EFFECT OF SLOW VELOCITY ISOKINETIC KNEE ACTIONS ON SLOW AND FAST VELOCITY CONTRALATERAL KNEE ACTION PERFORMANCE

By

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ABSTRACT

Fatigue is a complex, multifactorial phenomenon that affects the neuromuscular system from the muscle fibers and neuromuscular junction to the higher planning centers in the brain and reflects interactions along the entire system. 'Neuromuscular fatigue' refers to the decrease in physical performance associated with an increase in the real and/or perceived difficulty of a task, regardless if the force or power can be sustained, and is present and progressing from the onset of the task that is reversible with rest. It consists of central and peripheral components such as decreases in central drive (central fatigue) or contractile responses (peripheral fatigue) and is suggested to occur at any site involved in the muscle contraction. Fatigue also has a mental component that describes an emotion suggested to act as a warning sign for maintaining physical integrity. Neuromuscular fatigue may depend on both the muscles employed and on the type of exercise from which fatigue results and are specific to the task and dependent on the mechanisms which are the most stressed during the task.

Fatigue can either be localized or global, meaning it can affect the muscles exercised or the entire body system resulting in fatigue effects in non-exercised muscle groups. A growing body of research revolves around the effects of fatiguing exercise and their impact on the performance of non-exercised muscles, termed non-local muscle fatigue (NLMF). The presence of NLMF effects is conflicting, with effects seemingly dependent on many factors such as contraction intensity, fatiguing exercise volume, muscle group fatigued and tested, muscle action, and the detection method(s) used. NLMF research has many implications for rehabilitation and training purposes, as well as widening our understanding of global fatigue mechanisms. A relatively unexplored aspect of NLMF is whether the testing is velocity specific. The purpose of this study was to investigate the effects of fatigue induced by simultaneous low velocity unilateral

isokinetic knee extensions and flexions on contralateral knee slow and fast velocity extensor and flexor isokinetic force and electromyography (EMG). In a randomized, repeated measures, crossover design, peak torque, EMG, and rate of perceived exertion measures were measured from the non-dominant vastus lateralis and biceps femoris before and after unilateral fatiguing protocols of the dominant knee extensors and flexors. The fatiguing protocols consisted of 4 sets of 15 maximal isokinetic knee extension and flexion contractions. In addition, a fatigue resistance test was also completed post-intervention.

The current study used 16, university-aged (ages 18-30) participants (10 males and 6 females) who were resistance trained. Peak torque of the dominant (exercised) quadriceps and hamstrings decreased when tested at slow and high velocities. Peak torque of the non-dominant quadriceps and hamstrings during post-test ($p=0.6$ and $p=0.3$ respectively), or first or last repetition of repetitive fatigue test ($p=0.8$, $p=0.06$, and $p=0.8$, $p=1.0$, respectively) tested at slow velocity was not significantly different from control, demonstrating a lack of peak torque or fatigue endurance NLMF effects. In addition, there was no relative (normalized) differences in peak torque for velocity specific or fast test velocities. However, the fast velocity repetitive fatigue test resulted in a greater decrease from first to the last repetition than the slow test, as demonstrated by the fatigue index (FI), but was not significantly different from control. This study highlights that prior unilateral fatigue of the dominant quadriceps and hamstrings by repetitive slow maximal isokinetic actions did not demonstrate decreases in singular maximal peak torque or repetitive fatigue endurance in the contralateral muscles. In addition, velocity specific effects were not demonstrated in relative peak torque or relative fatigue endurance changes. There was also no observable effect on the rating of perceived exertion following control vs fatigue (4.6 vs 6.3, $p>0.05$), or slow vs. fast testing (5.8 vs 6.8, $p>0.05$) on post-repetitive test values.

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ABBREVIATIONS:

1RM = One Repetition Maximum

ANOVA – Analysis of variance

AP – Action Potential

ADP – Adenosine Diphosphate

ATP – Adenosine Triphosphate

BF – Biceps Femoris

CNS – Central Nervous System

CSE – Cortico-Spinal Excitability

EMG – Electromyography

ES – Effect Size

ECC - Excitation-Contraction Coupling

ITT – Interpolated Twitch Technique

M Wave – Muscle Response Wave

MEP – Motor Evoked Potential

MVC – Maximal Voluntary Contraction

NLMF – Non-local Muscle Fatigue

Pi – Inorganic Phosphate

RPE – Rating of Perceived Exertion

SD – Standard Deviation

SEM – Standard Error of the Mean

TMS – Transcranial Magnetic Stimulation

VA – Voluntary Activation

VL – Vastus Lateralis

LITERATURE REVIEW

1.1 INTRODUCTION (NEUROMUSCULAR FATIGUE)

Fatigue is a complex, multifactorial phenomenon (Enoka & Stuart, 1992; St. Clair Gibson et al., 2003) that affects the neuromuscular system from the muscle fibers and neuromuscular junction to the higher planning centers in the brain and reflects interactions along the entire system, and also describes an emotion (Noakes, 2012; St Clair Gibson, et al., 2003) suggested to act as a warning sign for maintaining physical integrity (Ament & Verkerke, 2009). 'Neuromuscular fatigue' refers to the decrease in physical performance associated with an increase in the real and/or perceived difficulty of a task (MacIntosh et al., 2006; Davis & Bailey, 1997), regardless if the force or power can be sustained (maximal or submaximal) (Bigland-Ritchie & Woods, 1984), and is present and progressing from the onset of the task (Bigland-Ritchie et al., 1986) that is reversible with rest (NHLBI, 1990).

Neuromuscular fatigue consists of central and peripheral components such as decreases in central drive (central fatigue) or altered contractile responses (peripheral fatigue) and is suggested to occur at any site involved in the muscle contraction (Kirkendall, 1990; Gandevia, 2001; MacIntosh et al., 2006). Changes which are rate-limiting may depend on both the muscles employed and on the type of fatiguing exercise (Bigland-Ritchie & Woods, 1984), and are task-specific (i.e. type and duration of the exercise, speed and duration of the muscle contraction) (Enoka & Stuart, 1992; Enoka & Duchateau, 2008). The physiological state of the system (e.g. energy reserves, ion concentrations, and the arrangement of contractile proteins) begins to alter at the onset of exercise, even before any external effects are present, progressing until exercise failure (Behm, 2004; Enoka and Stuart 1992). Identifying the extent to which central and peripheral fatigue mechanisms interact to affect performance is a major interest in exercise research. While

extensive literature examines muscle fatigue in the exercised muscles (Allen et al., 2008; Gandevia, 2001), effects of fatigue can either be localized or global (Halperin et al., 2015; Kennedy et al., 2013; Rattey et al., 2006), meaning it can affect the muscles exercised, or the entire body resulting in fatigue effects in non-exercised muscle groups. A growing body of research revolves around the effects of fatiguing exercise and their impact on performance of non-exercised muscles, termed non-local muscle fatigue (NLMF) (Halperin et al., 2015).

NLMF refers to a temporary performance deficit in a contralateral, ipsilateral, inferior, or superior uninvolved muscle distant from the fatigued muscle group (Gandevia et al., 1996; Graven-Nielson et al., 2002; Halperin et al., 2015; Kennedy et al., 2013). Synergist or stabilizer muscles are excluded from NLMF as co-contractions may lead to fatigue effects (Ben Othman et al., 2017; Paillard et al., 2010). By testing non-local muscles, research can drastically reduce influences of peripheral fatigue (however metabolites such as lactate may travel from one limb to another), defined as changes at or beyond the neuromuscular junction, which inhibits the contractile elements of the muscle, and focus on central fatigue, which refers to changes proximal to the neuromuscular junction resulting in a decreased neural drive (i.e. number and discharge rate of motor units) to the muscles (Bigland-Ritchie et al., 1978; Boyas & Guével, 2011). NLMF asks the question if fatigue is specific to the exercised muscles or a systemic response, and to what extent systemic responses may affect non-local performance. Answers to these questions would enhance the understanding of mechanisms responsible for muscle fatigue. Practical applications can involve insight into the types and order of exercise or rehabilitation programming to direct participants toward their training goals. For example, exercise-induced fatigue in one muscle group that induces fatigue elsewhere in the body might be programmed later to avoid systemic fatigue or injury.

NLMF research is conflicting. A review paper by Halperin et al., (2015) reported that approximately half of the studies demonstrated effects (32 of 58) and suggested that varying methodological considerations lead to the presence or absence of effects. When examining lower limbs, the group observed that 23 of 30 (76%) studies demonstrated effects, while only 32% (9 of 28) demonstrated effects in the upper body, suggesting NLMF might be muscle group dependent and that the legs are more susceptible than the upper body (Halperin et al., 2014b, Halperin et al., 2015). In addition, upper body fatigue appears more likely to induce lower body fatigue than vice versa (Bouhlel et al., 2010; Halperin et al., 2014b, c). The most studied version of NLMF might be crossover fatigue, which indicates a temporary deficit in performance of the non-exercised, contralateral, homologous limb muscles following a fatiguing protocol to the opposite limb (Doix., et al., 2013; Halperin et al., 2015, Martin & Rattey, 2007). The review by Halperin et al., (2015) also suggested that repetitive testing measures such as repeated maximal contractions, and time to exhaustion, are more likely to demonstrate effects than a single maximal effort or MVC (Halperin et al., 2014b, Triscott et al., 2008). As well, other measures of fatigue such as changes in muscle activity (electromyography: EMG), voluntary activation, or rating of perceived exertion have been used inconsistently. The contraction intensity and volume used to fatigue muscle groups may be one of the most variable and important influences for fatigue in non-exercised groups (Halperin et al., 2015). Studies using lower or submaximal intensity (lower percentage of maximal effort relative to another intensity used in the study, or simply less than maximal) or shorter duration (contraction time) resulted in less pronounced effects than maximal efforts (Kawamoto and Behm., 2014; Rasmussen et al., 2010; Kennedy et al., 2013; Paillard et al., 2010; Arora et al., 2015). While never directly compared, the contraction mode (isometric, cyclic, dynamic, isokinetic) may also account for the conflicting

results. Studies using dynamic or stretch-shortening cycle contraction seemed to be less likely to induce NLMF effects due to recovery periods (usually 1:1 work-rest ratio) or stretch-shortening cycle versus constant work modes such as isometric or cyclic protocols (Halperin et al., 2015). Only three studies have examined isokinetic exercise, and demonstrated minimal NLMF effects (Ben Othman et al., 2017; Grabiner & Owings, 1999, Strang et al. 2009). Within those studies, all of them used a contract-passive return methodology allowing a 1:1 work-rest ratio, and neither used concentric-concentric actions (with minimal rest between repetitions). The question can be asked, if isokinetic exercise were to be concentric-concentric, making it constant action like isometric or cyclic, would this improve the incidence of effects? Secondly, while Ben Othman et al., (2017) used isometric and high velocity (300°.s-1) fatigue and tests, it can be questioned if slow (60°.s-1) or fast (240°.s-1) velocity isokinetic test contractions demonstrate a velocity specific NLMF effect?

Before diving deeper into the physiological phenomena associated with neuromuscular fatigue, and more specifically non-local muscle fatigue (NLMF), a brief discussion regarding fatigue and its main components is warranted.

1.2. FATGUE COMPONENTS (PERIPHERAL AND CENTRAL)

With voluntary contractions, muscles are activated by complex pathways originating in the cerebral cortex traveling to the lower motor neurons in the spinal cord and the neuromuscular junction causing a contraction of the muscle fibers via action potentials (Allen et al., 2008). When identifying sites of fatigue, two main components are often considered: central (neural and psychological) and peripheral fatigue (Bigland-Ritchie & Woods, 1984).

Peripheral fatigue refers to changes at or beyond the neuromuscular junction, which inhibits the contractile elements of the muscle, and central fatigue refers to changes proximal to the neuromuscular junction resulting in a decreased neural drive (number and frequency of discharge rate to motor units) to the muscles (Bigland-Ritchie et al., 1978; Boyas & Guével, 2011). The central and peripheral components likely interact through multiple physiological mechanisms to cause fatigue (Place et al., 2010), with different exercise protocols causing different amounts of stress on different sites (Bigland-Ritchie, 1981). It can be suggested that any site or process involved in the muscle contraction could be a potential site of fatigue. Boyas and Guevel (2011) outlined nine potential sites of fatigue, listing "(1) activation of the primary motor cortex; (2) propagation of the command from the central nervous system (CNS) to the motoneurons (the pyramidal pathways); (3) activation of the motor units and muscles; (4) neuromuscular propagation (muscle action potential including propagation at the neuromuscular junction); (5) excitation-contraction coupling; (6) availability of metabolic substrates; (7) state of the intracellular medium; (8) performance of the contractile apparatus; (9) blood flow restriction". Sites 1-3 are considered central in origin, while sites 4-9 are considered peripheral in origin.

Mechanisms of fatigue have been examined by manipulating exercise duration and intensity, recovery (work to rest ratio, or time before testing), contraction velocity, and mode of activation (Boyas & Guével, 2011).

1.3 MECHANISMS OF FATIGUE: PERIPHERAL FATIGUE

1.3.1 NEUROMUSCULAR TRANSMISSION

Neuromuscular transmission takes place at the neuromuscular junction and is defined as the transformation of the nerve action potential into a muscle action potential, which is generated

when the sum of the excitatory and inhibitory presynaptic potentials reaches or exceeds the muscle cells' excitability threshold (Boyas & Guével, 2011). During exercise, Boyas and Guével (2011) suggested neuromuscular transmission can be altered by insufficient propagation of the nerve potential; a failure of the coupling between excitation and neurotransmitter secretion in the synaptic gap; reduced neurotransmitter release or depletion; a decrease in the sensitivity of the postsynaptic acetylcholine receptors and the post-synaptic membrane which can lead to decreases in force production (Allen et al., 2008; Sieck & Prakash, 1995).

1.3.2 EXCITATION CONTRACTION COUPLING

Excitation-contraction coupling (ECC) is the rapid series of action potentials along the muscle membrane leading to Ca^{2+} release from the sarcoplasmic reticulum and ending with the onset of muscle tension (Calderon et al., 2014; Sandow., 1952). The concentration of Ca^{2+} released decreases with fatigue which can reduce force production, and the reuptake also decreases increasing the relaxation time following a contraction (Ament & Verkerke, 2009; MacIntosh, et al., 2006). ECC can be affected by many factors, such as the propagation of the action potential along the sarcolemma and the transverse tubules, the sarcoplasmic reticulum's efflux, permeability, movement, and leading to the binding of Ca^{2+} to troponin and the myosin-actin interaction associated with the work performed by the cross-bridges (Allen et al., 1992).

In addition, differences in fatigue resistance between type I (slow-twitch) and type II (fast-twitch) muscle fibers are associated with differences in the ECC (Ament & Verkerke, 2009). Type I and type II muscle fibers within a muscle vary in their contractive speed, maximal force, and resistance to fatigue, while. Fast-twitch muscle fibers have higher ATPase turnover and cross-bridge cycle rates than slow-twitch fibers leading to faster contraction and relaxation; in addition, fast-twitch fibers have a lower concentration of enzymes catered to oxidative metabolism, which

gives them a faster onset of fatigue (Ament & Verkerke, 2009). Muscles are made up of different compositions of type I and II fibers with distribution based on function (i.e postural muscles containing more fatigue-resistant type 1 fibers) (Ariano et al., 1973; Johnson et al., 1973).

1.3.3 AVAILABILITY OF METABOLIC SUBSTRATES

During high-intensity exercise adenosine triphosphate (ATP) and phosphocreatine provide an immediate but short-duration source of energy required for muscle activation (~8 seconds) (see Behm (2004) for review). At high intensities, longer durations, or limited oxygen supply where glycolytic activity exceeds the mitochondria's oxidative capacity, metabolic by-products such as adenosine diphosphate (ADP), inorganic phosphate (Pi), creatine and hydrogen ions (H+) accumulate (Behm, 2004). As more ATP derived from glycolysis is demanded, further H+ production and decrease of intra- and extra-cellular pH will occur (Ament & Verkerke, 2009). Increasing concentrations of ADP, Pi, H+, and muscle acidity may decrease optimal cross-bridge interactions and impair ATP generation contributing to muscle fatigue (Ament & Verkerke, 2009; Behm., 2004; Fitss, 1994; Sahlin, et al., 1998).

1.3.4 STATE OF INTRACELLULAR MEDIUM

As mentioned previously, an intense or prolonged activity can lead to accumulations of ADP, Pi, H^+, and decreases in ATP availability. Fatigue is also influenced by changes in other intracellular metabolic substrates such as magnesium ions Mg^{2+}, ammonia NH_3, heat, and an increase in the efflux of potassium K^+ from the muscle fibers, as well as a decrease in glycogen, (Bigland-Ritchie, 1981; Boyas & Guével, 2011; Ament & Verkerke, 2009). It is suggested these mechanisms interact and progressively develop leading to decreased muscle force and contraction velocity giving the effects of fatigue (Ament & Verkerke, 2009).

1.3.5 ALTERED BLOOD FLOW

Exercise initiates vasodilation of the local muscular vascular region (Garrett and Kirkendall, 1999), and changes in blood flow to active muscles are likely to affect performance (Crenshaw et al., 2000; Sahlin et al., 1998). Increases in blood flow are necessary to supply active muscles with substrates, evacuate metabolites, and dissipate heat (Boyas and Guevel, 2011). However, intense muscle contraction increases intramuscular pressure and compresses the blood vessels, decreasing the blood supply to the active muscles, possibly even causing complete ischemia (Boyas and Guevel, 2011). It has been demonstrated by Crenshaw et al., (2000) that higher intensity contractions lead to a faster onset of ischemia. This leads to a rapid reduction of the oxygen supply, promoting anaerobic metabolic pathways causing a more rapid accumulation of muscle metabolites thus accelerating fatigue (Boyas and Guevel, 2011; Crenshaw et al., 2000; Sahlin et al., 1998, Sjogaard et al., 1998).

Exercise modalities allowing blood flow and oxygen to return to the muscles during brief relaxation periods may allow for more ATP to be supplied allowing higher effort contractions to be maintained for longer durations (Allen et al., 2008). In addition, the amount of recovery is likely related to the tie period of relaxation (Bellemare and Grassino, 1982). Thus, while altered blood flow might not be a direct mechanism of fatigue, it may exacerbate and increase the rate of fatigue.

1.4 CENTRAL FATIGUE

A progressive reduction in voluntary activation of muscle during exercise is termed ‘central fatigue’ and can be defined as the decrease in central drive to the motoneurons (Gandevia, 2001), which involves a decrease in recruitment and firing rates (rate-coding) leading to decreased activation of the muscle (Fulton et al., 2002). Changes in CNS excitation can affect conscious,

voluntary activation (VA) and neural drive affecting the motor unit pool and performance (Enoka & Stuart, 1992). The ability to voluntarily activate muscles is strongly influenced by interacting spinal and supraspinal changes in excitation (together, corticospinal excitability (CSE)), which can be decreased with exercise-induced fatigue delivering a net decrease in neural drive to the motoneuron pool or motoneuron responsiveness (Gandevia, 2001; Taylor & Gandevia, 2001), even in the absence of visible performance deficits such as loss of force (Aboodarda et al., 2015a,b; Behm, 2004). Central fatigue appears to contribute more significantly to the decrease in force generation during low-intensity exercise than peripheral fatigue (Millet and Lepers, 2004). Central fatigue may involve a drop in the central command (motor cortex, motoneurons) elicited by the activity of cerebral neurotransmitters and muscle afferent fibers, as well as decreases in motivation to continue (Boyas & Guével, 2011).

