AN ANALYSIS OF THE DURATION OF NON-LOCAL MUSCLE FATIGUE EFFECTS

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Abstract

Introduction Non-local muscle fatigue (NLMF) is a temporary impairment in the performance of a non-exercised muscle following a fatigue protocol of a different muscle group. Since the tested muscle has not experienced prior activity or fatigue, any impairments due to the fatigue of another muscle cannot be due to peripheral factors and thus must be due to global or central influences. The majority of NLMF post-tests were conducted immediately after the fatiguing protocols. Thus, how long these effects can last is unknown.

Purpose There is some uncertainty and conflicting results in literature regarding NLMF effects. The purpose of this study was to examine post-test durations of NLMF in four different time conditions (Control, 1, 3, and 5 min) to investigate the duration of the possible effects.

Methods In a randomized crossover study design with only five recreationally trained participants (due to COVID) were recruited for this study (four females: height 159.1 ±2.9 cm, body mass 62.7 ± 7 kg, age 26.6 ± 9.8 yrs. and one male: height 182.2 cm, body mass 90.3 kg, age 40 yrs.) to examine the duration of acute effects of unilateral knee extensors muscle fatigue on the contralateral homologous muscle strength, activation, and fatigue resistance (endurance). Four of the participants were determined to be right-leg dominant, while one participant was left-leg dominant. In five randomized separate sessions (48 hours between visits) each condition was presented which included testing at one, three, five minutes post-test or Control. Non-dominant knee extensors muscle force, and an endurance test as well as vastus lateralis and biceps femoris electromyography

(EMG) data were collected. The fatigue protocol consisted of two sets of continuous 100-seconds MVC by the dominant leg, separated by 1-min of rest.

Results The major finding was the lack of significant NLMF-induced single (discrete) MVC force decrements at any post-test duration.

Conclusions NLMF was not evident in both single discrete MVC and muscle endurance (fatigue resistance). This finding was in agreement with a recent meta-analysis that reported trivial NLMF effects on single MVCs but contradicts the review's finding of small to moderate NLMF effects on muscle endurance. The lack of NLMF effects on endurance might be attributed to a lack of statistical power, the recruitment of recreationally active rather than trained individuals, the greater fatigue endurance of female participants or recovery effects within 1-minute of the unilateral fatigue intervention.

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LIST OF ABBREVIATIONS

ADP - Adenosine Diphosphate
AP - Action Potential
ATP - Adenosine Triphosphate
BF - Biceps femoris
Ca++ - Calcium
Cm - Centimeter
CMEP - Cervicomedullary Motor Evoked Potential
CNS - Central Nervous System
EMG - Electromyography
Hz - Hertz
ICC - Intraclass correlation coefficients
K+ - Potassium
MAP - Mean Arterial Pressure
MEP - Motor Evoked Potential
MVC - Maximum Voluntary Contraction
M-Wave - Compound Muscle Action Potential
Na+ - Sodium
NLMF – Non-local muscle fatigue
P+ - Phosphate
RM – Repetition maximum
RMS – Root mean square
RPE – Rate of preserved exertion
S - Second
SR - Sarcoplasmic Reticulum
TMS - Transcranial Magnetic Stimulation
VL – Vastus lateralis

Chapter 1: Literature Review

An analysis of the duration of non-local muscle fatigue effects

1.1 Introduction

Most people know the uncomfortable feeling of muscle fatigue. It makes doing a physical task harder than normal. You feel strong and resilient at the beginning then you feel muscles getting tired and weaker. Fatigue can be defined as "any exercise induced reduction in the ability to exert muscle force or power, regardless of whether or not the task is sustained" (Bigland-Ritchie & Woods,1984). Accordingly, fatigue is not detected at the beginning or just when muscles reach failure. Rather, fatigue increases gradually after the onset of a physical task (Enoka & Duchateau, 2008). There is no one dominant cause for fatigue, Fatigue can be local (i.e., single muscle) or global (i.e., full body) causing temporary impairments of voluntary activation and force production (Rattey et al. 2006). Crossover or non-local muscle fatigue (NLMF) occurs when fatigue of one muscle group leads to a decrease of force in homologous or heterologous non-exercised muscle groups (Halperin et al. 2015). Yet, there is some uncertainty and conflicting results regarding NLMF moderating factors such as muscle specificity, the effect of the NLMF protocol, contraction intensity and sex differences. A neglected area of research is the post-test durations of NLMF. This factor will be the objective of this study, as the majority of NLMF post-tests were conducted immediately after the fatiguing protocols. Hence, further studies are needed to clarify the duration of the NLMF impairments.

1.1.1 Fatigue

One definition of fatigue is the inability to generate the required force for a specific task (Edwards 1981). But muscle fatigue cannot be explained with a single model because also holding a submaximal resistance (weight or load) during an isometric contraction induces fatigue although there is no reduction in externally applied force. In this case, there is an increase in the effort to maintain that contraction and keep the load in position. A more comprehensive definition is provided by Simonson and Weiser (1976): "a transient loss of work capacity resulting from preceding work regardless of whether or not the current performance is affected". Enoka and Duchateau (2008) summarized fatigue as an exercise-induced reduction in physical functions causing impairments of motor performance accompanied by sensation of tiredness.

Enoka and Duchateau (2016) considered fatigue as a disabling system and divided it into two parts; performance fatigability and perceived fatigability. Performance fatigability is the decline in performance over time, while perceived fatigability is the changes in sensations that affect the performer. Accordingly, the psychological state would have a global effect on the whole body not just the fatigued muscle group. Hence, fatigue includes both qualitative and quantitative measures.

The mechanism of voluntary muscle activation is a very complex process starting at the cerebral cortex through a series of action potentials transmits to the neuromuscular junction and transferred to the muscle membrane. The action potential reaching the sarcoplasmic reticulum to release calcium into the muscle cell to initiate crossbridge kinetics. Considering the breadth of this pathway, fatigue can be divided into peripheral

and central fatigue components. There is no one single dominant cause for fatigue. It is more of task dependency principle whether it is a sustained low-intensity or high intensity activity that identifies which mechanism is activated (Enoka and Duchateau,2016).

