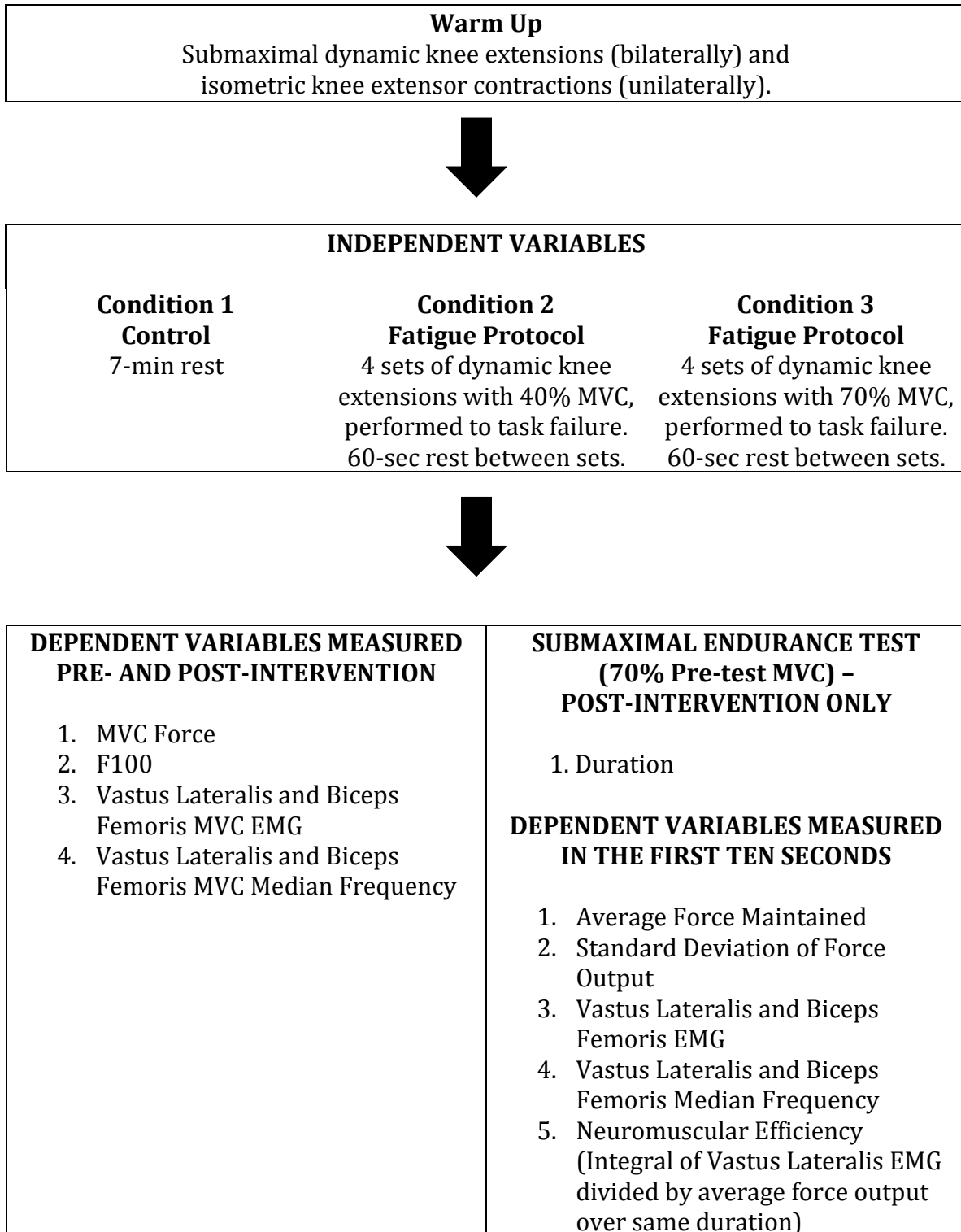| **DEPENDENT VARIABLES MEASURED PRE- AND POST-INTERVENTION**	**SUBMAXIMAL ENDURANCE TEST (70% Pre-test MVC) – POST-INTERVENTION ONLY**
1. MVC Force 2. F100 3. Vastus Lateralis and Biceps Femoris MVC EMG 4. Vastus Lateralis and Biceps Femoris MVC Median Frequency	1. Duration **DEPENDENT VARIABLES MEASURED IN THE FIRST TEN SECONDS** 1. Average Force Maintained 2. Standard Deviation of Force Output 3. Vastus Lateralis and Biceps Femoris EMG 4. Vastus Lateralis and Biceps Femoris Median Frequency 5. Neuromuscular Efficiency (Integral of Vastus Lateralis EMG divided by average force output over same duration)

Figure 2. Photo of Leg Extension Custom Apparatus

Figure 3a. MVC Force Pre-post Intervention – Representation of force in the dominant, fatigued leg (a) and non-dominant, non-exercised leg (b), pre- and post-intervention. Variation in data indicated by standard error. Significance was set at p < 0.05. Stars (★) indicate significant pre-post intervention differences. Whereas there were significant differences between all 3 conditions with the dominant fatigued leg post-intervention, there were no significant differences between the 40% and 70% conditions for the contralateral non-exercised limb post-intervention.