Voluntary activation (VA) is the level of neural drive to muscles during a voluntary action (Gandevia, 2001). VA measures central fatigue of the CNS and net interactions between spinal and supraspinal factors (Belanger & McComas, 1981; Gandevia 2001). While VA has demonstrated an inability to fully activate motor units during maximal effort tasks (Gandevia 2001), it is also been shown to vary among individuals, trials, days, and muscles (Allen et al., 1995; Belanger & McComas, 1981). In addition, muscle function and fiber type composition seem to play a role, with type II dominant (fast-twitch) quadriceps being more difficult to fully activate than the type 1 (slow twitch) dominant plantar flexors, dorsiflexors (Behm et al., 2002; Johnson et al., 1973). It is suggested this is possibly due to Henneman's size principle (1973) of motor unit recruitment and the type II motoneurons which would have higher recruitment thresholds, making them more difficult to fully activate. It is also worth noting that the ability to repeatedly sustain maximal efforts often depends on the motivation and training background of the participant

(Bigland-Ritchie et al., 1983). A lack of motivation has been shown to reflect a progressive reduction in effort during exercise (Gandevia, 2001). Thus, a full voluntary activation may be unlikely, and changes in activation with fatigue can give valuable insight into the development of central fatigue.

VA is commonly estimated using a single supramaximal electrical stimulation stimulus to the motor nerve during an isometric voluntary contraction (interpolated twitch technique (ITT)) (Merton, 1954) and stated that additional stimulation should not result in additional force if the muscle is fully activated, meaning all motor units have been recruited and are at maximum firing frequency. An increase in force following the electrical stimulation suggests a change in the ability of the CNS to activate the motoneuron leading to incomplete excitation of all motor units (recruitment), and/or the units were firing at a submaximal frequency (rate coding), indicating a decrease in VA, or a lack of motivation (psycho-physiological)(Behm et al., 1996). The larger the increase in force following stimulation demonstrates a lower level of VA and a greater decrease in neural drive (Loscher et al., 1976). While the ITT is useful for detecting voluntary activation, it does not distinguish between sites of central fatigue, only if a net effect exists (Gandevia, 2001).

Central fatigue development is accompanied by decreases within the motor cortex and motoneurons. The presence of fatigue decreases the amplitude of the motor evoked potential (MEP) (short-latency excitatory responses) and increases the length of the EMG silence (‘silent period’) which is a period of EMG quiescence following a MEP during a voluntary contraction to transcranial magnetic stimulation (TMS) of the motor cortex that can last longer than 200 milliseconds (Taylor and Gandevia, 2001). The silent period may represent both inhibitions of descending drive and decreased excitability of the motoneurons which can theoretically lead to a decrease in force (Taylor and Gandevia, 2001). TMS is a non-invasive and relatively painless

technique that can elicit targeted depolarization of axons and cell bodies in the motor cortex (Barker et al., 1985; Brasil-Neto et al., 1993) generating a corticospinal volley that results in contraction of one or more skeletal muscles. Increases in MEP by TMS demonstrate inadequate descending drive from the motor cortex that is overcome by an applied external magnetic stimulation (Taylor and Gandevia, 2001). TMS alone however does not distinguish between the sites of fatigue between the motor cortex and the motoneuron, only demonstrating the inhibition at the motor cortex plays a role (Taylor and Gandevia, 2001).

While TMS can be used to examine overall central fatigue from the motor cortex to the motoneuron, it cannot alone distinguish between sites. However, spinal stimulation below the motor cortex to the descending axons of the corticospinal tract and corticomedullary junction of the muscle(s) of interest elicits a corticomedullary motor evoked potential (CMEP), which have large monosynaptic components and can be used to test motoneuron excitability (Taylor, 2006). CMEPs activates motoneurons synaptically and evokes a short-latency excitatory response that can be recorded from muscle EMG (Taylor, 2006). TMS coupled with CMEPs allows the distinction between supraspinal and spinal influences on fatigue.

As earlier suggested by Bigland-Ritchie (1981) many possible sites within the CNS can result in fatigue effects, as well effects in non-exercised muscles, such as activation of the primary motor cortex; propagation of the command from the central nervous system to the motoneurons; and activation of the motor units.

1.4.1 PRIMARY MOTOR CORTEX

One of the causes of decreased central command during prolonged exercise could be the decreased excitation supplied by the motor cortex (Gandevia, 1998; Taylor et al., 2006).

Supraspinal fatigue refers to an exercise-induced decline in performance by suboptimal output from the motor cortex (Gandevia et al., 1996). The causes of supraspinal fatigue are poorly known although there are two generally accepted categories; mechanisms that reduce descending drive from the motor cortex, and mechanisms that decrease the efficacy of output from the motor cortex (motor drive decreases or becomes less effective) (Taylor and Gandevia, 1996). Mechanisms that decrease the output from the motor cortex are likely influenced by changes in properties of corticospinal neurons or input to corticospinal neurons which have been shown to decrease with fatiguing exercise (Gandevia, 2001, Gandevia et al., 1996).

Supraspinal fatigue may be linked to the depletion or accumulation of certain brain neurotransmitters. For example, exercise increases tryptophan entry into the brain increasing serotonin [5-HT] activity limiting central command and recruitment of motor units as well as giving the sensation of sleep, and relaxation (Jacobs and Azmitia, 1992; Newsholme et al., 1987). In addition, during exercise the plasma concentration of ammonium increases (Nybo et al., 2005) and affects cerebral brain blood flow, the activity of certain neurotransmitters, and synaptic transmission (Davis & Bailey, 1997; Felipo & Butterworth, 2002; Nybo et al., 2005; Nybo & Secher, 2004). Glycogen could also play a role in central fatigue because a decrease in central activation is associated with a drop in brain glycogen (Dalsgaard et al., 2002; Dalsgaard et al., 2003; Nybo, 2003; Swanson et al., 1992). It has also been suggested that increases in adenosine and gamma-aminobutyric acid [GABA] an inhibitory neurotransmitter with exercise plays a role in the development of central fatigue by decreasing descending neural drive (Guézennec, 2000; Tergau et al., 2000).

It may also be suggested that muscle afferents limit cortical activity. Pitcher & Miles (2002) demonstrated that supraspinal fatigue (as evidenced by a decrease in the motor-evoked potentials)

could be modified by muscle afferents, particularly group III/IV. Gandevia (2001) suggested that feedback on the muscles' biochemical status and force generation capacity is likely to reduce stimulation from cortical sites. Gandevia et al., (1996) demonstrated using ischemia that supraspinal fatigue persisted, and corticospinal and motoneuron activities appear to recover (Butler et al., 2003). It is likely that excitation changes to the brain will affect non-exercised as well as the exercised areas.

1.4.2 SPINAL MECHANISMS

Central fatigue at the spinal level can be caused by several mechanisms that lead to a decrease in the firing rates of motoneurons (Boyas & Guevel, 2011). Three interacting actions that lead to fatigue of the motoneuron include; a decrease in excitatory input; an increase in inhibitory input; and decreased responsiveness of the motoneuron (Taylor and Gandevia, 2008). Motoneuron activity can be affected by afferent influences (Behm, 2004). Inhibitory afferents from intramuscular receptors such as group III/IV muscle afferents (metaboreceptors), Golgi tendon organs (group Ib afferents), and decreases spindle activity (group Ia and II afferents) appear to be involved in the inhibition or disfacilitation of motoneuron activity (Avela et al., 1999; Gandevia, 1998; Kaufman & Rybicki., 1984; Macefield et al., 1991; Martin, 2006; Woods et al., 1987). It has also been shown that motoneuron discharge rates can be altered by peripheral reflexes in response to fatigue-induced metabolic variations within the muscle (Bigland-Ritchie et al., 1986) and intrinsic properties (Kernell & Monster, 1982; Daniel Kernell, 2006) such as late adaptation (Gardiner, 2001), and Renshaw cells (Hultborn et al., 1988).

Group III/IV muscle afferents (metaboreceptors) which are stimulated by ischemia (Lagier-Tessonnier et al., 1993), hypoxemia (Arbogast et al., 2000) and the extracellular accumulation of potassium (K+) and lactate (Darques et al., 1998; Rotto & Kaufman, 1988) may inhibit the alpha

motoneurons (Kaufman & Rybicki., 1984; Martin, 2006; Woods et al., 1987). Muscle spindle activity (group Ia and II afferents) that provide information on the muscle's length and changes in length (Proske & Gregory, 2002) decreases increasingly with prolonged submaximal contractions (Macefield et al., 1991), repeated contractions, or stretching (Avela et al., 1999). Golgi tendon organs (group Ib afferents) provide the CNS with feedback on muscular tension (Proske & Gregory, 2002), and are suggested to inhibit neuronal activity (Gandevia, 1998).

The decrease in motoneuron activity could also be due to its intrinsic properties (Kernell & Monster, 1982; Kernell, 2006). A motoneuron may reduce its discharge rate in response to constant excitation or the stimulation of group III/IV afferents modifying the cell's discharge rate of the motoneuron in a process called late adaptation (Gardiner, 2001). Late adaptation has been described by Behm (2004) as a decrease in motoneuron firing frequency attributed to an outward current mediated by a calcium-activated potassium conductance.

Motoneurons may also be inhibited by recurrent inhibition of Renshaw cells, which provide spinal inhibition relative to motoneuron excitatory inputs (Gandevia, 1998), as well as descending and peripheral influences. It has been suggested that Renshaw cell inhibition increases during maximal efforts (Kukulka et al., 1986). It is likely that the spinal mechanisms from muscle reflexes will more greatly affect the local musculature as they are more directly linked to the exercised limb than non-exercised muscles.

1.5 PATHWAYS OF NLMF

As peripheral fatigue is limited to the exercised muscle, central fatigue can help distinguish between the local and systemic effects of non-exercised limbs. Exercise of an affected limb has been shown to lead to fatigue of non-exercised limbs (Halperin et al., 2015). This phenomenon has

been termed crossover fatigue when the non-exercised limb is a contralateral homologous muscle (Arora et al., 2015; Doix et al., 2013; Martin & Rattey, 2007) and termed non-local muscle fatigue (NLMF) when any contralateral (Halperin et al., 2014c) or ipsilateral (Kennedy et al., 2013), non-exercised muscle is adversely affected (Halperin et al., 2015). To better understand NLMF, it makes sense to look at some pathways in which the fatigue effects might occur. Halperin et al., (2015) in an extensive review suggest four key pathways that may be responsible for the effects of fatigue in non-exercised muscles, including; biomechanical, biochemical, neurological, and psychological, with effects primarily attributed to neural factors.

1.5.1 BIOMECHANICAL FACTORS

Biomechanical factors of NLMF are effects that could be attributed to deficits in the ability of the fatigued muscle groups to optimally stabilize the body while the non-exercised muscles are tested (Halperin et al., 2015). It is important to consider that synergist or antagonist muscles are excluded from non-local muscle consideration due to co-contractions during exercise which may lead to peripheral fatigue (Ben Othman et al., 2017; Paillard et al., 2010). Biomechanical effects of NLMF include an inability to perform a muscle testing activity due to an inadequate ability to stabilize the body by fatigued muscles either directly involved in the fatiguing exercise, or that act as stabilizers (Halperin et al., 2015). Although antagonists and synergists are often removed from NLMF consideration, it is difficult, if not impossible to eliminate the effects of stabilizers, neutralizers, or heterologous muscles, especially during high-intensity exercise. Exercise has been associated with co-contractions or motor irradiation of many muscles around the body (e.g. contralateral activity) that increase with contraction intensity (Dimitrijevic et al., 1992; McKay et al., 1996). Although the tested, non-exercised muscles are often monitored for activity (usually EMG < 5% MVC), muscles that may stabilize the body to perform maximally may be the same

for the fatigued and tested muscles. For example, the muscles of the trunk (abdominal and lower back) act to stabilize the body during upper and lower body exercises (Kibler et al., 2006).

In testing procedures where trunk stabilization may be necessary for optimal performance Ben Othman et al., (2017) and Paillard et al., (2010) demonstrated contralateral unilateral balance impairments followed by unilateral fatiguing protocols. Similarly, McLean & Samorezov, (2009) found unilateral leg landing compromised by a fatigued contralateral leg. In all these studies it is possible fatigue of the trunk muscles induced with the fatigue protocol interfered with the performance of the contralateral leg. Ciccone et al. (2014) examined the effects of squats alone or squats with bench press and bench row between sets (maintaining 3 minutes between squat sets) on squat repetition maximum and average power after three sets of four repetitions at 80% repetition maximum. The total number and average power of squats decreased with upper body exercise between sets, demonstrating a fatigue effect when involving multi-joint upper body movement. The back squat, bench press, and bench pull all recruit large muscle groups and some of the same muscle groups are needed to stabilize. Thus, fatigue in the squat average power and repetitions may be attributed to peripheral fatigue of some of the prime movers, stabilizers, or synergists involved in the squat but also recruited in the bench press or bench row.

The possibility of biomechanical issues also arises in seated tasks such as cycling. Baker & Davies (2009) demonstrated a 20% decrease in peak power output (PPO) when unable to use the handgrips to stabilize. Therefore, it is possible that fatigue of the handgrip muscles could lead to decreases in cycling PPO, or that muscles involved in the handgrip could be fatigued during cycling. Grant et al., (2014) demonstrated that fatiguing the elbow flexors before Wingate cycling decreased PPO by 1%, although nonsignificant ($p>.05$, ES = .3). While not statistically significant, for elite performance a 1% decrease due to a confounding variable can dramatically affect

performance. This type of fatigue effect is a confounding variable that is more likely to result during higher intensity, full-body, or bilateral movement where other areas of the body are forced to stabilize. This effect can be minimized using straps and braces to hold the body still as well as monitoring muscles of interest with EMG, however it needs to be considered by the fatiguing protocol and tested muscle groups and roles of muscles during the tasks.

1.5.2 BIOCHEMICAL FACTORS

Prolonged or repetitive testing contractions may lead to an accumulation of metabolic by-products such as potassium, hydrogen and blood lactate (Bangsbo et al.,1996; Bogdanis et al. 1994; Grant et al. 2014; Halperin et al. 2014b; Johnson et al. 2014; Nordsborg et al. 2003), which may be distributed globally via the cardiovascular and lymphatic systems potentially causing performance decrements in non-exercised muscles (Halperin et al., 2015). Intense upper body exercise has been shown to elevate lower body blood and muscle lactate [La-], hydrogen ions [H+], and potassium [K+] (Johnson et al., 2014) and decrease pH without decreasing lower body concentrations of ATP, phosphocreatine, and glycogen, which are critical in anaerobic power (Bangsbo et al., 1996). It is suggested that an increase in metabolite accumulation in non-exercised muscles may also cause a decrease in maximal power. These mechanism(s) may affect non-local exercise tolerance and may be caused in part by the effect of elevated plasma metabolites on previously resting leg muscle function (Cairns & Lindinger, 2008). With prior exhaustive upper body cycling, Johnson et al., (2014) demonstrated a decrease in leg maximal cycling power and time to exhaustion decreased 8% (ES = 1.42 and 1.4 respectively). However, they showed no decrease in critical power (power that evokes the highest sustainable rate of oxidative metabolism), suggesting that dispersed metabolites may play a role in maximal efforts while having little effect on submaximal efforts. Bangsbo et al., (1996) also reported a decrease in high-intensity exercise

time to exhaustion (27%, ES = 2.77) and a 35% increase in blood lactate with lower body cycling following upper body cycling. As well, Nordsborg et al., (2003) also noted a decrease in time to exhaustion (33%, ES = 4.3) with an increase in interstitial [K+].

Performing Wingate tests following arm cycling, Bogdanis et al., (1994) reported increased blood lactate and decrease peak power (5 and 10% in 1^{st} and 2^{nd} Wingate, ES = 2.1). Furthermore, Elmer et al., (2013) using a self-paced 10-minute unilateral lower-limb cycling before contralateral maximal lower-limb cycling and handgrip MVC and found no change in peak power, handgrip MVC, or blood lactate, suggesting that the fatigue protocol might not have had sufficient muscle volume (unilateral vs bilateral) to induce large enough concentrations of metabolites to cause effects in the contralateral muscles of the upper body. In contrast to the idea that global and non-local changes in pH and metabolites affect non-local tissues, Rasmussen et al., (2010) found no change in resting twitch (no evidence of peripheral fatigue) but found a decrease in MVC and VA (via Interpolated twitch technique: ITT) (5% and 15%, respectively), suggesting a decrease in central drive as the cause of decreased performance. These studies examining the effect dispersed metabolites affecting non-local muscles are mixed but seem to demonstrate a small effect, if any on submaximal or short-duration maximal efforts, with a more possible influence on maximal time to exhaustion exercise.

1.5.3 NEUROLOGICAL FACTORS

Fatigue-induced nervous system alterations present strong evidence for contributions to NLMF. Just as training specificity research demonstrated training adaptations are specific and strongly neural (Behm & Sale, 1993), it is likely then that the fatigue induced during exercise is both specific to the task and neural in nature. With fatigue, the extent of muscle inactivation can increase (Behm, 2004). This effect is also demonstrated in non-exercised muscles with decreases

in voluntary activation (VA) (Doix et al., 2013; Halperin et al, 2014c; Kennedy et al., 2013; Martin & Rattey, 2007; Post et al., 2008; Sidhu et al., 2014) despite any mechanical loading of the musculature. Some of the mechanisms likely involved in neurological effects of NLMF are the activation of group III/IV muscle afferents, changes in corticospinal excitability, and specific shared neural networks between muscles/limbs.

1.5.3.1 GROUP III/IV MUSCLE AFFERENTS

When considering that NLMF tests non-exercised or remote muscles, the effects of peripheral fatigue altering the metabolic environment in working muscles may lead to performance deficits in remote areas. As mentioned previously, the exercise of working muscles can lead to a progressive change of the metabolic environment and buildup of metabolic by-products, such as H+ which may lead to activation of group III/IV muscle afferents (Amann, 2011, 2012; Amann & Dempsey, 2008), which relay fatigue-related metabolic information to the CNS (Kaufman., 2002) and in turn may cause a global system inhibitory effect leading to decrements in the central drive to the non-working muscles.