1.1.2 Peripheral Fatigue Mechanisms

Peripheral fatigue exists in the muscle producing a reduction of force induced by changes that occur at or distal to the neuromuscular junction (Enoka & Stuart, 1992). Peripheral fatigue can occur due to lack of blood flow, reduced metabolic substrates, mechanical disruption (i.e., myofilament crossbridge interactions) affecting muscle action potential, and excitation contraction (E-C) coupling (Bigland Ritchie 1981). Peripheral fatigue was found to be primarily responsible for the decrease in force at early stages when subjects were asked to hold 2-min MVC of biceps brachii with around 80% loss of voluntary force. (Schillings et al. 2003).

Energetic deficiency plays a significant role in muscle fatigue, during a physical task when adenosine triphosphate (ATP) consumption is no longar equal the rate of ATP production (Sahlin 1992). There is a strong correlation between rate of ATP production and performance (Sahlin 1992). The decrease in ATP production plus high ATP turnover is translated in the cell as an increase in the catabolism of adenine nucleotide pool. (Sahlin et al. 1990b). Fatigue-related cellular mechanisms can be either due to excitation-contraction coupling or the cross-bridge itself. The E-C coupling involves the action potential, which travels through the transverse (T) tubules to the muscle fibre. The action potential is responsible for opening the calcium channel in the sarcoplasmic reticulum so that calcium is released to initiate myofilament crossbridge interactions (muscle contraction) (Fitts 1996). Fatigue can inhibit the action potential propagation from

traveling along the T-tubule affecting the Ca^{2+} release, this would lead to a decrease in myofibrils activated and force development (Garcia et a1. 1991). Fatigued cells can experience changes in the sarcolemma resting potential from -70mV to -80mV in addition, the spike potential reaches +5mV compared to +20mV in normal circumstances. This membrane depolarization reduces the activity of the sodium channels. The increase in both inorganic phosphate (due to decrease in phosphocreatine), and hydrogen levels lead to fatigue as they prevent or reduce the ability of the myosin binding to actin to generate high force (Cooke & Pate 1990). Inorganic phosphate is also thought to be the reason for initial force drop in maximal force (Westerblad & Allen 1991). As fatigue develops, the working muscles become more acidic. The drop in pH contributes to the drop in force by decreasing Ca2+ release from the SR and sensitivity of troponin (Stackouse et al. 2001). That force deficit can be detected more in fast (type II) than slow (type I) fibres (Nosek et al. 1987). Also, fatigue slows the relaxation and contraction time by inhibiting the sarcoplasmic reticulum calcium reuptake (Fitts 1996).

1.1.3 Central Fatigue Mechanisms

Decreases in force with long, sustained, maximal, isometric contraction have been primarily attributed to central fatigue (Schillings et al. 2003). Central fatigue originates within the central nervous system (CNS), which decreases the neural drive to the muscle (Gandevia 2001). Central fatigue can occur at different sites such as the primary motor cortex and the pyramidal system (Bigland-Ritchie, 1981). During maximal intensity contractions, fatigue can be detected and observed in a short period of time with changes in motoneuron excitability in addition to other inhibitory mechanisms (such as short-interval intracortical inhibition and intracortical facilitation) (Bigland-Ritchie et al. 1978).

When all the motor units are activated and recruited at the beginning of an activity with high metabolic demand, it is then immediately followed by a decrease in force (Bigland-Ritchie et al. 1978). Central fatigue can be evident when observing the electromyographic (EMG) activity, as there is a decrease in the mean power spectrum frequencies (Kranz et al. 1985) due to the effect of fatigue with maximal intensity contractions. Mardsen et al. (1983) proposed the muscle wisdom hypothesis and suggested that the decrease in motor unit discharge during MVCs helped to minimize fatigue. In addition, other central processes such as the Renshaw cells directly inhibit the alpha motoneurons' excitability. This process is called recurrent inhibition and mainly affects nearby homonymous and synergist motor pools (McCurdy and Hamm, 1994; Trank et al., 1999). During a sustained maximal effort there is an increase in recurrent inhibition that prevents excessive force output and is also responsible for contributing to coordination of motor activity (Maltenfort et al., 1998).

The evidence for fatigue with submaximal intensity contractions is not always as externally evident as with maximal intensity contractions. With submaximal forces, it is a compromise between impairments due to fatigue and neuromuscular facilitation to sustain the effort (Behm 2004). Initially, there is not a need to fully activate (recruitment and rate coding) all the involved (agonist or prime movers and synergists) muscle fibres (energy conservation) (Behm 2004). But as time under tension persists these motor units will experience fatigue due to many factors such as recurrent inhibition, type III and IV afferent inhibition, and reduced reflex potentiation (Behm 2004). Subsequently, non-fatigued, higher threshold fibres are recruited, and existing fibres increase their firing frequency to compensate for the loss of intrinsic force (Behm 2004). In addition to the

increased recruitment and rate coding, there are other supraspinal strategies to sustain performance through catch-like properties (the insertion of an additional neural impulses into the train of stimuli which can result in force potentiation) and muscle wisdom (Behm 2004). When motor units reach full activation for a prolonged period to sustain the load, there can be a decrease in motor unit discharge frequency and eventually de-recruitment (Person & Kudina 1972; Garland et al.1994, 1997). One model that emphasizes central fatigue is crossover or non-local muscle fatigue (NLMF).