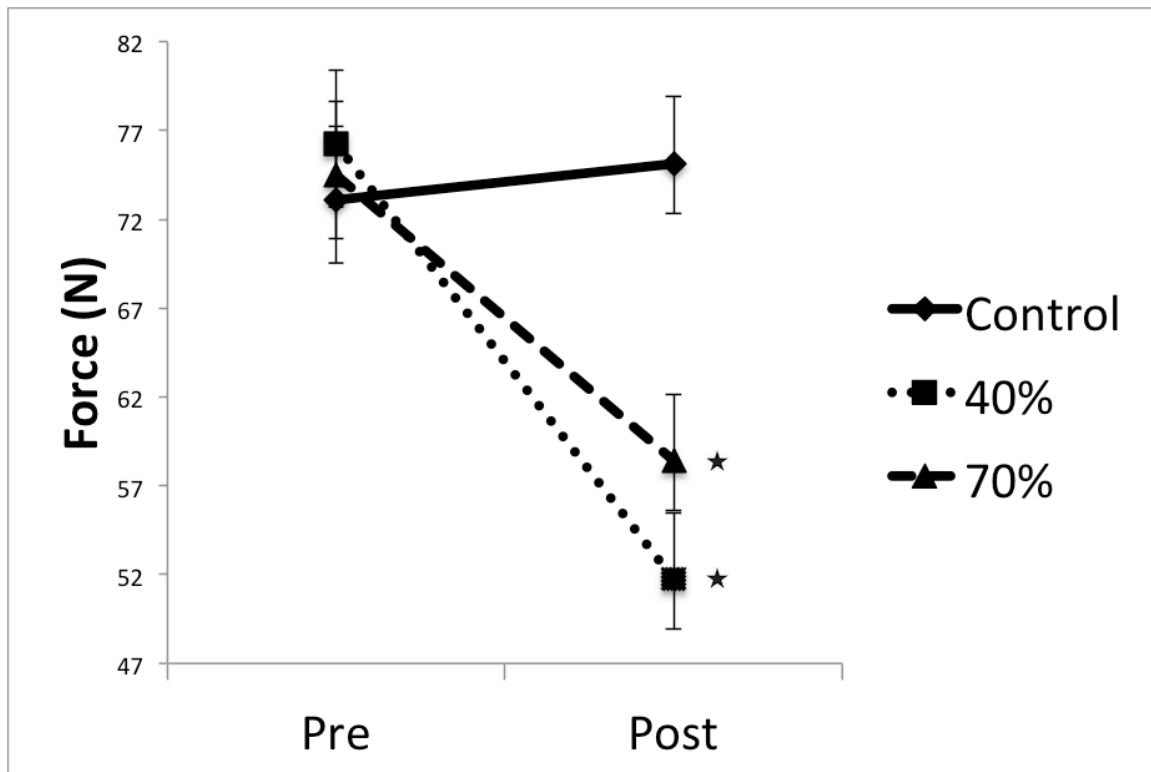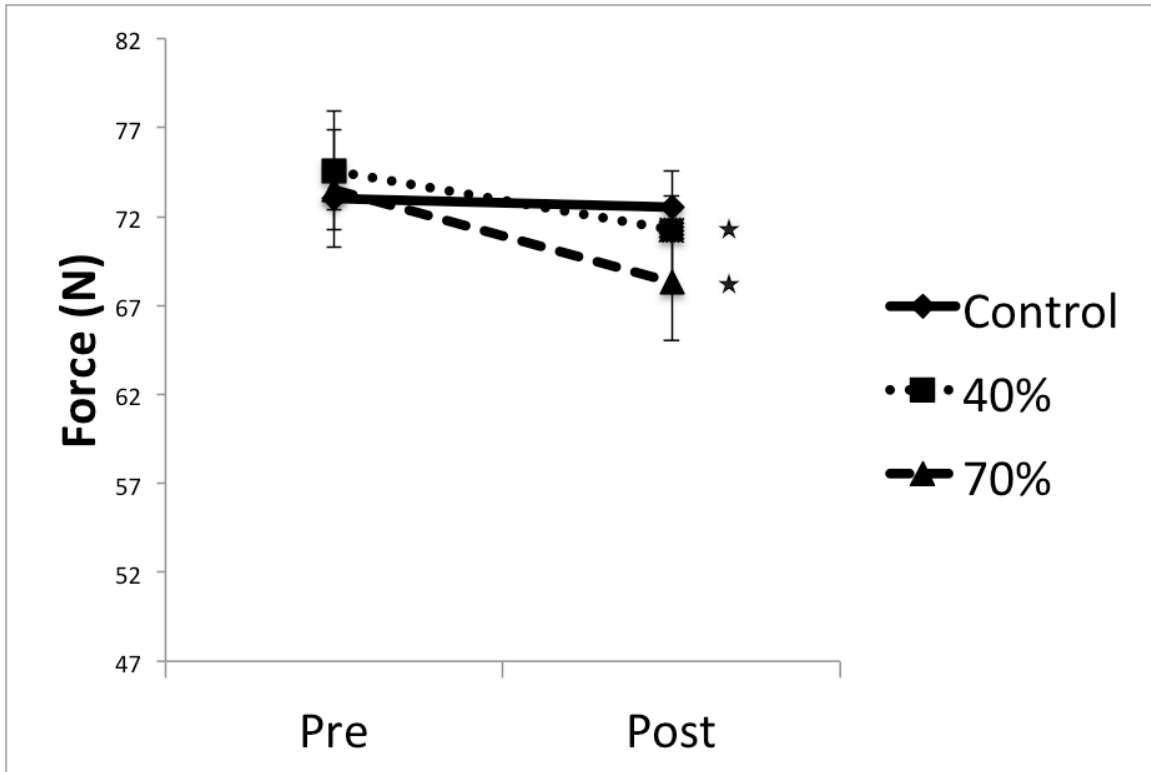
Figure 3b. MVC Force Pre-post Intervention

Figure 4a. F100 Pre-post Intervention - Representation of F100 in the dominant, fatigued-leg (a) and non-dominant, non-exercised leg (b), pre- and post-intervention. Variation in data indicated by standard error. Significance was set at p < 0.05. Stars (★) indicate significant pre-post intervention differences.
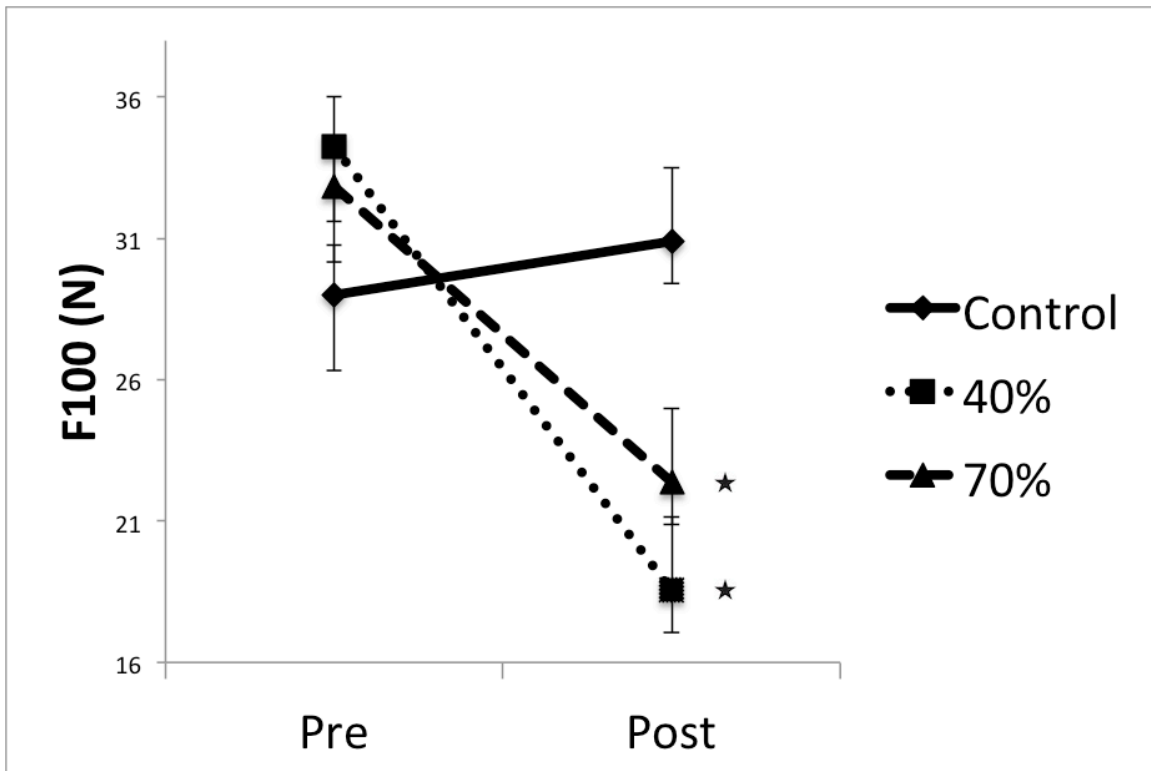
Figure 4b. F100 Pre-post Intervention