It is proposed that progressive activation of group III/IV afferent stimulation may play a role in the central governor theory, which suggests that a process in the brain subconsciously regulates exercise by decreasing activation (i.e. recruitment and rate coding) of muscle fibers to prevent catastrophic failures and thus prevent injury (Noakes et al., 2004). Thus, a critical threshold might exist in the CNS in which progressing afferent sensory information can reach a sensory tolerance limit from stimulation of group III/IV muscle afferents, which provides inhibitory input to the CNS during sustained or repetitive exercise and inhibits neural drive to muscles resulting in fatigue (Amann et al., 2006). Supraspinal inhibition of cortical sites can also be induced by muscle biochemical feedback coming from force-generating sites (Gandevia, 2001).

To examine more closely the effects of group III/IV muscle afferents on the development of muscle fatigue, studies have used pharmaceutical blockades to reduce sensory feedback, or blood flow occlusion to enhance sensory feedback, however the results are speculative as the afferents are not measured directly, and there are methodological considerations. Sidhu et al., (2014) evaluated the effect of blocking group III/IV afferents using a μ-opioid receptor agonist on cyclic exercise at exhaustion and measured performance in elbow flexors. Maximum voluntary isometric contractions (MVC) and VA were decreased by 5% with a large effect size (ES = 1.2), while remaining unchanged when group III/IV afferents were blocked, suggesting an increased effect of group III/IV afferents. In contrast, Kennedy et al., (2015) placed a sphygmomanometer cuff around the upper thigh occluding blood flow to maintain metabolite level and enhance group III/IV afferent stimulation following a 2-minute isometric MVC of the knee extensor. No differences in MVC or VA were seen in the contralateral limb for either control or "cuff" protocol, suggesting the stimulation of group III/IV afferents failed to contribute to an observable difference. The discrepancy in the results from Sidhu et al., (2014) and Kennedy et al., (2015) could involve the mode, or exercise endpoint. Sidhu et al., (2014) used bilateral cycling until exhaustion (drop in pedal frequency below 80% of individual target cadence), which lasted approximately 9 minutes, however Kennedy et al., (2015) used a shorter, discrete 2-minute unilateral isometric MVC, where a pacing strategy to avoid fatigue-induced pain may have been employed, inducing less fatigue. Furthermore, Amann et al., (2013) used unilateral dynamic knee extensors to failure either with or without previous fatigue in the contralateral leg. Contralateral knee extensor MVC or bilateral handgrip MVC did not change, however, time to exhaustion decreased (49%, ES = 8.8). This suggests that non-exercised muscles may be able to overcome some amount of fatigue to produce a maximal effort such as a singular MVC, but when asked to sustain a more prolonged

effort, previous fatigue seems to affect in part from group III/IV afferent stimulation. A possible explanation for the presence/absence of NLMF effects ascribed to group III/IV muscle afferents may be due to the type of fatiguing exercise, and its relative intensity and duration, with longer, exhaustive exercise seemingly playing a bigger role as pain often limits exercise performance and a tendency to quit exercise when it becomes painful or uncomfortable (Halperin et al., 2015). While it is possible group III/IV muscle afferents at least play a role within NLMF, changes in the excitability of the corticospinal pathway should be examined for possible links to NLMF.

1.5.3.2 CHANGES IN CORTICOSPINAL EXCITABILITY

Exercise can excite or inhibit components or the entire corticospinal pathway depending on multiple factors such as time of measurement and muscles involved leading to NLMF effects (Halperin et al., 2015). Following fatigue, MEPs amplitudes of non-exercised muscles have been shown to both decrease (Takahashi et al. 2011; Stedman et al. 1998), demonstrating decreased central drive, or increase (Bonato et al. 1996; Takahashi et al. 2009, 2011) demonstrating a net excitation. Studies by Aboodarda et al., (2015) and Takashi et al., (2011) suggest that spinal excitability seem to increase during exercise while supraspinal excitability decreases leading to an overall decreased neural drive to muscles that likely spread to non-exercised muscles (Halperin et al., 2015).

Generally, during exercise MEPs are facilitated for a few seconds before a longer-lasting inhibition occurs (Lentz & Nielsen, 2002). Whole-body exercise to exhaustion involving large muscle groups has been shown to reduce corticospinal excitability (Fulton et al., 2002), and intracortical facilitation (a measure of excitability of inter-neuronal circuits within the motor cortex) (Tergau et al., 2000; Verin et al., 2004) of the exercised muscles suggesting higher intensity

or greater volume of fatigue may be required to offset any potential faciliatory changes that may occur, resulting in an overall decrease in corticospinal drive.

In non-exercised muscles, it is indicated that high-intensity muscle contractions can also affect the corticospinal pathway responsiveness and motor performance in muscles not directly contributing in the task (Aboodarda et al., 2015; Amann et al., 2013; Halperin et al., 2015; Kennedy et al., 2013; Kennedy et al., 2015; Sidhu et al., 2014; Takahashi et al., 2011). During intense bilateral leg press (3 sets of 50% MVC) until exhaustion Takahashi et al. (2011) demonstrated an increase in MEPs of the first dorsal interosseous and biceps brachii during the exercise protocol but decreased up to 20 minutes into recovery. Further supporting the role of high-intensity fatiguing exercise on MEPs comes from Sidhu et al., (2014) who showed that MEPs during a 25% elbow flexor MVC were facilitated with light exercise but decreased significantly following leg cycling exercise to exhaustion.

Following 3 sets of 50% MVC bilateral knee extensions to exhaustion, Šambaher et al, (2016) did not demonstrate a decrease in MEPs of the biceps brachii. However, a decrease in supraspinal motor responses was suggested to occur due to a decreased MEP/CMEP ratio, without a decrease in spinal motoneuron excitability which likely masked a decrease in MEP with an increase in spinal motoneuronal response. On the other hand, Aboodarda et al., (2017) demonstrated an increase in MEP/CMEP ratio following two unilateral knee extensor 100s isometric MVCs suggesting that the supraspinal effort increased with the biceps brachii with an increase in MVC. The supraspinal motor response was significantly higher during 100% MVC (42%, $p = 0.027$) but lower during 5% MVC (28%, $p = .009$) following the fatiguing protocol. This is consistent with that of Stedman et al., (1998) who found an increased cortical input to rested flexor digiti minimi at increasing intensity levels (10, 20, 30, 70%) while MEP to contralateral

flexor digiti minimi was increased likewise at all intensities. These findings suggest the increased excitability was at the cortical level and the effect on the contralateral motoneurons might be due to a transcallosal pathway that excites the contralateral hemisphere in reaction to facilitation to the activated side, presenting a possible “spreading effect” of central excitation across hemispheres. The increase in cortical responsiveness might help explain why Aboodarda et al., (2017) did not see an MVC deficit. Aboodarda et al., (2015) were interested in specifically identifying if changes in corticospinal excitability from a fatiguing muscle (unilateral or bilateral elbow flexion) to a non-exercised knee extensor were located spinally or supraspinal. A decreased CMEP/Mmax ratio response following 5 sets of MVC to below 20% demonstrated decreased central activation with no decrease in MVC. A lower electromyographic (EMG) signal following bilateral fatigue might have been due to a reduction in supraspinal motor output because spinal motoneuronal response demonstrated a higher value (30 seconds post-exercise) and peripheral excitability showed no change. Lower EMG following bilateral fatigue, combined with higher spinal motoneuron excitability (post-exercise) and no changes in peripheral excitability (Mmax amplitude) suggest a supraspinal mediated decrease in voluntary central drive that seems to be more affected with bilateral exercise. The observed decrease in post-exercise MEP might be due to a decreased spinal cord excitability (assessed using H-reflex) that has been shown to recover within 30s (Brasil-Neto et al., 1993), which is included in TMS evoked MEPs.

Thus, it seems that during exercise both spinal and supraspinal excitation changes lead to an increase in overall CSE, with an increasing contribution coming from cortical outputs with higher intensity contractions. When fatigue is induced, spinal excitability seems to recover quickly while supraspinal excitability remains decreased for longer periods, leading to a decrease in overall CSE, which seems to be greater with more intense contractions. This decrease in CSE to non-

exercised muscles might occur due to transcallosal connections (Bonato et al., 1996) and/or intra-segmental spinal connectivity (Carroll et al., 2006; Hortobágyi & Maffiuletti, 2011; Hortobágyi et al., 2003).

1.5.3.3 SHARED NEURAL NETWORKS

It also seems that neural wiring between different muscle groups in the body might induce or prevent NLMF effects within shared neural networks. The cross-extensor reflex (Sherrington, 1910), cross-education (Carroll et al., 2006), and locomotor central pattern generators (Guertin, 2013) in contralateral extensor and flexors are possible examples that might be intensity and phase-dependent.

There seems to be a stronger NLMF effect between homologous versus heterologous muscles. Several studies testing the contralateral homologous muscle demonstrate fatigue effects (Amann et al., 2013; Doix et al., 2013; Halperin et al., 2014c; Martin & Rattey, 2007). Evidence demonstrating fatigue in the non-exercised, contralateral homologous, but not heterologous muscle was shown by Bäumer et al., (2002) using pinch grips at 50% MVC until failure (inability to reach a 50% MVC). Intracortical facilitation of the right first dorsal interosseous was significantly reduced after fatigue to the non-fatigued hand, however, MEPs to the adductor digiti minimi supplied by the same nerve (ulnar) showed no change. This finding suggests that there might be a direct link between contralateral homologous muscles that is mediated supraspinally through transcallosal inter-hemispheric interactions that reduce motor output to homologous muscles but not heterologous muscles (Baumer et al., 2002; Halperin et al., 2015).

An upper and lower body shared neural network might be related to locomotive type movements and gait. Huang (2004) investigated neuromuscular recruitment of the arms and legs

at different intensities and with different demands on the upper/lower body using a recumbent stepper. Active upper limb movement increased neuromuscular activation of the lower limbs during passive cyclic stepping, and the activity in the legs increased as the intensity of the upper body cycling increased. In addition, Kam et al., (2013) noted that EMG of flexors/extensors in the lower limbs appeared to coincide with the pattern of gate (e.g. lower leg extensors more highly activated during extension) suggesting a possible phase dependency of activation. While these studies examined the influence of locomotion movement of the arms with muscle activity in the leg, based on other research that demonstrated NLMF effects, it is likely with high-intensity volume to exhaustion that fatigue might also be induced from the upper to lower body in cyclic tasks. Halperin et al., (2015) in their NLMF review suggest that NLMF may be more predominant with the lower rather than the upper body musculature possibly because of differences in neural networks. While both the upper and lower extremities are connected by central pattern generators (Guertin, 2013; MacKay-Lyons, 2002), due to other factors the lower limbs can be more difficult to fully activate (Behm et al., 2002), and are activated less frequently (Kern et al., 2001) leading to increased susceptibility to NLMF.

NLMF studies fatiguing upper limb musculature and testing lower limb musculature have shown greater consistencies of fatigue (Aboodarda et al., 2015; Bangsbo et al., 1996; Kennedy et al., 2015) than lower body fatigue protocols exhibiting fatigue effects to the upper body (Decorte et al., 2012), but is not always the case (Rasmussen et al., 2010; Sidhu et al., 2014). A study by Bouhlel et al., (2010) fatigued either upper or lower body with brief, maximal cycling, and tested the opposite with the same protocol. The lower body demonstrated a peak power decrease of 4% following upper body fatigue, while the upper body demonstrated a 4% increase following the lower body protocol, suggesting that the lower body might be more susceptible to NLMF.

1.5.4 PSYCHOLOGICAL FACTORS

Just as performance and physiological variables are considered in fatigue, so too should perceptual responses (Borg, 1990; Enoka & Duchateau, 2016). Mental fatigue is a centrally mediated psychobiological state caused by prolonged periods of demanding cognitive activity and characterized by subjective feelings of "tiredness" and "lack of energy" (Boksem & Tops, 2008). Performance due to psychological factors and depend on the level of motivation at the time of activity or memory of previous experiences performing the task, mental fatigue (Boksem and Tops, 2008; Marcora, et al., 2009), and/or specific details of the task such task intensity (e.g. maximal vs. submaximal contraction) (Taylor and Gandevia, 2008).

Studies often use a rate of perceived exertion (i.e. effort and exertion) (RPE) to subjectively measure the psychological strain involved with a task. RPE encompasses the overall perceived exertion including the many signals from the peripheral working muscles, the cardiovascular and respiratory functions, and CNS (Borg, 1982). The perception of effort tends to increase with the duration and intensity of the physical work (Borg, 1990). Thus, it seems that exercise performance may be at least partly limited by perception of effort rather than contraction factors as individuals may withdraw from a task when it is perceived as too difficult, or exceeds their limit of desire (Wright, 2008), and intense cognitive effort has been shown to decrease exercise performance (Marcora et al., 2009). However, Pageaux et al., (2013) did not show mentally fatiguing tasks decrease discrete MVC but observed a decrease in time to exhaustion with the knee extensors after a mentally fatiguing task, suggesting perception of effort might have a greater observable impact on sustainable effort than a short duration maximal effort. In addition, Hamilton and Behm, (2017) demonstrated that an unknown test endpoint after contralateral fatigue resulted in a decrease in strength-endurance, due to a possible pacing strategy. Thus, it can be suggested that testing

endpoint should be known to allow participants to perform maximally. When participants knew they only had a 5-s MVC, they were able to maintain or even increase their effort in response to contralateral fatigue. The known endpoint conditions likely provided higher motivation, which has been shown to enhance self-control and help overcome performance impairments due to fatigue (Hagger et al., 2010). Even when every effort is intended to be maximal, higher forces can be produced when an individual is aware of a more immediate and known endpoint (Halperin et al., 2014; Hamilton and Behm, 2017).

Exercise also has a cognitive component and can affect non-exercised muscles. This is an observation also noted by Amann et al., (2013) who found an increase in RPE at the onset of exercise of the contralateral knee extensors after prior exhaustion of the ipsilateral leg, that was non-existent without fatigue. It was suggested that the increase in perceived exertion was arising from the fatigued leg and played a role in the significant decrease (49%, ES = 8.8) in time to exhaustion and increase in VO_2 and heart rate from the onset of exercise. Since MVC of contralateral knee extensors and bilateral handgrip MVC were unaffected, this study suggests that increases in psychological stress seem to play a greater role in sustained actions versus singular maximal efforts. Elmer et al., (2013) who also failed to find an MVC effect with contralateral muscle fatigue, also noted no change in RPE. This was likely due to the training background of their participants who were competitive cyclists who would be less likely to view 10 minutes of high intensity cycling as particularly stressful of painful.

1.6 NLMF FACTORS

Understanding that many interreacting physiological factors may contribute to NLMF effects, it is pertinent to consider how the research methods and confounding variables might contribute to the extent and presence of NLMF. Halperin et al., (2015) recognized that about 50%

of NLMF studies demonstrated effects. The questions then become apparent, what is causing the discrepancy in the research? Attempting to better understand mechanisms and effects relevant to their specific research question, researchers have manipulated many factors to examine NLMF and many methodological procedures. The effects seem to depend on factors such as the quantification of fatigue, exercise intensity, exercise volume, contraction mode, as well as the muscle groups tested. The wide use of different protocols both creates trends in the literature as well as introduces more questions involving NLMF.

1.6.1 FATIGUE QUANTIFICATION OF THE NON-EXERCISED MUSCLE

One likely cause of the discrepancy in the NLMF literature could be the way the non-local effects are monitored. Because the definition of fatigue has many components and definitions, it can be manifested in many ways in research. The most common measure used to determine whether fatigue has occurred is an MVC, which is "a maximal contraction that a subject accepts as maximal and that is produced with appropriate continuous feedback of achievement" (Gandevia, 2001). For example, some studies using singular MVCs have reported no effects (Arora et al., 2015; Decorte et al., 2012; Elmer et al., 2013; Grabiner and Owings, 1999; Halperin et al., 2014; Halperin et al., 2014; Kennedy et al., 2015; Paillard et al., 2010; Triscott et al., 2008; Zijdewind et al., 1998), while some have reported decrements (Aboodarda et al., 2015; Doix et al., 2013; Martin and Rattey, 2007) suggesting some methodological differences or that a single MVC does not highlight the full fatigue profile. As well, peripheral feedback has been suggested to be the key mediator of performance impairments at maximal intensities or shorter durations (Amann et al., 2013; Weir et al., 2006), and central fatigue during longer duration exercise (Boyas and Guével, 2011). Since peripheral fatigue is not induced in the tested non-exercised limb, it makes sense then, that short duration tasks like a singular MVC might not detect effects where repeated or sustained

tasks might. Prolonged testing demands more persistent neural input, which could exacerbate global neural failure (e.g. inter-hemispheric and/or corticospinal inhibition), and afferent inhibition of spinal and cortical motoneurons (Behm, 2004). For example, studies that use multiple MVCs (Halperin et al., 2014b; Rasmussen et al., 2010), time to exhaustion (exercise endurance) (Amann et al., 2013; Triscott et al., 2008), or voluntary activation (Todd et al., 2003), seem more likely to demonstrate effects that are not apparent with a single maximal voluntary contraction (MVC). Halperin et al., (2015) suggested that quantification methods that stressed multiple physiological pathways (neurological, biochemical, biomechanical, psychological) might provide a more observable net fatigue. These alternate methods of performance decrement detection justify the expanded definition of neuromuscular fatigue into an increased effort to sustain performance, regardless of whether it can be maintained.

Because neuromuscular fatigue includes any increase in real and/or perceived difficulty of a task or exercise (MacInstosh et al., 2006) and begins with the onset of exercise before any visible performance decrements occur (Allen et al., 2008) a decrease in voluntary activation (VA) from the CNS might occur in non-local limbs absent of any performance decrements such as loss of force (Aboodarda et al., 2015a,b; Behm, 2004). While an observable force decrement is not always demonstrated, a decrease in central drive may be present. Todd et al., (2003) found no decrease in force production during a sustained MVC but demonstrated a decrease in VA by ITT (2.8%). Several studies have demonstrated a decrease in VA with a decrease in force demonstrating a positive correlation in decreases in central neural drive and NLMF (Doix et al., 2013; Halperin et al., 2014b; Kennedy et al., 2013; Martin and Rattey, 2007). It is possible Todd et al., (2003) never noticed a decrease in force because the fatigue protocol demonstrated a decrease in VA of (2.9%), which was much lower than Doix et al., (2003) (6 and 9%), Halperin et al., (214b) (4.5 and 5.5%),

Kennedy et al., (2013) (15%), and Martin and Rattey (2007) (9%) that have demonstrated decreases in force and VA. In addition, Todd et al., (2003) suggested the similar voluntary force in the contralateral leg despite decrease VA might be due to systemic factors such as elevated adrenaline (Williams and Barnes, 1989) or blood pressure which increases contraction force (Hobbs and McCloskey, 1987; Wright et al., 2000).