1.1.4 Non-local muscle fatigue (NLMF)

NLMF is a temporary impairment in the performance of a non-exercised muscle after applying a fatigue protocol on a different muscle. The affected muscle can be located contralateral or ipsilateral to the fatigued muscle (Halperin et al. 2014c; Kennedy et al. 2013). Crossover fatigue refers to the muscle impairments of a contralateral homologous muscle (Martin and Rattey 2007, Doix et al. 2018), whereas NLMF can be deficits associated with any homologous or heterologous non-exercised muscle (Behm et al. 2021, Halperin et al. 2014c, 2015). Since the tested non-fatigued muscle has not experienced prior activity or fatigue, any impairments due to the fatigue of another muscle cannot be due to peripheral (local) factors (i.e. changes in pH, metabolite accumulation, E-C coupling or crossbridge kinetics disruption) and thus must be due to global or central influences (Behm et al., 2021). The magnitude of NLMF varies due to many factors, such as the fatigue protocol(s) used, the fatigued muscle group and the techniques used to test it (Halperin et al., 2015) and (Behm et al., 2021).

1.1.5 Central NLMF mechanisms

Feedback systems contribute to the behaviour of working muscles and maintaining the force output. That feedback can be either spinal or supraspinal. Thus, fatigue can lead to inhibition in the CNS and reduction in the neural drive of non-exercised muscles (Gandevia 2001). Fatiguing protocols that promote an accumulation of the metabolic by-products may lead to activation of group III and IV muscle afferents (Amann 2012). These sensory neurons affect the motoneuronal output and inhibit the corticospinal pathway (Sidhu et al., 2014). Muscle afferents are also important for determining the fatigue threshold, which is the level of peripheral fatigue that is never exceeded under intact sensory feedback conditions (Amann 2009; Amann et al. 2013). Sidhu el al. (2017) suggested that group III and IV muscle afferents have different effects on the corticospinal pathway depending on the existence or absence of fatigue. In the absence of fatigue, they facilitated motor cortical cells and inhibited motoneurons while with fatigue they inhibited motor cortical cells without affecting the motoneurons. However, recent studies showed that group III and IV do not contribute to NLMF effects. Kennedy et al (2016) showed that after fatiguing the knee extensors with maximal isometric contraction, group III and IV muscle afferents did not affect the corticomotoneuronal pathway.

On the other hand, transcranial magnetic stimulation (TMS) is used to monitor corticospinal responses by exciting the motor cortex (Klomjai et al. 2015) producing a measurable electrical potential from the muscle of interest using surface EMG (motor evoked potentials or MEPs). MEPs are the recorded electrical signals from the descending

motor pathways. MEPs amplitudes increase with isometric voluntary contractions, suggesting that corticospinal excitability is increased.

However, it depends on the group muscle tested. The biceps brachii muscle showed greater increases in MEP compared to distal muscles the brachioradialis and adductor pollicis during a stimuli wide range of intensities from zero to 75% MVC (Kischka et al. 1993; Taylor et al. 1997). Studies that used TMS showed decrease in force output during fatigue can be due to the descending drive from the motor cortex as evidenced by reduced amplitudes of MEPs (Taylor & Gandevia 2001). While during a sustained MVC, MEP increased in the first 15-seconds with no changes thereafter (Taylor & Gandevia 2001). Also, Šambaher et al. (2016) showed that bilateral knee extensors fatigue not only decreased the elbow flexors' force production but also induced a significantly lower MEP/CMEP ratio (25%) (the MEP/CMEP ratio is used to assess whether changes happened at spinal or supraspinal level). This inhibition was suggested to be due to the suppression of excitability of the supraspinal circuits.

However, Aboodarda et al. (2017) found significant increases in the MEP/CMEP ratio (32%) at 100% MVC following fatigue (two 100-s dominant leg MVIC knee extension) compared to control. It was suggested that fatiguing the elbow flexors made the supraspinal circuits more excitable. They also had similar results in another study investigating unilateral elbow flexion fatigue effects on MVC and corticospinal excitability of the contralateral non-exercised biceps brachii with significantly higher MEP during 100% MVC of unilateral elbow flexion muscles and greater supraspinal motor response (Aboodarda et al. 2016a). However, Aboodarda et al. (2019) later did not find any changes in right knee extensors muscles neuromuscular functions nor

corticospinal responses after fatiguing the contralateral knee extensor. Takahashi et al. (2011c) showed that fatiguing lower limb muscles decreased the excitability of the corticospinal tract and disinhibition of the intracortical circuit in the non-exercised upper limb muscles. These contrasting findings between studies showing higher MEP/CMEP and other showing lower MEP/CMEP after fatigue even by the same research team highlights the need for more studies and conditions tested to elaborate the influence of NLMF on the excitability of supraspinal and corticospinal circuits.

1.1.6 Biochemical mechanisms

During exercise, the depletion of energy substrates metabolic by-products start accumulating and contribute to fatigue. These by-products include: magnesium ions, adenosine diphosphate (ADP), inorganic phosphates, lactate ions, hydrogen ions and ammonia. These by-products can be transferred through the cardiovascular system around the body (Halperin et al., 2015) . In NLMF studies, hydrogen ions and blood lactate were found after testing the non-exercised muscles (Bogdanis et al. 1994). Grant et al. (2014) used biceps curls as an arm fatigue protocol before performing two maximal 30-second sprints on a cycle ergometer. The prior upper body exercise significantly affected peak power output suggesting that metabolic by-products have effects on maximal force production. Intense exercise is also related with high levels of lactate, which correlates with increases in the acidity inside the working muscles (Lannergren & Westerblad, 1991). Bangsbo et al. (1996) suggested that the decrease in muscle pH by 0.2 (from 6.82 to 6.54) did not affect glycogenolytic and glycolytic pathways. Acidity level is not the only cause of fatigue in high intensity exercise as there is a link between potassium in muscle and fatigue as well. High intensity exercise causes a loss of potassium from

working muscles and an increase of extracellular levels of potassium leading to a loss of force (Sejersted and Sjøgaard 2000). Hence, fatigue-induced metabolic disruptions are not isolated to the exercising muscle but can be distributed globally impairing non-local contractile functions.