It has been demonstrated that NLMF may have greater effects on repeated or sustained exercise than on single attempts of maximal force production, suggesting that NLMF effects may affect fatigue resistance more than a single maximal contraction (Halperin et al., 2015). While repeated MVCs can refer to brief, singular maximal contractions separated by very brief recovery periods (Halperin et al., 2014b), ‘‘limit of endurance time’’ can be defined as the length of time over which a muscle may be exercised to the point of exhaustion (inability to perform to some relative or absolute criteria) (Triscott et al., 2008). It is possible that a decreased neural drive from fatigue may be overcome by motivation for a single discrete contraction, but that prolonged or repetitive contractions stress several physiological systems to a greater extent exposing the fatigue effects (Halperin et al., 2015). Because fatigue is present and progressing from the onset of the task regardless of whether force can be maintained (Bigland-Ritchie et al., 1986), it may be demonstrated in difficulties in sustaining performance as well as a single, discrete deficit in force. Prolonged or sustained contractions require more persistent neural input, which may amplify fatigue mechanisms such as inter-hemispheric and/or corticospinal inhibition, muscle afferent inhibition to spinal and cortical motoneurons, and a greater accumulation of metabolic by-products that may travel to nonlocal muscles giving the effect of fatigue (Behm, 2004; Halperin et al., 2015).

When examining repeated MVCs (Halperin et al., 2014b) demonstrated no change in a single MVC following contralateral fatigue, however in the last 5 of 12 MVCs (separated by 10s),

a 5% decrease (ES = .58) was demonstrated. As well, Halperin et al., (2014a) noted a more marked force decrease during the first 6 MVCs (13%), and a plateau in force over the last 6 MVCs (3% decrease), suggesting a decrease in fatigue resistance that appears to reach a plateau versus a constant decrease. Similarly, Amann et al., (2013) found no decrease in contralateral MVC or handgrip MVC. However, time to exhaustion following fatigue of the contralateral leg decreased 49%. This study suggests the multisystem strain of constantly calling effort from the motor system to muscles seems to affect endurance exercise but not single MVC performance. Triscott et al., (2008) also found no decrease in a single MVC following a unilateral fatigue protocol but reported a 20% decrease in time to exhaustion. Hamilton and Behm, (2017) however demonstrated an increase in singular MVC force following contralateral fatigue, demonstrating a potentiation rather than inhibition to the opposite limb. However, during a sustained strength-endurance 30s MVC an overall 12% decrease in force was demonstrated. Kawamoto et al., (2014) also noted an 8.8% (ES = .29) decrease in isometric time to exhaustion using 70% of MVC with a minor decrease in singular MVC (7.1%, ES = .53).

1.6.2 EXERCISE INTENSITY OF THE INTERVENTION

Contraction intensity is often used as a measure of how hard the muscle(s) is working to achieve a desired outcome. In resistance training, it is often referred to as the percentage of one-repetition maximum (1RM) (Alcarez et al., 2008; Ciccone et al., 2014), but often refers to the relative percentage of MVC (%MVC) and refer to the magnitude of effort coming from neural drive and peripheral factors to cause a muscle action (Gandevia, 2001). Intensity seems to play a predominant role in fatigue as high-intensity activities using higher or maximal efforts decline the speed, force, and power outputs more than lower intensity protocols (Chidnok et al., 2013).

It has been demonstrated that higher intensity exercise is more likely to cause NLMF effects than low-intensity exercise when the same relative failure (Kennedy et al., 2013) or until exhaustion (Kawamoto et al., 2014) versus lower intensity submaximal exercise (Arora et al., 2015; Paillard et al., 2010). Kawamoto et al., (2014) compared four sets of 70% and 40% MVC dynamic knee extensions until failure on contralateral knee extensor performance force and time to exhaustion. They found greater force decrements after the high (70%) versus low (40%) protocols (7.1% ES = .53, 4.4% ES = .29, respectively). They also a much faster time to exhaustion in the high versus low intensity protocol (8% ES = .29 vs 2% ES < .01, respectively). Kennedy et al., (2013) compared 100% and 30% bilateral isometric handgrip MVC until failure (20% decrement) and their effect on MVC immediately and 2-minute post-fatigue, as well as voluntary activation (VA). The maximal protocol resulted in an immediate (23%) and 2-minute post (10%) MVC decrement versus an immediate (8%) and 2-minute (7%) for the submaximal protocol. As well, the VA was greater affected following the maximal protocol (15%) versus the submaximal (2%). It has also been demonstrated that lower intensity protocols are less likely to induce MVC effects at 30% (Arora et al., 2015) and 10% (Paillard et al., 2010) whom both tested the contralateral knee extensors, while maximal protocols demonstrated effects (Doix et al., 2013; Martin and Rattey, 2007). The greater deficits in force and VA with higher intensity protocols might be due to greater stress placed on the CNS (Rasmussen et al., 2010).

Intensity might be a greater factor in the lower body versus the upper body as a larger amount of muscle mass is used (Post et al., 2008). The lower body seems more susceptible to effects than the upper body possibly due to larger, harder to activate lower body muscles such as with the greater number of muscle fibers in the quadriceps) (Bouhlel et al., 2010; Humphry et al.,

2004). Bilateral exercise causes greater effects than unilateral exercise possibly due to the total amount of exercise or work performed (Aboodarda et al., 2015).

1.6.3 EXERCISE VOLUME OF THE INTERVENTION

Exercise volume refers to the total amount of exercise performed. It can be quantified as the total contraction time or time under tension in a given period (Fleck and Kraemer, 1997). The amount of time in which the exercise is ongoing may also affect NLMF effects. Longer, sustained contractions lead to greater central fatigue effects than shorter higher intensity contractions (Gandevia, 2001). This is likely due to the total duration a lower intensity exercise protocol can be sustained, requiring a longer neural input demand, where central fatigue likely become the limiting factor for exercise, while shorter, higher intensity contractions can only be sustained for shorter periods and likely limited by peripheral fatigue mechanisms (Bigland-Ritchie et al., 1978; Gandevia, 2001).

One hundred seconds has been shown to induce contralateral knee extensor deficits in MVC and VA using sustained isometric contractions (Doix et al., 2013; Martin and Rattey, 2007 [male subjects]). However, 100-second contractions have not been shown to induce contralateral single MVC effects (Martin and Rattey, 2007 [Female subjects]; Halperin et al., 2014c) or sustained force (Todd et al., 2003). It seems NLMF is greater with an increased exercise volume. When shorter and longer durations are compared the longer protocol seems to induce greater effects. Doix et al., (2013) and (Halperin et al., 2014c) used one of two, 100s maximal contractions of the knee extensors before testing MVC and VA, or by Humphry et al., (2004) using unilateral bicep curls to exhaustion and 25% of that time to exhaustion. It can be suggested that giving the

same relative intensity with a longer contraction volume will accumulate more total fatigue through the stress of multiple physiological systems leading to an observable NLMF effect.

1.6.4 CONTRACTION MODE

Many methods of exercise have been used in non-local muscle fatigue literature, including isotonic (concentric and eccentric), isometric, isokinetic, and cyclical (locomotive action with the upper or lower body) (Halperin et al., 2015). Many studies use isometric protocols (Aboodarda et al., 2015; Arora et al., 2015) or cyclic (Bogdanis et al., 1994; Bouhlel et al., 2010; Decorte et al., 2012) protocols with fewer studies using isotonic contractions (Alcarez et al., 2008; Amann et al., 2013; Ciccone et al., 2014), with only three studies (to my knowledge), using isokinetic contractions (Ben Othman et al., 2017; Grabiner and Owings, 1999; Strang et al., 2009). The type of contractions used in the fatigue protocol seems to affect the presence of NLMF, with isometric and cyclical contractions tend to increase NLMF effects compared to isotonic contractions (Halperin et al., 2015). However, the lack of volume of studies using other methods, other methodological considerations, as well as a lack of studies comparing methods, make drawing conclusions based on contraction mode premature (Halperin et al., 2015).

Isometric contractions occur when resistance prevents motion and no visible shortening of the muscle occurs (Baechle et al., 2008), allowing maximal loading during the entire contraction protocol, but only at one point in the joint range of motion. Isotonic contractions consist of concentric (muscle shortening) or eccentric (muscle lengthening) actions involving exercise through a joint range of motion with a set resistance that is constantly varied due to physiological levers (Smith and Merton, 1981). Isokinetic contractions involve movement throughout a joint ROM with a constant angular velocity and the resistance is varied by the forces exerted against the device. Isokinetic actions accommodate for pain and fatigue while maximally loading a muscle

throughout a full range of motion allowing the muscle to experience greater torque at stronger ranges of motion and less torque at weaker ranges, where repetition failure would occur with isotonic or isometric actions (Smith & Merton, 1981). The variable to be manipulated is the velocity of muscle shortening or lengthening, and not the resistance load itself. The resistance becomes proportional to the dynamic tension produced through the ROM, or torque, and can be constantly measured by an isokinetic dynamometer. Cyclic exercise consists of locomotive type actions involve phasing opposite and alternating patterns of the arms and/or legs (Bouhlel et al., 2010; Elmer et al., 2013; Huang, 2004; Kam et al., 2013).

Isometric protocols have been used by many researchers in NLMF research to demonstrate effects (Aboodarda et al., 2015; Doix et al., 2013; Halperin et al., 2014b, c; Kennedy et al., 2013. 2015). One suggestion as to why isometric protocols cause a greater consistency to show NLMF effects is the inhibition of blood flow to the area (Halperin et al., 2015), whereas isotonic, isokinetic, or cyclic contractions often have brief recovery periods or passive phases of contraction permitting intermittent blood flow.

Cyclic protocols have also been regularly used in NLMF research (Bogdanis et al., 1994; Bouhlel et al., 2010; Bangsbo et al., 1996; Johnson et al., 2014; Nordsborg et al., 2003), usually consisting of bilateral leg cycling or arm cranking (Bouhlel et al., 2010) or unilateral leg cycling (Elmer et al., 2013). Cycling effects might be predominant in NLMF due to a large amount of muscle mass used (entire lower or upper musculature, as well as trunk) and high demand on cardiovascular responses which might also cause NLMF effects due to cerebral deoxygenation causing a decrease in oxygen flow to the brain decreasing neural drive to the muscles (Rasmussen et al., 2010). While there are brief recovery periods of working muscle during cycling as the opposite limb contracts, large muscle groups are constantly in use as well as co-contractions and

antagonist contractions which may increase overall work performed leading to a greater overall development of fatigue. Elmer et al., (2013) who used unilateral leg cycling and did not find a decrease in handgrip MVC or peak power during a 4.5-second maximal cycling task, while other studies using bilateral leg cycling found decreases in handgrip (Decorte et al., 2012) and peak power output (Bouhlel et al., 2010).

Isotonic contractions have been used by researchers to observe NLMF in such modalities as unilateral knee extensions (Amann et al., 2013; Kawamoto et al., 2014), bilateral knee extensions (Halperin et al., 2014b; Šambaher et al., 2016) squats (Ciccone et al., 2014), bilateral elbow flexing (Grant et al., 2014), unilateral elbow flexion (Humphry et al., 2004; Triscott et al., 2008) plantar flexion (Alcarez et al., 2008). Isotonic contractions seem less likely to demonstrate NLMF effects than cyclic or isometric (Halperin et al., 2015). One likely reason is the impact of brief recovery periods during the return phase of isotonic contractions which is absent during sustained isometric protocols. In addition, isometric contractions allow a constant torque to the muscle, while isotonic contractions have changing torque to the muscle do to a changing joint angle as well as altering length tensions relationships of the muscle, resulting in inconsistent loading to the muscles.

Only three studies (to my knowledge) have used isokinetic contractions to evaluate NLMF effects (Ben Othman et al., 2017; Grabiner and Owings, 1999; Strang et al., 2009). Grabiner and Owings, (1999) used either 75 (3 sets of 25 repetitions: about 3 mins of contraction time) unilateral knee extensions or eccentric flexions of the quadriceps at $30°.s^{-1}$. Their results failed to demonstrate crossover fatigue with the concentric protocol, and surprisingly demonstrated an increase in eccentric MVC with the eccentric protocol (11%). It can be suggested that although three minutes of contraction time seems sufficient to induce crossover effects, the 1:1 work-rest

ratio associated with a passive return of the dynamometer might have caused central nervous system recovery to offset induced fatigue. Ben Othman et al., (2017) compared similar volumes (60 seconds of contraction time) of isometric 10 sets of 6s) and isokinetic (10 sets of 20 repetitions at $300°.s^{-1}$) protocols (with 10s rest in between sets) on unilateral knee extensors using intermittent MVCs in children (ages 10-13). MVC versus high speed isokinetic was used to help distinguish task specificity on fatiguability, and joint angle specificity was measured at 90° (MVC) and 120° as well for isokinetic actions. There was no significant difference in the response to the isometric- or isokinetic-fatigue intervention protocols. Results indicated that NLMF was evident with the contralateral knee extensor MVC at 90° ($p = 0.008$; 8.9%), knee extensor isokinetic torque at 90° ($p < 0.001$; 11.4%), and 120° ($p = 0.05$; 5.4% handgrip ($p = 0.06$; 4.5%), and elbow flexors ($p < 0.001$; 7.7%). There was an indication of angle-specific NLMF with knee extension MVC at 90° fatigue deficits but no significant MVC at 120° impairments. However, there was no evidence of task specificity as isometric and isokinetic fatigue protocols provided similar NLMF effects. While Grabiner and Owings, (1999) and Ben Othman et al., (2017) allowed a passive return of the dynamometer, Strang et al., (2009) used concentric/concentric unilateral knee extension/flexion to test contralateral knee extension and flexion MVC. Using seven sets of 20 repetitions at $110°.s^{-1}$ (piloting finding in which participants felt they were best able to produce maximal force without being limited by speed) their results demonstrated a significant ($p > .05$) increase in MVC of the contralateral quadriceps (12%, $p < .05$) with no change in the contralateral flexors. The finding is important as it demonstrates an unexpected increase in MVC following a fatiguing protocol of 229 seconds of contractions (1:1 ratio of extension and flexion). The authors suggested that although the fatiguing protocol was meant to induce fatigue of the exercising limb, which it did (20% and 18% decrease in extensors and flexors respectively), it seemed insufficient to cause fatigue to the

contralateral limb and may have caused a ‘warm-up effect’ (Strang et al., 2009). However, the pre-test MVCs may not have been true MVCs as there was no explicit warm-up prior, potentially accounting for a lower pre-test MVC.

Due to the unevenness in the number of studies using different contraction modes, it is difficult to make conclusions based on which mode is most likely to induce a NLMF effect. However, it seems that isometric and cyclical are most effective at inducing NLMF effects due to their constant contraction mode. Isometric activity can restrict blood flow and amplify the number of metabolites and afferent activity, while cyclic has an alternating phasic rhythmic pattern that allows constant contraction of agonists and antagonists in the same limb. Traditional isotonic activity has an uneven resistance along the exercise range of motion and allows the use of momentum, as well as a passive return, which may cause a decrease in the incidence of NLMF due to recovery. Finally, within isokinetic exercise, the passive return utilized by Ben Othman et al., (2017), Grabiner and Owings (1999) might help explain the minimal effects. However, Strang et al., (2009) who used concentric knee extensions and flexions did not notice a NLMF effect, therefore the area of NLMF and isokinetic exercise requires further exploration.

1.6.5 VELOCITY

A confounding variable involving dynamic contraction modes within the NLMF research is the velocity in which the fatiguing and testing contractions occur. NLMF may follow similar rules of velocity specificity as the exercised leg, and fatigue will be most affected at or near the exercise velocity. It is also possible that fatigue of primarily type 2 (fast) fibers with maximal intensity exercise might cause an inability of the type 2 fibers of the unaffected leg to perform at higher velocities versus type 1 (slow) and give the effect of fatigue due to the velocity requirement. With many studies using isometric contractions (velocity = distance / time = 0) they can be

excluded. In addition, isotonic or cyclical actions do not precisely control the velocity of movement throughout the range of motion and therefore can be excluded. A rising question to be answered is how the velocity of fatiguing contractions affect fatigue of the uninvolved limb. To control for a specific velocity of muscle action, the use of an isokinetic dynamometer must be used. Constant load actions such as free weights, do not produce constant resistance over the arc of motion because they require the greatest force at the beginning of the movement (weight plus inertia), a moderate amount in the middle (just weight), and the smallest force at the end (weight minus inertia). As well, length-tensions relationships during the arc of motions may allow greater forces to be exerted at different ranges of motion, altering the velocity of contraction. Thus, a constant resistance device such as a dynamometer allows minimal inertia and a fixed velocity of movement throughout a full range of motion.

It is difficult to establish comparisons between fatigue of different velocity contractions often due to a discrepancy in contraction times and/or work-rest ratios, which could both influence the extent of fatigue. Higher velocities result in faster repetitions, leading to a decreased contraction time or time under tension, influencing the amount of fatigue. Celes et al., (2009) reported greater losses in peak torque and total work with three sets of 10 ($60°.s^{-1}$ versus $300°.s^{-1}$ isokinetic knee extensions in the ipsilateral leg). However, contraction time was different for the two protocols. Therefore, to compare different velocities, repetitions need to be changed to equalize contraction time. When contraction time and work/rest ratio are controlled, higher velocity contractions have demonstrated a greater MVC decrease than a slower or isometric protocol, however, voluntary activation seems to be affected to a lesser extent, suggesting an increase in peripheral fatigue, but a decrease in central fatigue (Morel et al., 2015). This result occurred despite maximal isokinetic torque being shown to decrease with an increasing speed of

velocity, with isometric MVC torque demonstrating greater values at all angles as well as maximal dynamic torque at 180°.s-1 corresponding to only about 50% of maximal isometric torque (Thorstensson et al., 1976). As the speed of contraction increases, the ability to produce force decreases for concentric actions and increases for eccentric actions (force-velocity relationship) (Fenn and Marsh, 1935). For concentric actions, this is postulated to be due to the actin-myosin filaments kinetics with the filaments not having sufficient time to produce the optimal tension needed for full force (Burke et al., 1971; Edstrom and Kugelberg, 1968). Therefore, it might be suggested that a higher velocity fatiguing protocol may influence the contralateral leg to a lesser extent than a slower, or isometric protocol due to less development of central fatigue. However, the impact of contraction velocity in non-exercised limbs has not been directly studied.

Velocity specificity indicates that training adaptations of strength/power are greatest near the training velocity, but high-velocity training demonstrated greater transference to slow-velocity actions (Coyle et al., 1981; Kanehisa and Miyashita, 1983). One possible explanation is that higher velocity contractions appear to fatigue primarily type 2 fibers, which hypertrophy to cause increased force (Coyle et al., 1981; Thorstensson and Karlsson, 1976). EMG was added to a follow-up study and demonstrated a small increase in EMG (that plateaued at 75 contractions), despite a large decrease in MVC torque of 50% that seemed to plateau after 50 contractions. The increase in EMG could be due to an increase in motor unit recruitment (primarily type 1) and increase in the firing frequency. A positive correlation was found between initial torque, work, and power to the proportion of fast-twitch muscle fibers within a muscle group, suggesting that fast-twitch fibers were fatigued faster, leading to a decrease in performance. However, muscle hypertrophy does not directly account for a lack of gains on higher than trained velocities. Coyle et al., (1981) suggested a neural mediated response might also exist, which might help explain why

strength gains show a trend towards slower than higher velocities rather than the training velocity. Thus, higher velocity contractions might result in smaller NLMF effects due to an overall shift towards peripheral versus central fatigue development, which has fewer implications on non-exercised limbs.

In attempt to control velocity, some studies using isotonic contractions to induce NLMF fatigue have often used a metronome (Alcarez et al., 2008; Amann et al., 2013; Ciccone et al., 2014; Grant et al., 2014; Halperin et al., 2014b; Kawamoto et al., 2014), and studies using cycling often use repetitions per minute (Bangsbo et al., 1996; Nordsborg et al., 2003). However, these methods do not control velocity throughout the ROM precisely, and only the assumption can be made that increases in resistance result in a slower movement velocity and increases in repetitions per minute result in increased velocity. As well, it is likely the velocity is altered throughout the ROM by momentum and changing length-tension relationships of the muscles involved.

Of the three studies using constant velocities to evaluate NLMF effects, none of them compared different velocities, except Ben Othman et al., (2017) compared 300°.s-1 isokinetic actions to isometric contractions ($0°.s^{-1}$). However, as mentioned previously, isometric actions do not have velocity and can be excluded. According to the concept of training specificity (Behm, 1995), for sports that involve explosive and high-speed contractions, training should involve similar contraction velocities and intensities. Most athletic performances occur at limb speeds greater than 30 rpm (180°.s-1) (Moffroid and Whipple, 1970). However, a Behm and Sale (1993) training study demonstrated that high-velocity specific adaptations rely primarily on the ‘intent to move quickly’ rather than the actual movement speed. However, they used a within-subject design, where one leg used an isometric training protocol, while the other used isokinetic contractions at 300°.s-1. Therefore, a cross-over effect of strength gains from one limb to the other could therefore

have occurred and prevented the identification of velocity-specific strength gains. Grabiner and Owings, (1999) used 30°.s-1 knee extensions or flexions and did not find a decrease in concentric torque but reported an increase in eccentric torque (11%) following the eccentric protocol. This study demonstrated a few issues, first that a relatively slow velocity (30°.s-1) seemed unable to produce crossover effects, and that eccentric muscle action seems to be more resistant to fatigue. Ben Othman et al., (2017) compared isometric to high speed (300°.s-1) protocols and found that there were no effects between velocities, and they seemed to affect MVC similarly (8.9% and 11.4% for isometric versus isokinetic respectively). Strang et al., (2009) only used one velocity (110°.s-1) of concentric-concentric actions and tested isometric MVC extension and flexion. Their results demonstrated a contralateral knee extension improvement of 11% with no change in contralateral knee flexion enhancement

The inability of any of the three isokinetic studies to induce NLMF effects may be due to the fatigue protocol, or testing protocol. The isokinetic protocols had a discrete endpoint, whereas studies to exhaustion or failure (Amann et al., 2013; Halperin et al., 2014b; Kawamoto et al., 2014) seem to demonstrate greater incidences of fatigue. In addition, the isokinetic studies only used singular or a few discrete MVCs, whereas repeated (Halperin et al., 2014c; Kennedy et al., 2013) or time to exhaustion (Amann et al., 2013; Bangsbo et al., 1996; Johnson et al., 2014; Kawamoto et al., 2014; Nordsborg et al., 2003; Triscott et al., 2008) studies seem to demonstrate greater effects.

1.7 CONCLUSION

In conclusion, a gap currently exists in exercise literature surrounding velocity specific fatigue effects in non-local limbs. Most of the research uses isometric fatigue protocols, which do not transfer well to functional, sport, or rehabilitative movements, and a lack of controlled velocity

movement protocols exist. As well, most dynamic protocols are performed with submaximal loads to exhaustion, versus maximal efforts. Importantly, with dynamic protocols it is very difficult to control for the contraction time, which can lead to difficulty isolating effects. If isokinetic contractions are used, total contraction volume might not be adequate to elicit effects. If isokinetic contractions were used, it was only one velocity, versus an isometric. In addition, the work-rest ratios of different contraction modes make it difficult to compare results as even a brief rest period seem to alleviate or alter NLMF effects. Research performed using a metronome or repetition per minute protocol does not precisely control for velocity throughout the range of motion. A study is needed which compares isometric, as well as high-and-low speed isokinetic contractions with similar contractions time, work/rest ratio, and testing protocols to help distinguish possible differences in different modes of contractions on non-exercised limbs.

1.8 RESEARCH QUESTION:

The purpose of this study was to investigate the effects of low velocity ($60°s^{-1}$) fatiguing contractions produced by unilateral knee extension and flexion on contralateral knee extensor and flexor performance at low ($60°s^{-1}$) and high velocity ($240°s^{-1}$).

1.9 RESEARCH HYPOTHESIS:

It was hypothesized that following unilateral leg fatigue at a low velocity ($60°s^{-1}$) that the low velocity testing protocol of the contralateral, homologous muscle groups would experience greater deficits (decreased peak torque, fatigue endurance, and increases in electromyography and ratings of perceived exertion) than the high velocity ($240°s^{-1}$) protocol.

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“Effects of fatigue using slow velocity isokinetic knee actions on low and high velocity contralateral knee action performance”

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2.1 ABSTRACT

Non-local muscle fatigue (NLMF) describes exercise-induced fatigue effects on non-exercised muscle groups. An unexplored aspect of NLMF is whether the testing is velocity specific. The purpose of this study was to investigate fatigue effects induced by simultaneous low velocity ($60°.s^{-1}$) unilateral isokinetic knee extensions (KE) and flexions (KF) on contralateral knee extensors and flexors isokinetic force at low ($60°.s^{-1}$) and high velocity ($240°.s^{-1}$) and electromyography (EMG). In a randomized, repeated measures, crossover design, peak torque (PT), EMG, and rate of perceived exertion (RPE) were measured from the non-dominant KE and KF before and after unilateral dominant KE and KF fatigue. The fatiguing protocols consisted of 4 sets of 15 maximal isokinetic KE and KF contractions at $60°.s^{-1}$. In addition, a fatigue resistance test was also completed post-intervention.

Dominant (exercised) knee extensors and knee flexors PT decreased significantly ($p<.05$) 24% (ES=1.01), and 15% (ES=.65), respectively when tested at a low velocity, and 20% (ES=.57) and 17% (ES=.55), respectively, when tested at high velocity. Non-dominant quadriceps and hamstrings PT during post-test, or fatigue endurance test were not significantly different from control, demonstrating a lack of PT or fatigue endurance NLMF. In addition, there were no relative differences in PT for low (60°.s-1) or high (240°.s-1) test velocities. However, the high-velocity fatigue test resulted in a 30% (ES 1.54) greater fatigue index from the first-to-last repetition than the slow test but was not significantly different from control. In conclusion, this study highlights that prior slow (60°.s-1) maximal isokinetic, unilateral, dominant quadriceps, and hamstrings fatigue did not demonstrate decreases in singular maximal PT or fatigue endurance in the contralateral muscles. In addition, velocity specific effects were not demonstrated in relative PT or fatigue endurance.

Keywords: central fatigue; isokinetic; non-local muscle fatigue; crossover fatigue; velocity specificity.

2.2 INTRODUCTION

Fatigue is a complex, multifactorial phenomenon (Enoka & Stuart, 1992; St. Clair Gibson, et al., 2003). Neuromuscular fatigue refers to the decrease in physical performance associated with an increase in the real and/or perceived difficulty of a task or exercise (MacIntosh et al., 2006; Davis & Bailey, 1997), regardless of whether the force can be sustained (Bigland-Ritchie & Woods, 1984), and is present and progressing from the onset of the task (Bigland-Ritchie et al, 1986). While extensive literature examines muscle fatigue in the exercised muscles (Allen et al., 2008; Gandevia, 2001), effects of fatigue can either be localized or global (Halperin et al., 2015; Kennedy et al., 2013; Rattey et al., 2006), meaning it can affect the exercised muscles or fatigue effects in non-exercised, non-local, muscle groups (non-local muscle fatigue: NLMF) (Halperin et al. 2015).

NLMF refers to a temporary performance deficit in a contralateral, ipsilateral, inferior or superior, uninvolved (non-exercised) muscle distant from the fatigued muscle group (Gandevia et al., 1996; Graven-Nielson et al., 2002; Halperin et al., 2015). Synergist or stabilizer muscles are excluded from NLMF as co-contractions may lead to fatigue effects (Ben Othman et al., 2017; Paillard et al., 2010). The most studied version of NLMF might be crossover fatigue, which indicates a temporary deficit in the performance of the contralateral, homologous, non-exercised, limb muscles following a fatiguing protocol to the opposite limb (Doix et al., 2013; Martin & Rattey, 2007).

By testing non-local muscles (homologous or heterologous), peripheral fatigue, defined as changes at or beyond the neuromuscular junction, is primarily eliminated as a mechanism for the observed effect(s). It is thus likely that crossover or NLMF is due primarily to central fatigue, which refers to changes proximal to the neuromuscular junction resulting in a decreased neural drive (i.e. recruitment and discharge rate of motor units) to the muscles (Bigland-Ritchie et al., 1978; Boyas & Guével, 2011),

While NLMF focused research is relatively new, the research is conflicting. A review by Halperin et al., (2015) reported that approximately half of the studies reported NLMF effects with the presence or absence of NLMF likely related to methodological considerations. When examining lower limbs, 23 of 30 (76%) studies reported effects, while only 30% of studies examining upper limbs reported effects, suggesting NLMF might be muscle group dependent and that the lower legs are more susceptible than the upper body (Halperin et al., 2014b, Halperin et al., 2015). In addition, the upper body fatigue appears more likely to induce lower body fatigue than vice versa (Bouhlel et al., 2010; Halperin et al., 2014b,c). Halperin et al., (2015) also suggested that repetitive testing measures (repetitive MVCs, time to exhaustion, endurance time) demonstrated more consistent impairments whereas discrete or single, maximal efforts were less consistent (Halperin et al., 2014b). As well, other measures of fatigue such as changes in muscle activity (electromyography: EMG), voluntary activation, time to exhaustion, or rating of perceived exertion have been used inconsistently.

The intensity and volume of contractions used to fatigue muscle groups may be some of the most variable and important influences in eliciting NLMF (Halperin et al., 2015). Studies using lower intensity (submaximal efforts) or shorter duration (contraction time) fatigue protocols resulted in less pronounced effects (Kawamoto et al., 2014; Rasmussen et al., 2010; Kennedy et

al., 2013; Paillard et al., 2010; Arora et al., 2015). While never directly compared, the contraction mode (isometric, cyclic, dynamic, isokinetic) may also account for the conflicting results. Studies using dynamic or stretch-shortening cycle contraction seemed to be less likely to induce NLMF effects due to recovery periods (usually 1:1 work-rest ratio) or stretch-shortening cycle versus constant work modes such as isometric or cyclic protocols (Halperin et al., 2015). In addition, Ben Othman et al., (2017) suggested the possibility of task specificity demonstrating isometric fatigue affecting isometric MVC more greatly then isokinetic fatigue affecting isometric MVC. However, some studies have used a dynamic fatigue protocol and have tested isometric MVCs and demonstrated (Kawamoto et al., 2014) and have not demonstrated (Amann et al., 2013; Strang et al., 2009) effects. Only three studies have examined isokinetic exercise, and they demonstrated minimal NLMF effects (Ben Othman et al., 2017; Grabiner and Owings, 1999, Strang et al. 2009). However, only Strang et al., (2009) used a concentric-concentric fatiguing protocol, neither used different velocities (except Ben Othman et al., (2017) who used isokinetic and isometric), which raises two main questions. Firstly, if isokinetic exercise were to be concentric-concentric, making it a constant action like isometric or cyclic, would this increase the incidence of isokinetic effects? Secondly, might low or high-velocity test contractions demonstrate a velocity specific NLMF effect? Velocity specificity indicates that training adaptations of strength/power are greatest near the training velocity, but high-velocity training demonstrated greater transference to low-velocity actions (Coyle et al., 1981; Kanehisa and Miyashita, 1983). Thus, the question can be asked if low-velocity fatiguing contractions can affect low or high-velocity crossover fatigue effects.

A benefit of using an isokinetic dynamometer is the control of the volume and velocity, allowing consistency in the contraction time, work-rest ratio, and exercise durations. Equalization of contraction times using different velocities can be completed by increasing the number of

repetitions over the same range of motion since velocity will remain constant, may help determine whether NLMF may be velocity specific.

This study aims to determine if the existence or extent of lower limb NLMF (crossover) fatigue is velocity-dependent. More specifically, this study asks the question; how do constant, maximal intent, slow ($60°.s^{-1}$) isokinetic knee extension and flexion contractions influence maximal contralateral knee extensions and flexions at low ($60°s^{-1}$) and high ($240°s^{-1}$) velocity (maximal torque, fatigue endurance, EMG parameters and rate of perceived exertion)? The research outcomes may provide practical insights into the order of exercises used in training or rehabilitation programs. Differential velocity effects may provide some insights into the mechanisms of NLMF.

2.3 MATERIALS & METHODS

2.3.1 PARTICIPANTS

Based on prior NLMF force data (Halperin et al., 2014b,c, Kawamoto et al. 2014, Doix et al. 2013, Bogdanis et al. 1994), a statistical "a priori" power analysis (G*Power: Dusseldorf Germany) indicated that 4-8 participants would be needed to achieve an alpha of 0.5 with a power of 0.8. Sixteen healthy (absence of knee pain within the last 6 months) participants (10 males (172.20 ± 6.86cm, 82.1 ± 8.07 kg, 24.2 ± 2.53 years), and 6 females (169.34 ± 4.65 cm, 70.46 ± 11.26 kg, 22.83 ± 1.83 years)) resistance-trained (resistance train at least three times a week for over two years (Halperin et al., 2014b)) were verbally explained the experimental procedures, completed the Physical Activity Readiness Questionnaire, (Canadian Society for Exercise Physiology, 2011) and read and signed a letter of informed consent. Thirteen participants were determined to be right-leg dominant, while three participants were left-leg dominant (Oldfield,

1971). Ethical approval for the study was granted by the institutional Health Research Ethics Board (ICEHR: # 20200137) and conducted accorded to the latest version of the Declaration of Helsinki. To minimize confounding variables, participants were requested to avoid intense exercise training a day before the testing days and avoid caffeine or other drugs within eight hours of testing. In addition, testing was attempted to be completed at the same time each day, and participants had a minimum rest interval between test days of 48 hours following American College of Sports Medicine (ACSM) recommendations for exercise recovery (ACSM, 2009).

2.3.2 EXPERIMENTAL DESIGN

A randomized, repeated measure crossover design was used to examine the acute effects of unilateral knee extensor and flexor isokinetic muscle fatigue on the performance of the contralateral homologous muscles (Figure 1). Participants visited the laboratory for 4 sessions (2 control and 2 experimental) and completed them in a random order separated by a minimum of 48 hours. The sessions consisted of (i) Control-slow (no prior fatigue: slow-isokinetic test: 60°s-1), (ii) control-fast (no prior fatigue: fast isokinetic test: 240°s-1), (iii) slow-slow (prior slow isokinetic fatigue: 60°s-1: slow isokinetic test: 60°s-1), (iv) slow-fast (prior slow isokinetic fatigue: 60°s-1: fast isokinetic test: 240°s-1). The prior intervention fatigue protocol of the dominant leg was completed at $60°s^{-1}$ and consisted of 4-sets of 15 consecutive repetitions, separated by 15-s, totaling 2-minutes of contraction time. For the testing protocols of the contralateral non-dominant leg, a single maximal intent effort (contraction) at the prescribed angular speed was used. However, to determine post-intervention fatigue resistance, the slow testing protocol consisted of 12 consecutive repetitions at $60°s^{-1}$ with a similar duration achieved with the high-speed protocol by using 48 consecutive repetitions at $240°s^{-1}$. During the experiment, muscle torque (via an isokinetic dynamometer) was measured in both the dominant and non-dominant quadriceps and hamstrings

muscles, muscle EMG activity in the non-dominant knee extensors (vastus lateralis) and hamstrings (biceps femoris) was recorded, as well as rating of perceived exertion (RPE) was measured with the Borg 1-10 scale (Borg, 1990) (figure 3).

2.3.3 GENERAL PROCEDURES

2.3.3.1 General Warm up:

Participants first performed a general warm-up on a stationary cycle ergometer (Monark, WA, U.S.A) for 5 minutes at 70 revolutions per minute at 0.5kp resistance. They were then prepared for EMG.

2.3.3.2 Electromyography (EMG)

EMG of the non-dominant vastus lateralis (VL) and biceps femoris (BF) were monitored using self-adhesive Ag/AgCl bipolar electrodes (MeditraceTM 130 ECG conductive adhesive electrodes, Syracuse, USA) placed parallel to the muscle fibers according to the area specifications of Hermens et al., (2000) after area shaving, abrading, cleaning with isopropyl alcohol swabs, and left to dry. A ground electrode was placed on the femoral lateral epicondyle. EMG activity was collected from the mid-belly (midway between the anterior superior iliac spine to the superior edge of the patella) of the VL and BF (midway between the gluteal fold and the popliteal space) at 2 cm apart (Hermens et al., 2000). Following electrode placement electrodes were taped to minimize movement and tested for inter-electrode impedance noise (<5 kOhms).

All EMG signals were amplified (×1000) (CED 1902 Cambridge Electronic Design Ltd., Cambridge, UK) and filtered using a 3-pole Butterworth filter with cut-off frequencies of 10–1000 Hz. All signals were analog digitally converted at a sampling rate of 5 kHz using a CED 1401 (Cambridge Electronic Design Ltd., Cambridge, UK) interface, and recorded with a sampling rate

of 2000 Hz using a commercially designed software program Signal 5.0 (Cambridge Electronic Design Ltd., Cambridge, UK) and stored on a personal computer for further analysis.

2.3.3.3 Isokinetic Dynamometry

Following placement of EMG electrodes, participants were instructed to sit comfortably on the dynamometer seat according to manufacturer's specifications for seated knee extension/flexion (NORM; CSMI, Inc., Stoughton, MA) (figure 2). One manufacturer procedure that was changed for our protocol was the switch from using hand grips to placing the hands-on the shoulders without the use of shoulder straps. This change was made due to the possibility of NLMF effects due to the upper body and arm fatigue from bracing (stabilizing) (diminish the possibility that fatigue of the upper limbs acting as stabilizers affect the contralateral leg). A dual crossover strap was used to secure the torso, a waist strap for the hips, and individual thigh straps for the legs. Special care was taken to minimize extraneous movement as movement could affect the force and values and biomechanical moments (Weir et al., 1996).

The lever arm attachment was placed just proximal to the medial malleolus and stabilized tightly against the limb with Velcro straps. The isokinetic device lever axis was positioned in line with the axis of the knee. All isokinetic chair and apparatus settings were recorded for each participant to ensure an identical setup for each session. Isokinetic data was collected and analyzed using the CSMI Humac Norm (2010) internal software, gravity corrected internally for seated knee extension/flexion, and collected at 1250Hz (manufacture settings). Example of Humac Norm (2010) data in figure 17.