1.1.7 Biomechanical mechanisms

Core stability is a term that has been used extensively in sports strength and conditioning lately as an important aspect that athletes need to maximize their performance (Behm et al. 2010). Anatomically, the core is the axial skeleton and all proximally attached soft tissues whether they end on the axial or appendicular skeleton (Behm et al. 2010). Developing the core muscles not only helps in the prevention of lower back injuries but may enhance performance (Behm and Anderson 2006). However, Behm et al. (2015) found in their meta-analysis that unstable resistance training has limited effect on power and balance compared to stable resistance training. In addition, core muscles can either facilitate generation and transfer of force to extremities (kinetic chain) (Kibler et al. 2006) or resist motion (Behm et al. 2010). Core muscles do not only work in isolation, but they also connect upper body to lower body muscles and vice versa with minimal dissipation of energy (Shinkle, et al. 2012). Upper body exercises can highly activate trunk muscles. Bilateral shoulder extensions had significantly higher EMG amplitudes for rectus abdominis and external oblique compared to trunk flexion exercise (Tarnanen et al. 2008). Hence, when a fatigue protocol is applied that exhaust stabilizer muscles, it hinders their function to stabilize the body and affect the kinetic chain of the movement leading to a decrease in force production of the non-exercised muscles as another possible indirect cause of NLMF (Halperin et al. 2015).

1.1.8 Psychological mechanisms

The psychological side of the fatiguing protocol plays a predominant role. Psychological state, feelings like anger or fatigue are a mental representation of the physiological state. The mind is aware of the physiological change due to the physical activity exerted whether maximal or submaximal, which leads to changes in neural networks. It is suggested that a primary region in the brain involved is the prefrontal cortex (Miller 2000). These psychological effects are facilitated through perceived fatigability, which is related to the changes in the sensations that regulate the integrity of the subject during the required task (Enoka and Duchateau, 2016). Perceived fatigability can be measured in both conditions of rest or during the task. Naturally, a participant would want to stop as the task becomes uncomfortable (Halperin et al. 2015). For example, when the fatiguing protocol is prolonged (e.g., 100-second MVC) the participant is then asked to repeat the same intensity again using a non-exercised muscle. The participants may be already fatigued mentally affecting focus and concentration, which impairs physical performance therefore lower activation may be experienced in the muscle that was not exercised (Marcora et al. 2009).

The pre-induced fatigue from one task makes the group III/IV muscle afferent feedback higher in the non-exercised tested limb even if the work rate is the same (Amann et al. 2013). Studies with a known end point (e.g., a known duration or distance of the task) had higher force and EMG outputs (Billaut et al. 2011). The unknown duration of the protocol limits the performance when asking the participant to maintain MVC for the entire duration of the test (Mauger et al. 2009) due to the absence of a pacing plan (the variation of force over the time by regulating the rate of energy

expenditure) based on the knowledge of endpoint throughout the task (St Clair Gibson et al. 2006), which will decrease the motivation for optimum performance.

Pacing strategies helps to delay fatigue development and the associated discomfort feelings. Previous experiences can also affect participant's decision making of pacing or maintaining that effort level for a longer duration. Stone et al. (2012) showed that performance feedback also influenced average power output for trained cyclists performing time trials. Hence, mental fatigue can have negative effect on motivation and force output respectively. Besides the greater perceived exertion specially with prolonged submaximal fatiguing protocols.

NLMF effects mainly exist due to neural and psychological factors (Halperin et al. 2015). The psychological element of experiencing discomfort or pain during longer fatiguing protocols can affect both fatigued and non-exercised muscles (Halperin et al. 2015). Hamilton and Behm (2017) examined the presence of NLMF in known versus unknown testing endpoints and showed that unknown testing endpoints produced lower force and muscle activity. In addition, known endpoint condition provided the participants with more motivation to overcome any drop in performance due to fatigue (Hagger et al. 2010). Hence, knowing the test endpoint can change NLMF effect.

1.2 Factors affecting NLMF

1.2.1 Effect of fatiguing protocol intensity on NLMF

Intensity was one of the main NLMF factors, as higher intensity muscle contractions were found to have more impact on NLMF magnitude than lower intensity contractions (Kennedy et al. 2013). In the Kennedy et al. (2013) study, upper body

muscle fatigue protocols (forearm) led to NLMF of lower body muscles (plantar flexors) when MVC and voluntary activation were tested post-intervention.

Kawamoto and Behm (2014) tested the effect of fatiguing, non-dominant limb, dynamic, knee extensions at 70% and 40% MVC (4-sets till failure with one-minute recovery) on the contralateral non-exercised knee extensors muscle group. Both conditions resulted in significant F100 (force produced in the first 100 ms of an MVC) and MVC peak force decrements, yet the higher intensity condition (70% MVC) had larger magnitude decrements compared to the lower intensity (40% MVC).. Hence, in accordance with these previous studies (Doix et al. 2013; Halperin et al. 2015; Hamilton and Behm 2017) they all showed that high intensity fatiguing protocols can lead to NLMF especially when combined with high volume (two bouts of 100 s maximal voluntary isometric contractions).

1.2.2 Muscle specificity

NLMF can be considered muscle specific as not all muscle groups have the same level of decrement in force after different fatiguing protocols. The majority of the research found that lower body muscle groups observed more NLMF effects compared to the upper body. This was supported when Alcaraz et al. (2008) tested heavy loading circuit training with maximum effort 6-repetition maximum (RM) bench press including passive and active recovery (leg and ankle extensions). Their findings showed that both conditions did not significantly affect the performance regarding bar speed or number of repetitions. When participants did upper body exercises (bench press and bench pull) as an active recovery between back squats sets, impairments were observed in the number of repetitions till failure (Ciccone et al. 2014). These findings conclude that lower body

muscles (quadriceps were the most tested lower body muscle group) are more affected by NLMF than the upper body muscles mainly due to its large mass and higher number of fast twitch fibres (Miller et al. 1993). These functions require the neural drive to be fully activated. Due to the fatigue of the lower body muscles, the ability of the nervous system to fully activate this high volume of motor units (Galea et al. 1991) is hindered compared to upper body muscles (Behm et al. 2002). Therefore, fatiguing lower body muscles promotes a higher sensation of the effort as it also affects the rate of perceived exertion (RPE). RPE was found to be higher in back squats compared to bench press even with the same intensity, volume, and rest (Mayo et al. 2014), demonstrating that fatiguing lower body muscles leads to a greater NLMF effect.

1.2.3 Sex differences

The difference in the effect(s) that NLMF has between sexes is not very clear and there are limited studies that compare males and females. Martin and Rattey (2007) showed that although both sexes were affected by NLMF, greater central fatigue was observed in males with a 13% decrease in MVC compared to an 8% impairment with females (MVC tested before and after a 100-second MVC). More studies are required to determine if NLMF is sex specific. Based on studies included in the meta-analysis from Behm et al. (2021), females only represent approximately 8% of total participants in NLMF studies. Physiologically, females have less muscle mass, which will affect oxygen demand and perfusion. Less muscle mass produces less absolute force, less intramuscular pressures and occlusion of blood flow while performing the same task compared to males at the same relative intensity (Hunter 2009). Moreover, they were found to have less decrement in maximal force while sustaining submaximal isometric contractions (20-70%

of MVC) for many of the muscles tested (Hunter et al. 2006). While males depend more on efficient glycolytic energy pathway, females depend less on carbohydrates metabolism, have higher fat oxidation rate and less respiratory exchange ratio during endurance exercises (Tarnopolsky 1999). Research also suggests that estrogen has glycogen-sparing properties (Tarnopolsky 1999) meaning that females are more fatigue resistant with longer duration activities. However, with only a single study comparing NLMF responses between sexes, it is not clear whether the generally greater fatigue resistance of females transfers to differential NLMF responses.

1.2.4 NLMF testing protocols.

The type of testing protocols used may differentially affect the magnitude of NLMF. Most studies either do 1-3 single post-fatigue MVC tests with sufficient rest intervals, or a submaximal exercise to exhaustion. Doix et al. (2013) found that a unilateral fatigue protocol (two bouts of 100-second knee extension) reduced the MVC (~10%) of both the ipsilateral and contralateral muscles. While Halperin et al. (2014b,c) found a decrease in force production (~8%) of the rested knee extensors after the subjects performed 12 MVCs with 5-seconds of work and 10-seconds of rest between each repetition. Halperin's (2015) summarized that time to exhaustion and repetitive MVCs fatiguing protocols have a greater effect on NLMF due to the additional stress put on other systems (neural, biochemical, and psychological) compared to single contraction. Behm et al. (2021) in their meta-analysis concluded that NLMF was more evident (moderate effect size magnitude) when a post-test fatigue protocol is applied rather than a single or discrete strength (trivial magnitude effects overall) measure. Time to exhaustion and repetitive MVCs fatiguing protocols accumulate a greater concentration of metabolic

by-products such as hydrogen ions, blood lactate and potassium in the fatigued muscles (Halperin et al. 2015). These by-products can also be distributed around the body through the cardiovascular system affecting resting muscles' performance and ability to contract (Bangsbo et al., 1995; 1996). Elevated levels of hydrogen ions inhibit force production as they inhibit the cleavage of ATP (Fitts 2008). With pH decreasing and inorganic phosphate (P_i) starts accumulating during fatigue, they both also reduce myofibrillar Ca^{2+} sensitivity and tension during fatigue (Fitts 2008).

In addition, the activation of type III and IV muscle afferents inhibits the central motor drive in both exercised and non-exercised muscles (Amann 2012, 2011; Sidhu et al. 2014; Amann et al. 2013). Yet more studies are needed to confirm the exact roles and effects of group III/IV muscle afferents. As Sidhu et al. (2014) were studying the roles of group III/IV muscle afferents which demonstrated that the feedback from these afferents from the lower body muscles led to supraspinal fatigue in upper body muscles in a cycling to exhaustion test. Kennedy et al. (2015) also studied the activity of muscle afferents and found no crossover of fatigue in contralateral knee extensors after sustaining a two-minute unilateral MVC and no NLMF was recorded. Hence, as other studies consistently demonstrated similar results (Halperin et al. 2014a, b; Kawamoto et al. 2014) the longer the duration of fatigue protocol used, the more significant NLMF effects were measured compared to single maximal voluntary isometric contractions (Halperin et al. 2015, Behm et al. 2021).

1.2.5 NLMF Post-test durations

The search for crossover fatigue studies resulted in 37 related articles. Twenty-one of these studies found NLMF effects (significant reduction in EMG activity and force) on

the tested non-exercised muscle group. From the reviewed NLMF studies, 95% performed the post-test within the first minute after the fatiguing protocol. Only 11% tested at different times (1, 5 and 10-minutes). While one study tested at 3-minutes only after the fatiguing protocol was done. Hence, more studies are needed to discover the duration of the NLMF effects.

The physiological and neurological fatigue effects on the exercised muscles endured for extended periods post-test in many studies. Arora et al. (2015) found significant 44.8% and 39.9% decreases in the peak force and F100 respectively 10-minutes after the fatiguing protocol. Prieske et al. (2017) indicated a 4-24% decrease in neuromuscular efficiency at a test velocity of 60°/s up to 5-minutes post-test and Humphry et al. (2004) reported a 26% decrease in MEP for fatigued biceps brachii up to 9-minutes post-test and remained approximately the same value for 30-minutes, even though it increased to 58% after 60-minutes yet still was significantly depressed compared top pre-test. Thus, while the exercised limb has shown fatigue effects for 30 minutes post-fatigue, there is inadequate information regarding the duration of NLMF effects.