Specific Warm-Up:

Following the dynamometer physical setup (chair and lever arm), participants completed an isokinetic specific warm-up. Most people had not completed unilateral isokinetic concentric-concentric knee actions due to a lack of equipment availability. Therefore, an explanation in addition to familiarization repetitions was warranted. The specific warm-up consisted of 12 unilateral knee extension and flexions contractions at $60°s^{-1}$ and $240°s^{-1}$ over 90° range of motion (90°-0°, with the knee flexed at 90° as a start) at 50% of self-perceived maximal with the dominant leg, then repeated with the non-dominant leg. Before contractions at each velocity, participants were informed that with isokinetic actions, the lever arm would have zero resistance until the setting velocity is reached ($60°s^{-1}$ or $240°s^{-1}$) at which point it will maintain that velocity and torque is measured as the force exerted against the arm at that velocity. This meant participants must kick (contract) at the set velocity to register torque. In addition, because momentum cannot be used, participants were instructed to maintain effort throughout the range of motion (ROM) repetition to complete 'work' during the entire protocol. Computer settings for ROM prevented hyperextension/flexion to reduce the risk of injury, and rubber stoppers were placed as an extra precaution. To better understand the isokinetic principles, the computer screen, displaying torque, position, and velocity was visible for the participant. Finally, the isokinetic action was concentric knee extension and concentric knee flexion (no eccentric phase). Participants were instructed to 'push' to extend their leg and activated their knee extensors, and 'pull' to activate their knee flexors to return the lever arm to the start position as verbal encouragement has been shown to improve performance (Lauber & Keller, 2014).

Pre-Test (Peak Isokinetic Torque)

Following familiarization, three pre-test maximal isokinetic contractions were completed with the dominant and non-dominant leg with 30-seconds recovery between repetitions to measure

peak torque. Participants were instructed and encouraged to exert maximally as fast as possible over the full ROM for both the knee extensors and flexors. Participants were able to see the computer monitor to compare trials to encourage them to outperform previous trials. EMG was recorded from the non-dominant leg during non-dominant trials.

Fatigue Protocol

Following the pre-tests, with the intervention protocols (sessions slow-slow and slow-fast) the dominant leg was initially fatigued, as cross-education studies have demonstrated greater effects from dominant to dominant limbs (Carroll et al., 2006). The fatigue protocol consisted of four sets of 15 repetitions with minimal rest between repetitions over 90° range of motion, with sets separated by 15 seconds (four minutes of contraction time (two minutes of extension, two minutes of flexion), with one minute of rest total (4x15s), totaling five minutes for the protocol). The control sessions (control-slow and control-fast) consisted of 5 minutes of seated rest before post-tests. Participants were told to keep their leg relaxed and reminded if it moved. Participants were verbally encouraged and able to view the computer screen demonstrating torque values to encourage them to outperform previous repetitions to promote maximal contractions. Following each fatigue set, participants were asked their rate of perceived exertion.

Post-Fatigue Protocol & Endurance Test

Fifteen seconds following the intervention fatigue protocol of the dominant leg (or 5 minutes of seated rest for the control sessions) one maximal isokinetic contraction with the dominant leg at either $60°s^{-1}$ (slow-slow and control-slow conditions) or $240°s^{-1}$ (slow-fast and control-fast conditions), and then with the non-dominant leg was completed to view differences in maximal torque. Fifteen (15) seconds following the non-dominant maximal contraction,

participants completed a maximal endurance test of 12 maximal contractions at 60°s^{-1} for sessions control-slow and slow-slow, and 48 contractions at 240°s^{-1} for sessions control-fast and fast-fast with the non-dominant leg. The 240°s^{-1} protocol consists of four-fold greater repetitions to equalize total contraction time (volume of work). Following the final contraction in the endurance test, participants were asked again for their rating of perceived exertion.

2.3.3.4 Rate of Perceived Exertion (RPE)

Prior to the specific warm-up, participants were explained how and when the rate of perceived exertion scale would be used to minimize time and questions during the protocol. The Borg Rating of Perceived exertion scale (Borg, 1990) (figure 3) was used to subjectively quantify perceived effort on a 1-10 scale at 2-time points. RPE would be taken after the final fatigue set (or 5 minutes seated rest for control) and once after the post-fatigue test.

2.4 MEASUREMENTS AND DATA ANALYSIS

Changes in isokinetic peak torque (highest values achieved), pre- and post-fatigue (or rest), with the dominant and non-dominant knee extensors and flexors were recorded. During the endurance test, changes in peak torque for the first and final contractions were used to calculate a fatigue index ({final contraction peak torque / first contraction peak torque} x 100). Isokinetic torque was calibrated upon the initial installation of the CSMI Humac Norm (2010) isokinetic dynamometer and is analyzed at 1250Hz (recommended) internally on the internal software and expressed in Newton Meters (N/m).

EMG activity of the VL & BF were also investigated pre- and post-fatigue (or rest). A finite response high pass filter with a frequency cut-off of 20 Hz was used. Due to the COVID-19

pandemic, collected EMG data was unavailable for analysis. The EMG data will be analyzed and included in the published manuscript.

2.5 STATISTICAL ANALYSIS

Statistical analyses were calculated using SPSS software (Version 26.0, SPSS, Inc, Chicago, IL). This study employs a repeated measure within-subjects cross-over design. Normality (Kolmogorov–Smirnov) tests were conducted for all dependent variables. Significance was defined as $p < .05$. For the significant interactions, Bonferroni post-hoc analysis was used to identify differences between values. Intraclass correlation coefficients (ICCs) were measured for the pre-test trials of each condition to assess the consistency of this data (table 1). Cohen effect size statistics (ES) were conducted to evaluate the magnitude of the changes following various exercise protocols to the criterion of >0.80 large; 0.50-0.80 medium, <0.50 small and <0.2 trivial (Cohen, 1988). ES calculated as $(mean_1\text{-}mean_2)/((SD_1+SD_2)/2)$.

For examining maximal contraction peak torque and EMG with slow angular velocity testing, a 2x2x2: 3-way repeated-measures ANOVA comparing 2 conditions (Control-slow vs. Slow-slow) x 2 limbs (dominant vs. non-dominant) x 2 times (pre- vs. post-test) was used for both quadriceps and hamstrings. Similarly, a single maximal contraction peak torque with fast angular velocity testing was examined using a 2x2x2: 3-way repeated measures ANOVA comparing 2 conditions (Control-fast vs. Slow-fast) x 2 limbs (dominant vs. non-dominant) x 2 times (pre- vs. post-test) for both quadriceps and hamstrings. Separate ANOVAs were used for single absolute maximal peak torques with slow and fast isokinetic testing due to the inherent torque differences associated with the force-velocity muscle characteristics. When examining the slow fatigue test, a 2x4: 2-way repeated measures ANOVA comparing 2 conditions (Control-slow vs. Slow-slow) x 4 tests (pre-test, post-test, first and last fatigue repetitions) was used. Likewise, the same setup was

used for examining the fast fatigue test. To compare the slow versus fast peak torque and EMG (normalized to the pre-test single maximal contraction peak torque or EMG) testing a 2x4: with 2 limbs (Dominant vs. Non-dominant) x 4 conditions (Control-slow, Slow-slow, Control-fast, Fast-fast) was conducted for the quadriceps and hamstrings. To compare slow versus fast testing for fatigue a fatigue index was used, followed by a 2x4: 2-way repeated measures ANOVA with 2 limbs (Dominant vs. Non-dominant) x 4 conditions (Control: slow, Slow-slow, Control-fast, Fast-fast). Fatigue index was calculated by dividing the last repetition of repetitive fatigue test by the first repetition, then multiplying by 100.

For examining the effects of fatiguing exercise and repetitive exercise tests on the rating of perceived exertion (RPE), a 2x2x2: 3-way repeated measures ANOVA comparing 2 conditions (Control vs. fatigue) x 2 times (slow test vs fast test) x 2 (pre- vs post-test) was used.

2.6 RESULTS

2.6.1 *Summary*

Peak torque of the dominant (exercised) quadriceps and hamstrings decreased 24% (ES = 1.01), and 15% (ES = .65) respectively when tested at a slow velocity, and 20% (ES = .57) and 17% (ES = .55) deficits when tested at a high velocity. Peak torque of the non-dominant quadriceps and hamstrings during the post-test, or first or last repetition of repetitive fatigue test were not significantly different from control, demonstrating a lack of peak torque or fatigue endurance NLMF effects. In addition, there were no relative (normalized) differences in peak torque for velocity specific (slow (60°.s-1) or fast (240°.s-1) test velocities. However, the high-velocity repetitive fatigue test resulted in a 30% (ES = 1.54) greater decrease from the first to the last

repetition than the slow test, as demonstrated by the fatigue index (FI), but was not significantly different from control.

Although EMG was monitored, due to the COVID-19 isolation regulations, the laboratory was locked, and the data was not available for analysis (see limitations section).

2.6.2 Quadriceps

Single MVC Peak Torque - Slow Test Condition (figure 4)

A significant interaction was seen for intervention*time ($F_{(1,15)}$ = 17.44, p=.001), revealing a significant decrease from pre- vs. post-test for control (p=.001, ES = .27) and slow-slow test (p<.001, ES = .57) of 6% and 14%, respectively. The difference between control and intervention protocol responses was not significant. A significant dominant*time ($F_{(1,15)}$ = 23.49, p<.001) interaction found significant (p<.001 ES = .70 & p<.01 ES = .17) decreases of 16% and 4% for pre- to post-test for dominant and non-dominant limbs, respectively. A significant intervention*dominance*time interaction ($F_{(1,15)}$ = 9.21, p=.008) showed a significant decrease (p<.001, ES = 1.04) of 25% from pre- vs. post-test for dominant quadriceps with the intervention slow test condition. Post-test in the dominant leg during the intervention condition was demonstrated to be significantly (p<.008, ES = .53) lower than in control by 13%.

Single MVC Peak Torque - Fast Test Condition (figure 6)

An intervention*time interaction ($F_{(1,15)}$ = 5.94, p=.03) demonstrated a significant (p=.005, ES = .30) 11% decrease pre- to post-test for the intervention protocol. In addition, the post-test for the intervention was significantly (p=.02, ES = .26) lower than control post-test by 9%. An intervention*dominance*time interaction ($F_{(1,15)}$ = 12.77, p=.003) found a significant (p=.006, ES = .57) decrease of 20% for pre- vs post-test for the dominant leg intervention.

Slow Fatigue Test (figure 8)

A significant main effect was found for time ($F_{(1,15)} = 46.88$, $p<.001$). A significant ($p=.002$, ES = .24) decrease of 6% was demonstrated for the pre-test vs. first fatigue test repetition. In addition, a significant ($p<.001$, ES = .67) decrease of 18% was demonstrated between the first and last repetition of the fatigue test in both the control and intervention sessions.

Fast Fatigue Test (figure 10)

A significant main effect for time ($F_{(3,45)} = 43.78$, $p<.001$) indicated a significant ($p<.001$, ES = .25) 9% decrease between pre-test and repetition one of the fatigue test. In addition, there was also a significant ($p<.001$, ES = 2.1) decrease of 53% between the first and last repetition of the fatigue test. There were no significant differences between slow and fast tests.

Slow vs Fast Test (figure 12)

A significant interaction between conditions*dominance ($F_{(1,15)} = 13.96$, $p=.002$) indicated a significant ($p<.001$, ES = 1.04) decrease of 16.6% in dominant leg performance with the intervention vs. control condition.

Fatigue Index (figures 14 & 15)

A significant main effect for conditions ($F_{(1,15)} = 6.27$, $p=.02$) revealed that the intervention condition peak torque during the repeated maximal test decreased 11% significantly ($p=.02$, ES = .34) more than control. In addition, a significant main effect for tests ($F_{(1,15)} = 31.26$, $p<.001$) indicated that high velocity peak torque fatigue index decreased 37% ($p<.001$, ES = 1.77) more than slow test.

2.6.3 Hamstrings

Single MVC Peak Torque - Slow Test Condition (figure 5)

A significant dominance*time interaction ($F_{(1,15)} = 8.42$, p=.011) indicated that peak torque of the dominant & non-dominant hamstrings decreased significantly 9.1% (p<.001, ES = 44) and 4.7% (p=.001, ES = .23) pre- vs post-test respectively. A significant intervention*dominance*time ($F_{(1,15)} = 10.57$, p=.005) interaction illustrated pre- to post-test decreases for slow-dominant of 14.6% (p<.001, ES = .65). When comparing post-test conditions, the dominant leg post-test in the fatigue condition was 11% (p=.03, ES = .49) lower than in control.

Single MVC Peak Torque - Fast test condition: (figure 7)

A significant intervention*dominance interaction ($F_{(1,15)} = 5.77$, p=.03) exhibited a significant (p=.02, ES .25) decrease of 8% for dominant leg post-test in the intervention test vs. control. A significant interaction effect for intervention*dominance*time ($F_{(1,15)} = 9.35$, p=.008) disclosed a significant (p=.001, ES = .55) 17% decrease in pre- to post-test dominant leg hamstrings in the intervention protocol.

Slow Fatigue Test (figure 9)

A significant main effect for time ($F_{(3,45)} = 63.29$, p<.001) revealed a significant (p<.001, ES = .98) decrease of 19% in first and last repetition of the repetitive fatigue endurance test. In addition, there was a significant (p=.001, ES = .43) 8% decrease from the pre-test to the first repetition of the fatigue test.

Fast Fatigue Test (figure 11)

A significant main effect for time ($F_{(3,45)} = 41.32$, p<.001) demonstrated a significant but trivial magnitude (p=.03, ES = .16) decrease of 5% in pre-test and the first repetition of the fatigue

test. As well, the fatigue test resulted in a significant (p<.001, ES 1.78) decrease of 43% between the first and last repetition.

Slow vs. Fast Test (figure 13)

A significant interaction between conditions*dominance ($F_{(1,15)}$ = 9.54, p=.007) indicated a significant (p=.002, ES = .94) decrease of 11.7% in dominant leg performance with the intervention vs. control condition.

Fatigue Index (figures 14 & 15)

A significant main effect for conditions ($F_{(1,15)}$ = 8.322, p=.011) displayed that the intervention condition peak torque during repeated maximal test decreased 10% significantly (p=.005, ES = .41) more than control. Furthermore, analysis revealed a significant effect for tests ($F_{(1,15)}$ = 14.94, p<.002) revealing that high velocity peak torque endurance decreased 30% significantly (p<.003, ES = 1.54) more than slow test.

2.6.4 Ratings of Perceived Exertion (RPE): (figure 16)

A significant RPE main effect for interventions ($F_{(1,15)}$ = 57.78, p<.001) revealed an increase of 4.3 points on the Borg 1-10 scale (56%, ES = 2.07) from control to intervention conditions. In addition, a significant ($F_{(1,15)}$ = 568.05, p<.001) interventions * time interaction showed that RPE increased significantly 489% (4.9 on the RPE scale) (p<.001, ES = 6.90) from post-test to repetitive fatigue post-test during control and demonstrated a significant decrease of 21% (1.8 on RPE scale) (p<.001, ES = 1.56) from post-test to repetitive post-test for interventions.

2.7 DISCUSSION:

The most important finding in this study was that prior unilateral fatigue of the dominant quadriceps and hamstrings by repetitive slow (60°.s-1) maximal isokinetic actions did not demonstrate decreases in singular (discrete) maximal peak torque or repetitive fatigue endurance in the contralateral, homologous muscles. In addition, velocity specific effects were not demonstrated with relative peak torque or relative fatigue endurance changes between slow (60°.s-1) or fast (240°.s-1) testing.

Contraction Mode:

The contraction mode has been suggested to play a role in NLMF (Halperin et al., 2015), with constant action fatiguing protocols such as isometric (Aboodarda et al., 2015; Doix et al., 2013; Halperin et al., 2014b,c; Kennedy et al., 2013), and cyclical (alternating, rhythmic, unidirectional about an axis) (Bogdanis et al., 1994; Bouhlel et al., 2010; Bangsbo et al., 1996; Johnson et al., 2014; Nordsborg et al., 2003) are more likely to demonstrate effects than dynamic (back and forth about a range of motion), however, effects have been demonstrated (Amann et al., 2013; Ben Othman et al., 2017; Kawamoto et al., 2014; Šambaher et al., 2016; Ciccone et al., 2014). The use of isokinetic exercise has been rare in NLMF research, and to the best of our knowledge has only been used in three other studies (excluding the present study) (Ben Othman et al., 2017; Grabiner and Owings, 1999; Strang et al., 2009). A lack of isokinetic dynamometry equipment likely leads to its minimal use. Of the three other isokinetic studies, only Strang et al., (2009) used concentric-concentric unilateral knee extensions and flexions (shortening contractions for both extensors and flexors), but at 110°.s^{-1}, and tested isometrically where the current study tested at slow (60°.s^{-1}) and high velocity (240°.s^{-1}). In contrast to the current study, Grabiner and Owings (1999) used slower (30°.s^{-1}) unilateral knee extensions or flexions, and Ben Othman et al., (2017) used faster (300°.s^{-1}) unilateral knee extensions and isometric. Within these four isokinetic

studies, only one demonstrated NLMF effects (Ben Othman et al., 2017). In addition, to employing higher velocity fatiguing contractions, Ben Othman and colleagues tested youth rather than the young adults recruited for this study. They reported global, non-local muscle fatigue (i.e. knee extensors, elbow flexors, handgrip, and balance test), suggesting that NLMF may be more susceptible in youth. A possible reason for the lack of NLMF in the current study is due to the concentric-concentric knee extension/flexion leading to systemic excitation that balanced fatigue effects to result in no net change on performance. Strang et al., (2009) who also used this type of isokinetic action noted that the absence of fatigue in the contralateral leg might have been due to a global 'warm-up effect' caused by activity in the ipsilateral leg that balanced any induced fatigue. This is highly possible as a lack of change in performance may be attributed to a balance between excitation and inhibition factors (Gandevia, 2001). In the current study, when participants underwent the fatigue protocol they were visually much more 'warmed up' than during control sessions. Participants were often flushed and sweating, signs of increased sympathetic drive and excitation hormones such as adrenaline, which may augment performance and balance any fatigue effects. It is also likely that additional factors, such as contraction intensity, volume, fatigue quantification and other methodological considerations contribute to observable NLMF effects (Halperin et al., 2015).

Fatigue Intervention

Methodological considerations of the fatigue intervention are also considered a NLMF factor, and whether it is sufficient to induce fatigue in the non-exercised limb (Halperin et al., 2015). It seems that the presence of NLMF is not only dependent on factors that increase the amount of fatigue induced to the exercise leg. In the present study, the fatigue protocol consisting of four sets of 15 unilateral isokinetic knee extensions and flexions utilizing maximal intent. This

resulted in similar deficits in the fatigued muscle torque of 24% (ES = 1.01) in quadriceps and 15% (ES = .65) in hamstrings torque when tested at a slow velocity, and 20% (ES = .57) and 17% (ES = .55) deficits when tested at a higher velocity. These fatigue-induced deficits of the exercised leg are similar to Kawamoto et al., (2014)(32%), Doix et al., (2013)(17%), Martin and Rattey (2007)(16%) and Ben Othman et al., (2017) with 12.6% and 11.3% at 90° and 120° respectively. In contrast, Grabiner and Owings (1999) and Strang et al., (2009) exhibited greater fatigue induced torque impairments of the exercised muscle of 39% and 19% respectively.