1.3 Conclusions

Although the most recent meta-analysis (Behm et al. 2021) reported overall trivial NLMF effects upon single or discrete strength measures, there were a substantial number of studies that did report NLMF. Even with these differing and conflicting findings, there are some conditions in studies that report NLMF that show greater observable NLMF effects. Fatiguing lower body muscles leads to greater NLMF compared to upper body

when tested as lower body muscles promotes a higher sensation of effort and RPE. Also fatiguing stabilizer muscles can indirectly lead to NLMF since the diminished stabilization can decrease force production in non-exercised muscle. The longer the duration of the fatigue intervention used, the more significant NLMF effects. Generally, high-intensity and high-volume fatigue protocols show more NLMF effects than a single MVIC. Additionally, unknown testing endpoints produced lower force and muscle activity, which can modify NLMF while known endpoint conditions provided the participants with more motivation to overcome any drop in performance. However, NLMF between sexes was not very clear as not enough studies were available to demonstrate whether the female's greater fatigue resistance influenced NLMF. The majority of NLMF post-tests were primarily completed in the first minute if not immediately after finishing the fatiguing protocols to identify if the NLMF exists using previously mentioned factors and protocols.

1.4 Objectives

The objective of the present study was to examine the duration of NLMF effects by testing at different time conditions (1, 3, and 5min) to investigate the duration of possible effects.

1.5 Hypothesis

NLMF effects last less than five minutes.

Chapter 2: Research

2.1 Methods

2.1.1 Participants

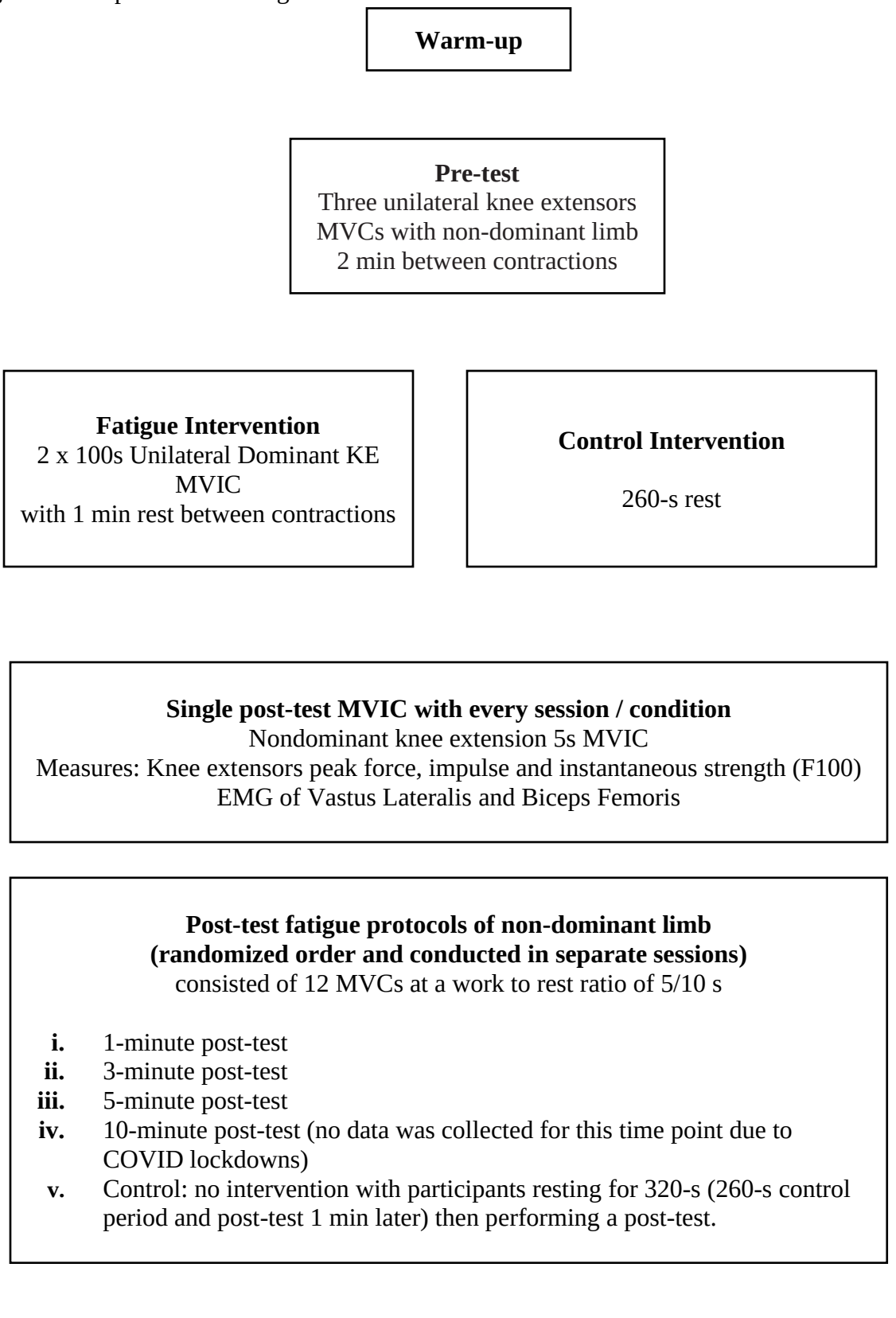
An “a priori” statistical power analysis (software package, G * Power 3.1.9.2) was conducted based on the force measures of related studies (Behm et al., 2016b; Behm, 2019; Chaouachi et al., 2017) to achieve an alpha of 0.05, effect size of 0.5, and a statistical power of 0.8 using the F-test family. The analysis indicated that between 8-13 participants per group should be sufficient to achieve adequate statistical power.

Due to the COVID lockdown only five recreationally trained participants were recruited for this study, four females (height 159.1 ±2.9 cm, body mass 62.7 ± 7 kg, age 26.6 ± 9.8 yrs.) and one male (height 182.2 cm, body mass 90.3 kg, age 40 yrs.). Four of the participants were determined to be right-leg dominant, while one participant was left-leg dominant by asking them which leg they would prefer to kick a soccer ball and would be more accurate. Prior to testing and after a brief explanation of the study and procedures of the experiment, each participant completed the physical activity readiness questionnaire plus (PAR-Q+ 2020), read and signed the informed consent form, and filled the COVID-19 daily self-assessment tool. Prospective volunteers who reported injury to the quadriceps muscles or knee joint or neurological conditions were excluded from the experiment. Participants were instructed to avoid intense activity and cease consumption of alcohol, caffeine, or nicotine for the 24-hour period prior to their lab visit. The Health Research Ethics Authority of the Memorial University of Newfoundland approved this research protocol (#20210760).

2.1.2 Experimental design

A randomized crossover study design was used to examine the duration of acute effects of unilateral knee extensors muscle fatigue on the contralateral homologous muscle strength, activation and fatigue resistance (endurance). An initial familiarization session oriented the participants with the testing procedures and the equipment. Participants visited the lab for five separate testing sessions (separated by at least 48 hours) including control. Experimental conditions were presented randomly and included testing at one, three, five minutes post-test or Control: (no intervention with participants rested for 260 seconds then performed a post-test at 1-min after the control inactivity period). The original protocol included a 10-minute post- testing period, but due to COVID restrictions, we were not able to collect this data at this time point. Non-dominant knee extensors muscle force, instantaneous strength (F100: maximum force produced in the first 100 ms) and an endurance test as well as vastus lateralis and biceps femoris electromyography (EMG) data were collected. A series of 12; 5-second isometric maximal voluntary contraction (MVIC) knee extensions with 10-second recovery between repetitions (endurance test) were performed with the non-dominant knee extensors after the fatiguing intervention.

Figure 2.1: Experimental Design



2.1.3 Protocol

2.1.3.1 Electromyography (EMG)

Each session started with the placement of surface EMG electrodes on the vastus lateralis (VL) and biceps femoris (BF) of both legs. Self-adhesive Ag/AgCl electrodes (MeditraceTM 130 ECG conductive adhesive electrodes) were placed according to previous studies (Hermens et al. 2000; Paddock and Behm 2009; Kawamoto et al. 2014). The surface electrodes were placed at 66% of the line between anterior superior iliac spine and lateral side of the patella for the VL. The mid-point between the gluteal fold and popliteal space was used for the BF. The electrodes were placed 2 cm apart (centre to centre) and parallel to the direction of the muscle fibers. The ground electrode was placed on the lateral femoral epicondyle. The skin was prepared prior to electrode placement by shaving the area, rubbing with sandpaper, and cleansing with an isopropyl alcohol swab to ensure minimal skin resistance.

To ensure an adequate signal-to-noise ratio, an interelectrode impedance of <5 kΩ was obtained prior to testing. The EMG signal acquisition system (Biopac System Inc., DA 100: analog–digital converter MP150WSW; Holliston, Massachusetts) recorded all signals at a sampling rate of 2000 Hz. All EMG signals were filtered with a Blackman − 61 dB band-pass filter between 10 and 500 Hz, amplified (bi-polar differential amplifier, input impedance = 2 MΩ, common mode rejection ratio >110 dB min (50/60 Hz), gain × 1000, noise >5 μV), and analog-to-digitally converted (12 bit) for storage and analysis on a personal computer. A commercially designed software program (AcqKnowledge III, Biopac Systems Inc.) was used for the establishment of signal parameters and for data analysis.

A 3-s window root mean square (RMS) EMG was used over the peak MVIC force (1.5-s prior to and after the peak force). RMS values were determined using a window width of 50-ms. Once RMS was calculated the mean value was selected. As EMG measures typically have lower reliability values and greater test to re-test variability than MVIC force, these EMG values were then normalized to the highest pre-test value and reported as a percentage.

2.1.3.2 Pre-test Single MVIC Force Measures

Subjects started a general warm up of lower body cycling (Monark cycle ergometer: Sweden) for 5-min at a pace 70 rpm. Next, in a randomized order, participants performed a pre-test with 2 knee flexion and extension MVICs for each muscle tested (BF and VL of both legs). Each MVIC was performed for 5-s with 2-min rest between MVICs. Subjects were asked to contract the involved muscles as hard and as fast as possible throughout the 5-s. The MVIC with the highest peak force was used for analysis. If the second MVIC was 10% higher an additional MVIC was added. To eliminate upper body involvement, a five-point harness was placed around the waist and shoulders of the participants and they were instructed to cross their arms across their chest. The ankle was inserted in an ankle cuff which was attached to strain gauges (Omega engineering Inc., LCCA 250, Don Mills, Ontario) by a non-extensible chain. The strain gauge and the chains were hooked to either the chair (for VL MVICs) or the wall (for BF MVICs) and the chair was positioned at a distance from the wall that maintained the chain with no slack. The MVIC warm-up consisted of three 5-second contractions at approximately 50% MVIC followed by two 5s contractions at approximately 75%.

2.1.3.3 Unilateral Fatigue Intervention

After the MVICs pre-tests, a fatigue protocol or rest (260-seconds) was presented as an intervention depending on the experimental condition. The fatigue protocol utilized for this study has been shown to elicit NLMF in contralateral knee extensors (Doix et al. 2013; Halperin et al. 2014b). With the same setup as for the pre-MVIC testing, the dominant leg performed a continuous knee extension MVIC for two sets of 100-seconds, separated by 1-min of rest. The dominant leg was used for all fatiguing protocols and the participants were encouraged to keep the contralateral leg relaxed during leg contractions. The EMG of the contralateral leg was monitored throughout the fatigue protocol to ensure it was relaxed (<5% MVIC EMG). Data for both legs were saved throughout the fatigue protocol for later analysis. A fatigue index (by dividing the last 2 MVICs mean values by the first 2 MVIC for forces and applying the same equation for EMG values) was calculated accordingly to test endurance outcome.

2.1.3.4 Post-test Single MVIC Force Measures

A single MVIC was performed at the post-tests after the fatigue protocol based on the condition (1-, 3-, and 5-min and, control). Starting with dominant leg knee extension then the non-dominant leg, followed by non-dominant leg knee flexion. Each MVIC was performed for 5-seconds and switched rapidly to the next. Peak force, impulse (work x time) and instantaneous strength (F100) were measured for each knee flexion and extension MVIC of both legs.