It has been demonstrated that maximal or high-intensity exercise (Kawamoto et al., 2015, Kennedy et al., 2014) has demonstrated greater NLMF effects than lower intensity exercise (Arora et al., 2015; Paillard et al., 2010). In addition, the amount of contraction time might play a role as fatigue accumulates over time and is progressing from the onset of the task (Bigland-Ritchie et al., 1986). It seems NLMF is greater with an increased exercise volume. When shorter and longer durations are compared the longer protocol seems to induce greater effects, at least for isometric protocols (Doix et al., 2013). However, for isokinetic protocols, the data is mixed even though all protocols used maximal intent. Of the isokinetic studies, Grabiner and Owings (1999) used 3-minutes of contraction time, Strang et al., (2009) used 3.8-minutes, and the current study used 2-minutes and did not demonstrate NLMF effects, whereas Ben Othman et al., (2017) used 60s and demonstrated effects. These results demonstrate that methodological considerations such as intensity and volume affect the incidence of NLMF. In addition, Grabiner and Owings (1999) suggested the allowance of a passive return of the dynamometer giving the protocol a 1:1 work-rest ratio might have allowed a recovery effect. Therefore, within isokinetic NLMF research, maintaining a constant concentric contraction of the extensor and flexor antagonist pair (allowing no recovery between repetitions) might influence fatigue differently than concentric extension or

flexion with passive return (allowing brief recovery between repetitions). However, the present study and Strang et al., (2009) used concentric-concentric actions of the quadriceps and hamstrings, not allowing recovery and did not demonstrate deficits, while Ben Othman et al., (2017) utilized concentric only actions of the quadriceps and demonstrated NLMF effects. It might then be possible that the velocity used to fatigue might play a role, as isokinetic actions allow control over movement velocity. While Grabiner and Owings (1999) used slower velocity ($30°.s^{-1}$), the current study used $60°.s^{-1}$, and Strang et al., (2009) used $110°.s^{-1}$ and did not demonstrate effects, Ben Othman et al., (2017) used a much faster $300°.s^{-1}$ protocol and reported impairments. In addition, the current study, Grabiner and Owings (1999), and Strang et al., (2009) used adults, while Ben Othman et al., (2017) used children. Ben Othman et al., (2017) suggested the use of children might be a contributor to the NLMF effects as children as they rely more on neurological mechanisms of fatigue than adults, and neurological mechanisms have been suggested by Halperin et al., (2015) to be a strong component of NLMF.

Fatigue Measures:

A common limiting factor in NLMF research has been the fatigue detection method(s) used. The most commonly used fatigue detection method has been peak force during a singular, maximal contraction, but because the NLMF definition of fatigue has many components and definitions, it can be manifested in many ways such as the rating of perceived exertion, and multiple repetitions (fatigue endurance changes) (Halperin et al., 2015). Several studies have (Aboodarda et al., 2015; Ben Othman et al., 2017; Doix et al., 2013; Martin & Rattey, 2007) and have not (Arora et al., 2015; Decorte et al., 2012; Elmer et al., 2013; Grabiner & Owings, 1999; Halperin et al., 2014; Halperin et al., 2014) demonstrated deficits in singular maximal contractions. Some studies that did not demonstrate NLMF with single maximal contractions have detected

deleterious effects when other measures or methods are also used, such as rate of perceived exertion (RPE) (Amann et al., 2013) and repeated maximal contractions (Amann et al., 2013; Halperin et al., 2014b; Rasmussen et al., 2010; Triscott et al., 2008). As a repetitive fatigue endurance test, the current study used one set of 12 repetitions at 60°.s-1 or 48 repetitions at 240°.s-1 (equalizing contraction time at 24 seconds). It can then be suggested that the fatigue induced using most NLMF studies might not be sufficient to elicit a deficit in a singular maximal contraction, however prolonged or repetitive testing demands could reveal effects. Therefore, due to the wide definition of neuromuscular fatigue, studies that utilize multiple methods of fatigue detection might be better able to identify fatigue and perhaps help explain its mechanisms and implications.

Velocity Specificity:

Velocity specificity suggests that training adaptations of strength/power are greatest near the training velocity (Behm et al. 1993). However, there are conflicting studies that have shown high-velocity training providing greater transference to slow-velocity actions (Coyle et al., 1981). A relatively unexplored aspect of NLMF is whether effects are velocity specific. Although Behm at al., (1993) suggested intended rather than actual movement directs velocity specificity, it has yet to be explored in NLMF research. Most studies test for fatigue in a non-local group at the same mode or velocity as the fatigue intervention. The current study examined the effects of slow velocity (60°.s-1) fatigue on slow and fast velocity (240°.s-1) fatigue, repetitive fatigue endurance, and RPE. No velocity specific effects were demonstrated in peak torque or RPE. Velocity specific differences were observed for the non-dominant, contralateral, repetitive fatigue endurance test, with the fast velocity test demonstrating a 30% (ES = 1.54) greater decrease in peak torque from the first-to-last repetition. This difference however was not deemed NLMF as it was not

significantly different from control. It is likely the greater decrease in repetitive fatigue endurance in the fast velocity protocol is due to the greater fatiguability of fast (type 2) muscle fibers at higher velocities. The only study that also arguably compared velocity specific effects was Ben Othman et al., (2017) who compared isometric (0°.s-1) and fast velocity (300°.s-1) fatigue protocol on isometric and fast velocity peak torque (even though technically isometric movements have zero velocity). In contrast to the current study, they found evidence of NLMF for both isometric and isokinetic protocols, however there was no difference between protocols, also demonstrating a lack of velocity specific NLMF effects.

Strengths and limitations

A limitation was the time required to switch the isokinetic device from the dominant to non-dominant legs (approximately 1 minute). NLMF effects seem to diminish quickly following a recovery of the exercised limb, and therefore a quick transition to the non-exercised leg may be critical to monitor immediate responses. Furthermore, EMG was monitored, but due to the COVID-19 isolation regulations, there was no access to the data and thus it could not be analyzed for this thesis. The EMG data will be analyzed and incorporated into the manuscript when it is submitted for publication post-COVID-19 restrictions.

2.8 CONCLUSION:

In conclusion, this study highlighted that prior unilateral fatigue of the dominant quadriceps and hamstrings by repetitive slow (60°.s-1) maximal isokinetic actions did not demonstrate decreases in singular maximal peak torque or repetitive fatigue endurance in the contralateral muscles. In addition, velocity specific effects were not demonstrated in relative peak torque or

relative fatigue endurance changes. There was also no observable effect on the rating of perceived exertion following fatigue vs. control, or slow vs. fast testing on repetitive contraction test values.

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2.10 TABLES:

Table 1: Intraclass Correlation Coefficients

Leg	Muscle	Variable	ICC Cronbach's Alpha
Dominant	Hamstrings	Peak Torque	0.87
Non-Dominant	Hamstrings	Peak Torque	0.90
Dominant	Quadriceps	Peak Torque	0.91
Non-Dominant	Quadriceps	Peak Torque	0.89

Table 2: Rating of Perceived Exertion (RPE) using Borg 1-10 scale.

	Mean	Standard Deviation
Control - Slow Test – Pre-Test	1.00	0.00
Control – Slow Test – Post-Test	5.58	1.47
Control – Fast Test – Pre-Test	1.00	0.00
Control – Fast -Test – Post-Test	6.22	1.38
Fatigue – Slow Test – Pre-Test	8.72	1.14
Fatigue – Slow Test – Post-Test	6.72	1.18
Fatigue – Fast Test – Pre-Test	8.66	1.19
Fatigue – Fast Test – Post-Test	6.94	1.40

Table 3: Mean peak torque & standard deviation of quadriceps and hamstrings expressed in Newton Meters (N*m) during slow test (60°.s-1) Non-Dom: non-dominant leg

Peak Torque – Slow Test (N*m)				
	Quadriceps		Hamstrings	
	Mean	Std. Deviation	Mean	Std. Deviation
Control – Pre-Test – Dominant	189.36	37.23	133.68	27.97
Control – Post-Test - Dominant	175.20	47.20	127.98	25.60
Control – Pre-Test – Non-Dom	189.07	39.07	127.78	27.08
Control – Post-Test – Non-Dom	181.17	42.00	119.62	25.67
Control – Post-Test – Non-Dom 2	177.72	45.41	132.93	27.59
Control – Post-Test – Non-Dom 3	154.22	43.13	118.29	25.16
Fatigue – Pre-Test - Dominant	198.57	47.39	97.69	21.30
Fatigue – Post-Test – Dominant	151.12	46.23	113.63	33.36
Fatigue – Pre-Test – Non-Dom	185.29	47.61	129.34	25.67
Fatigue – Post-Test – Non-Dom	177.48	55.60	125.34	28.82
Fatigue – Post-Test – Non-Dom 2	175.51	51.65	117.27	26.06
Fatigue – Post-Test – Non-Dom 3	136.92	50.18	92.03	23.47

Table 4: Mean peak torque & standard deviation of quadriceps and hamstrings expressed in Newton Meters (N*m) during fast test (240°.s-1). Non-Dom: non-dominant leg

Peak Torque – Fast Test				
	Quadriceps		Hamstrings	
	Mean	Std. Deviation	Mean	Std. Deviation
Control – Pre-Test - Dominant	98.31	37.78	81.58	29.72
Control – Post-Test - Dominant	98.04	36.80	79.60	30.12
Control – Pre-Test – Non-Dom	102.34	33.62	79.03	31.37
Control – Post-Test – Non-Dom	99.64	38.07	73.59	30.51
Control – Post-Test – Non-Dom 2	90.65	32.87	73.23	23.86
Control – Post-Test – Non-Dom 3	46.26	15.47	45.32	12.79
Fatigue – Pre-Test – Dominant	102.79	41.70	80.54	29.73
Fatigue – Post-Test – Dominant	82.74	28.91	66.98	21.41
Fatigue – Pre-Test – Non-Dom	99.09	37.68	79.01	26.03
Fatigue – Post-Test – Non-Dom	96.64	37.18	74.67	28.05
Fatigue – Post-Test – Non-Dom 2	93.61	32.63	76.51	22.86
Fatigue – Post-Test – Non-Dom 3	41.17	13.67	39.65	12.42

Table 5: Relative peak torque & standard deviation for slow vs. fast test of the quadriceps & hamstrings. Non-Dom: non-dominant leg

	Slow vs Fast Tests			
	Quadriceps		Hamstrings	
	Mean	Std Dev.	Mean	Std Dev.
Control – Slow - Dominant	.91	.11	.96	.05
Control – Fast – Dominant	1.00	.16	.96	.14
Control – Slow – Non-Dom	.95	.07	.94	.08
Control – Fast – Non-Dom	.96	.10	.92	.08
Fatigue – Slow - Dominant	.75	.13	.84	.15
Fatigue – Fast - Dominant	.84	.17	.85	.11
Fatigue – Slow – Non-Dom	.94	.11	.96	.11
Fatigue – Fast – Non-Dom	.98	.14	.92	.15

Table 6: Fatigue Index for peak torque between 1st and last repetition of fatigue endurance tests.

	Fatigue Index			
	Quadriceps		Hamstrings	
	Mean	Std Dev.	Mean	Std Dev.
Control – Slow	87.01	12.66	83.51	12.01
Control – Fast	55.25	20.28	64.79	14.13
Fatigue – Slow	77.92	14.05	78.82	13.86
Fatigue – Fast	48.33	22.16	54.89	18.21

2.11 FIGURES

Figure 1: Experimental Design

Control-Slow	Control-Fast	Slow Fatigue-Slow	Slow Fatigue-Fast

5 minutes warm up on stationary bike at 70rpm
Warm-up: 12 knee extensions and flexions repetitions at 60°/s and 12 at 240°/s at 50% of self-perceived maximal intensity of dominant and non-dominant leg
Pre-test: 3 maximal isokinetic voluntary knee extension & flexions (MIVC) of dominant and non-dominant leg
Intervention: 5-minute seated rest [2 control session] or 4 x 15 60°/s with 15s rest between sets with dominant leg [intervention sessions], with RPE taken after each set
Post-test: Single maximal knee extension and flexion with dominant then non-dominant knee at 60°/s (control-slow test & slow fatigue-slow test) or 240°/s (control-fast test & fast fatigue-fast test)
Post-fatigue test: 12 maximal contractions at 60°/s [control-slow test & slow fatigue-slow test] or 48 at 240°/s [control-fast test & fast fatigue-fast test] with non-dominant knee with RPE taken after the last contraction

Figure 2: CSMi Humac Norm in Seated Knee Extension/Flexion Position (We opted to change hand position to cross-shoulder position for methodological concerns)

Figure 3: Borg Rate of Perceived Exertion Scale

Figure 4: Peak torque for slow test in the quadriceps. Variation in data indicated by standard error. Significance was set at $p < 0.05$ and indicated with horizontal bars.

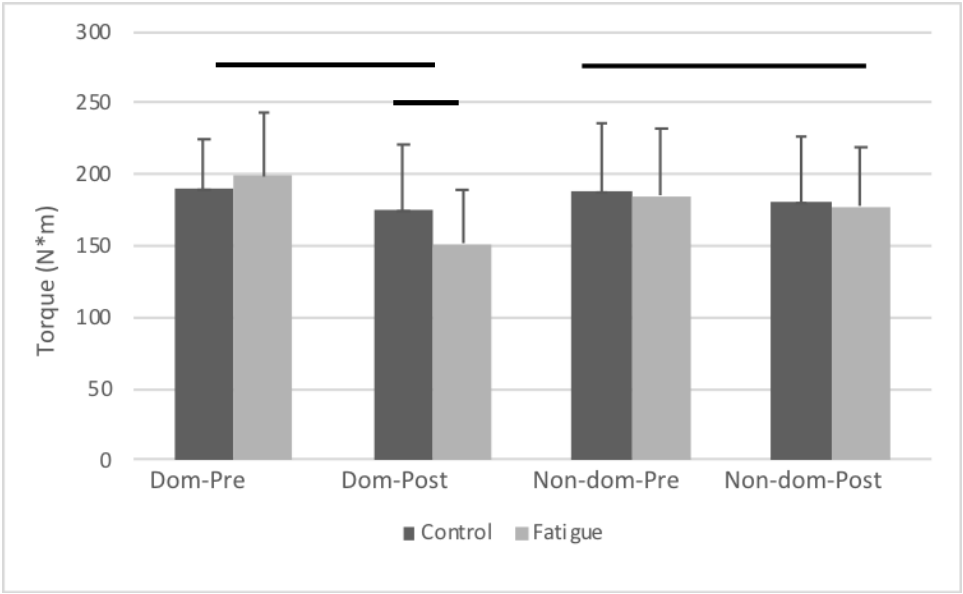

Figure 5: Peak torque for slow test in the hamstrings

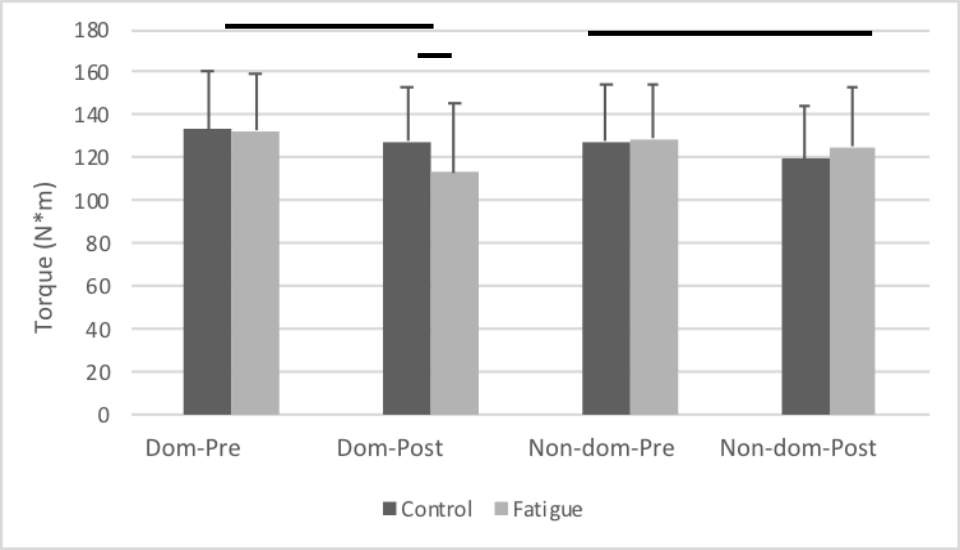

Figure 6: Peak torque for fast test in the quadriceps.

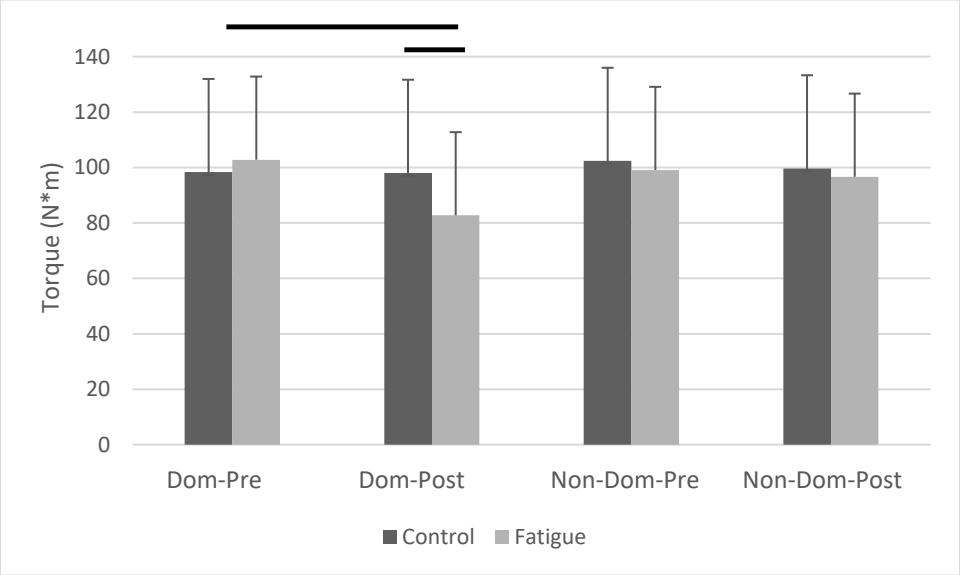

Figure 7: Peak torque for fast test in the hamstrings.

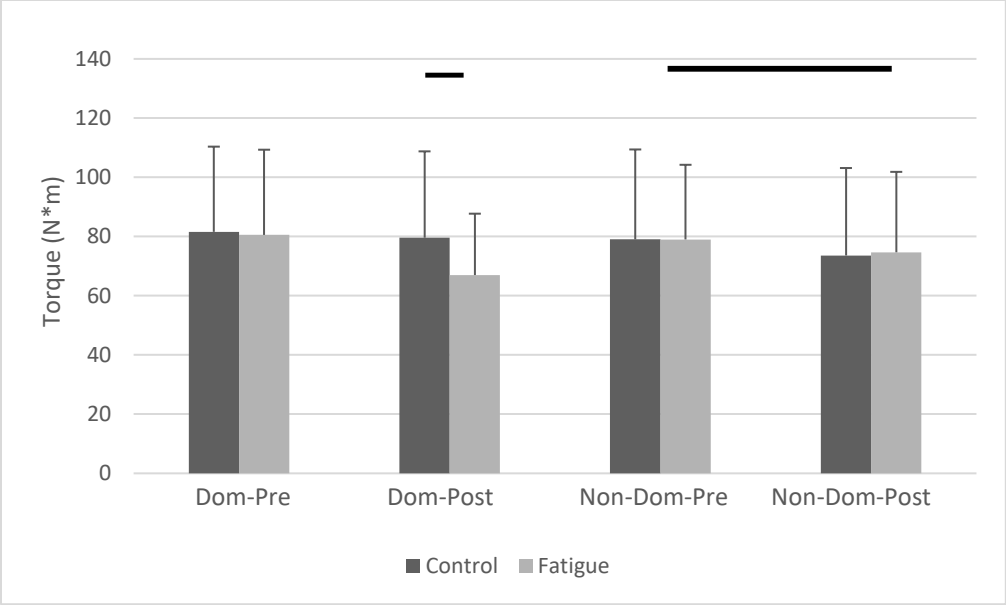

Figure 8: Peak torque of singlar and repetitive test using slow test in the quadriceps.

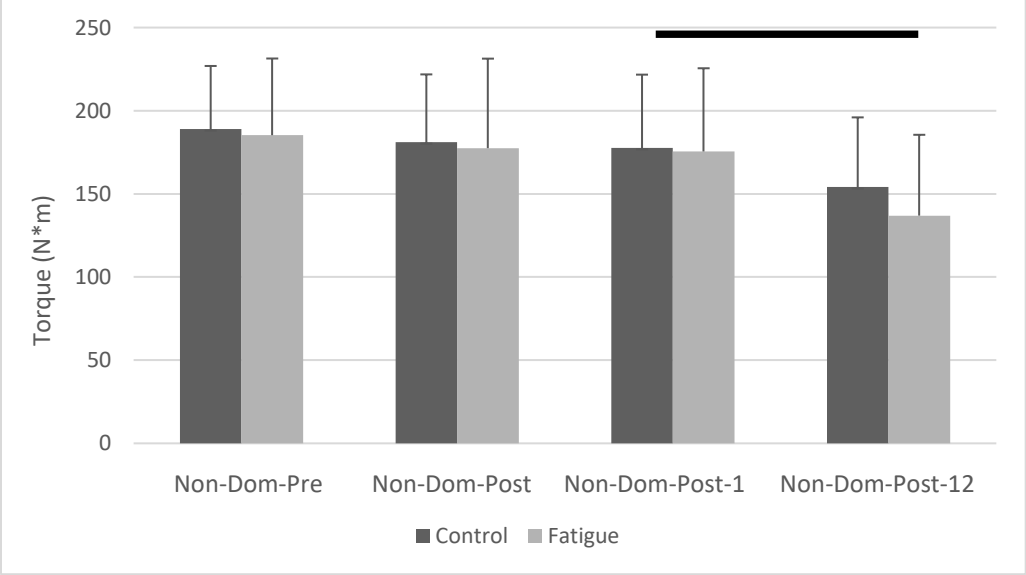

Figure 9: Peak torque of singlar and repetitive test using slow test in the hamstrings.

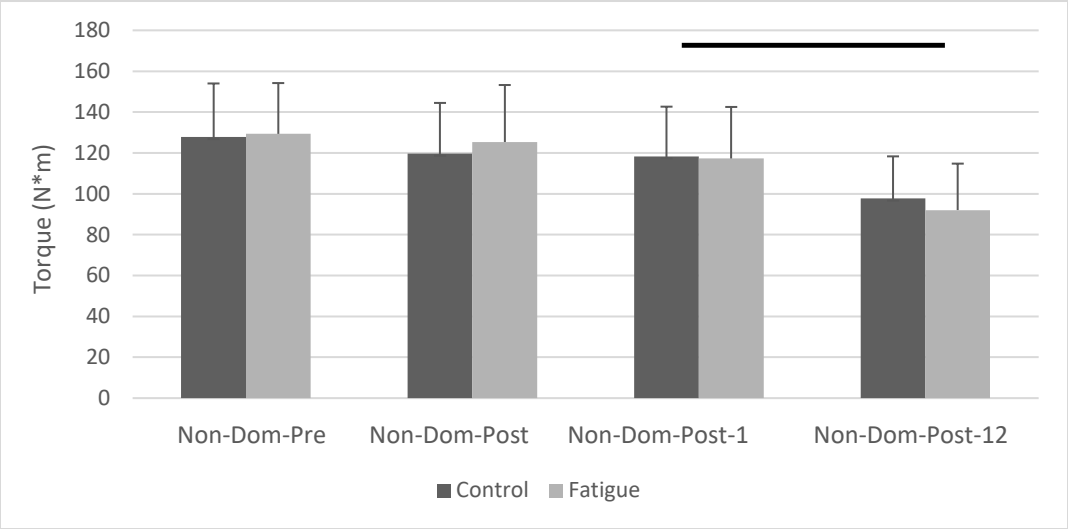

Figure 10: Peak torque of singlar and repetitive test using fast test in the quadriceps.

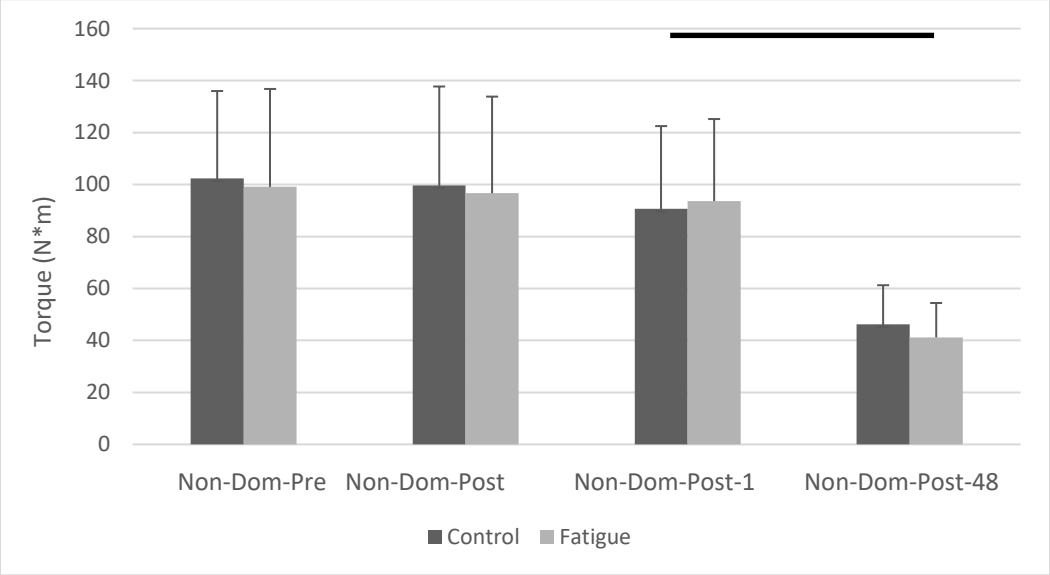

Figure 11: Peak torque of singlar and repetitive test using fast test in the hamstrings.

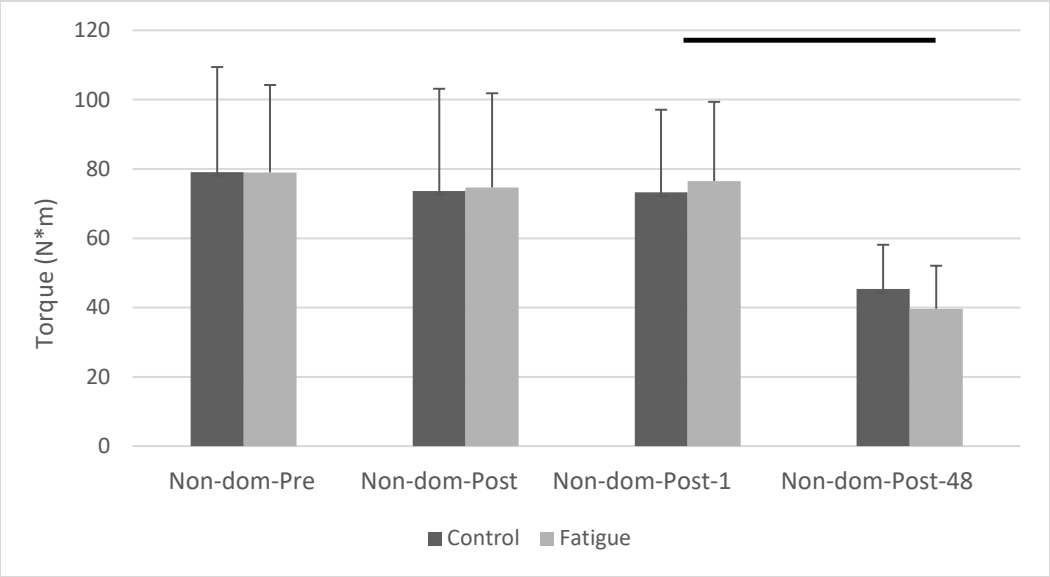

Figure 12: Slow vs fast test in the quadriceps.

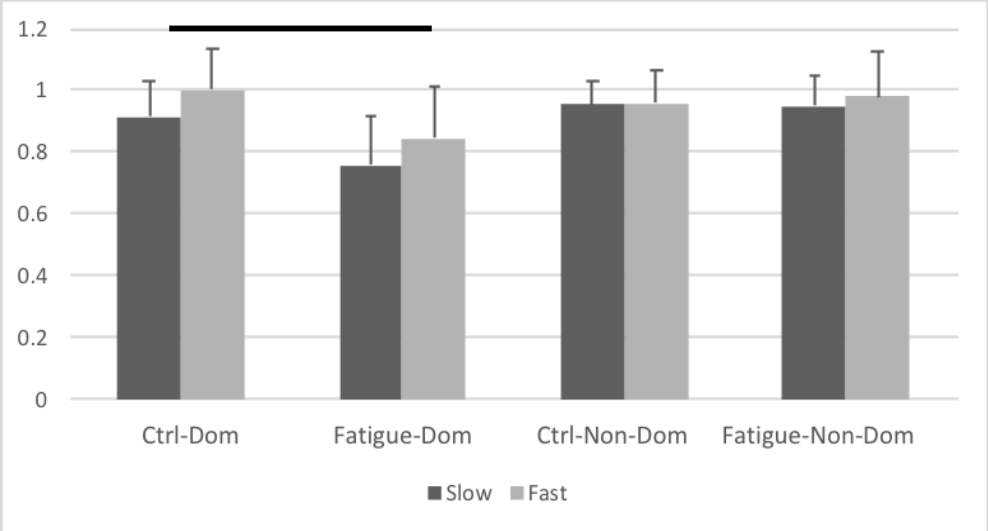

Figure 13: Slow vs fast test for the hamstrings.

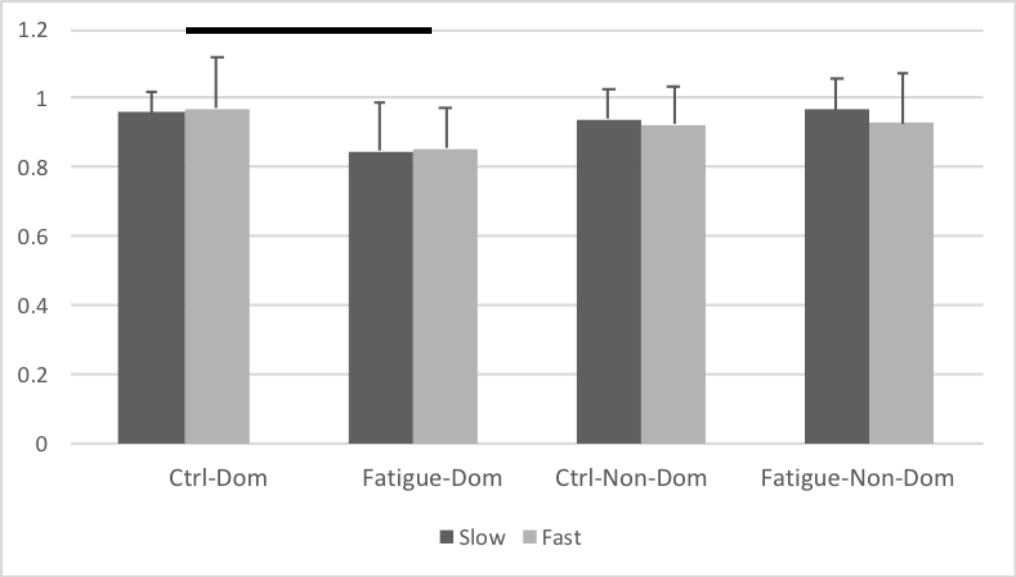

Figure 14: Fatigue index for conditions.

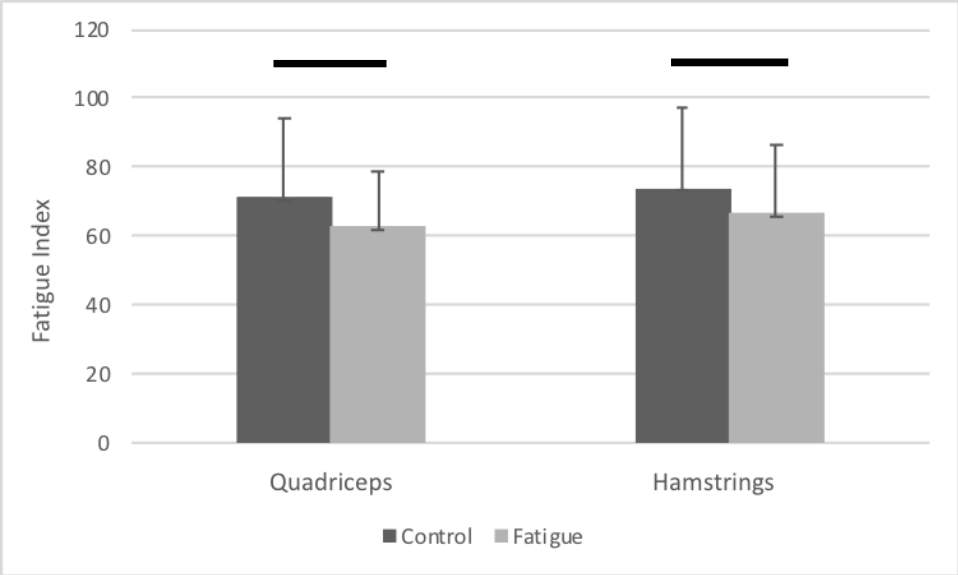

Figure 15: Fatigue index for tests.

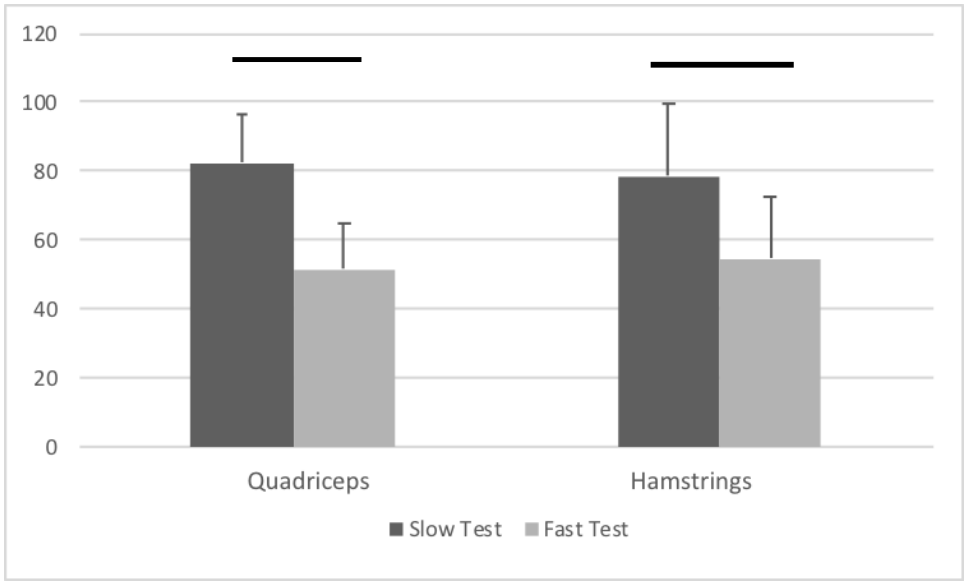

Figure 16: Rating of perceived exertion for intervention and time.

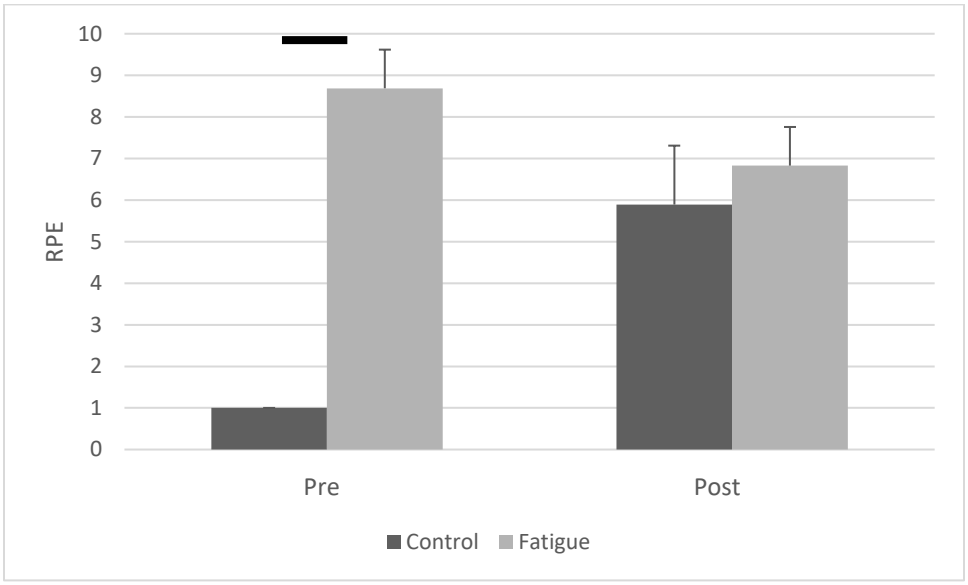

Figure 17: Example of Humac Norm (2010) isokinetic data converted to Microsoft Excel output displaying torque and velocity for slow condition repetitive fatigue test. Positive values represent knee extension (quadriceps torque and velocity) and negative values represent knee flexion (hamstring torque and velocity).