2.1.3.5 Post-test Fatigue Measures

Since NLMF has been shown to be more evident with fatigue testing (Halperin et al.,2014a, Behm et al. 2021), a post-test fatigue protocol involved participants performing

a repeated MVIC protocol of the non-exercised knee extensors consisting of 12 MVICs at a work to rest ratio of 5/10 seconds. Each visit had a different time for the post-test (1-, 3-, and 5-min), while during the control session, participants followed the same pre-test protocol but instead of doing the fatiguing protocol they rested for 260-seconds followed by a post-test at 1-min after the control inactivity period. The 12 MVICs were used for calculating a fatigue index to detect if there was a significant decrease in forces or EMG during the endurance test in the non-exercised muscle group showing NLMF effects. This was done by dividing the last 2 MVICs mean values by the first 2 MVIC for forces and applying the same equation for EMG values.

2.1.4 Statistical Analysis

Statistical analyses were calculated using SPSS software (Version 27). Intraclass correlation coefficients (ICC) were to be calculated for MVIC force, VL and BF EMG in the non-dominant limb. Normality (Kolmogorov-Smirnov) and assumption of sphericity tests were conducted for all dependent variables. When normality and sphericity were met, the effect of fatiguing protocol on pre- and different timing post-test measurements (1, 3, 5, minutes), were performed for MVIC force and EMG using a two-way repeated measures ANOVA 2 (pre- and post-test) x 4 (Control, 1, 3, and 5 min) for the single MVC measures. Also, for the fatigue index a one-way repeated measures ANOVA (4 post-testing conditions Control, 1, 3, and 5 min) was employed. Both ANOVAs were for the non-exercised leg. If significant main effects were observed, Bonferroni correction post-hoc tests were used to compare different conditions and times. Significance was defined as $p < 0.05$. Cohen's d effect sizes (Cohen, 1988) were also be calculated, with

effect sizes of, <0.2: trivial, 0.2 to <0.5: small, 0.5 to <0.8: medium and 0.8 or greater: a large effect size. Data was reported as means ± SD.

2.2 Results

The normality and homogeneity of variances within all the MVIC collected data were confirmed with the Shapiro–Wilk and Levene's tests, respectively except for the pre-test for dominant quadriceps forces. Unfortunately, due to the low subject recruitment due to COVID lockdowns there were insufficient data points to accurately calculate reliability with ICC.

2.2.1 Fatigue intervention on the non-dominant knee extensor MVIC:

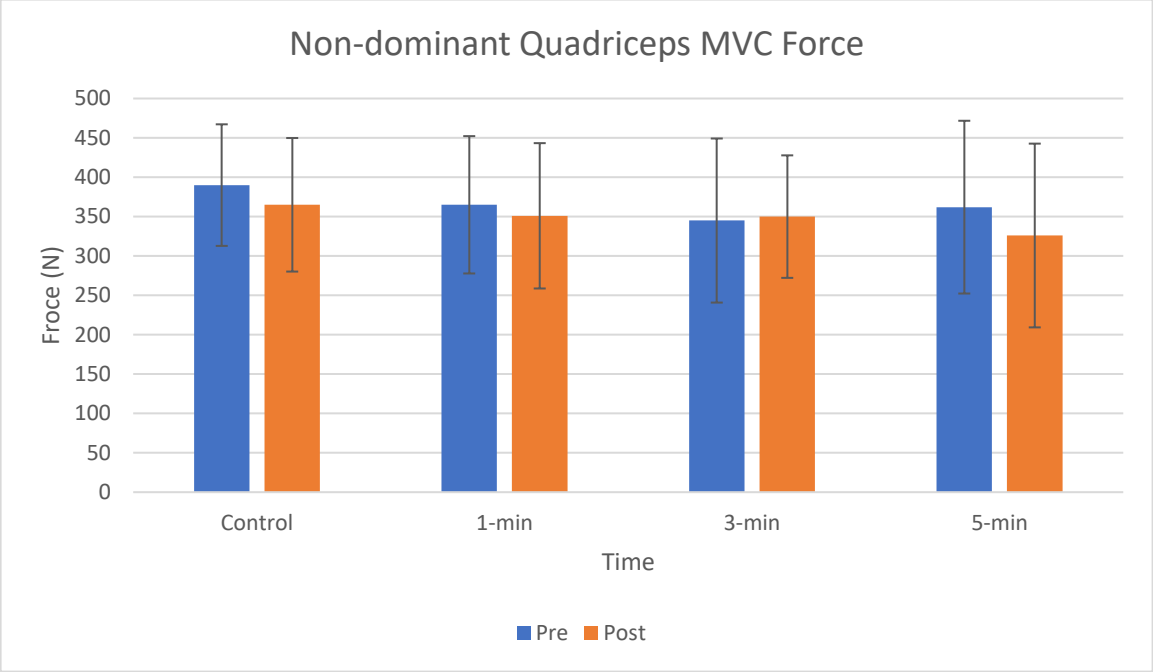
An insignificant, small magnitude, interaction ($F_{(1,16)} = 3.51$, $p = 0.08$, $d = 0.2$) revealed that the non-dominant quadriceps showed decreases in single MVIC forces. Compared to the pre-test, MVIC forces decreased 3.7% at 1-min post-test, increased 1.4% at 3-min, and decreased 10% at 5-min post-test. The control group showed a pre- to post-test decrease of 6.4% (Table 1 and Figure 1).

Table 2.1

Effects of fatigue intervention on the non-dominant knee extension (quadriceps) MVIC force:

	Pre-MVIC	Post-MVIC	Percent difference (%)	Effect size
Control force (N)	390.8 ±109.7	365.8 ±116.7	-6.4	0.2
1-min force (N)	365 ±77.2	351.6 ±84.8	-3.7	0.2
3-min force (N)	345.4 ±87.2	350.2 ±92.3	+1.4	0.2
5-min force (N)	362.6 ±104.2	326.4 ±77.8	-10.0	0.2

Figure 2.2



2.2.2 Effects of fatigue intervention on the non-dominant knee flexion MVIC force:

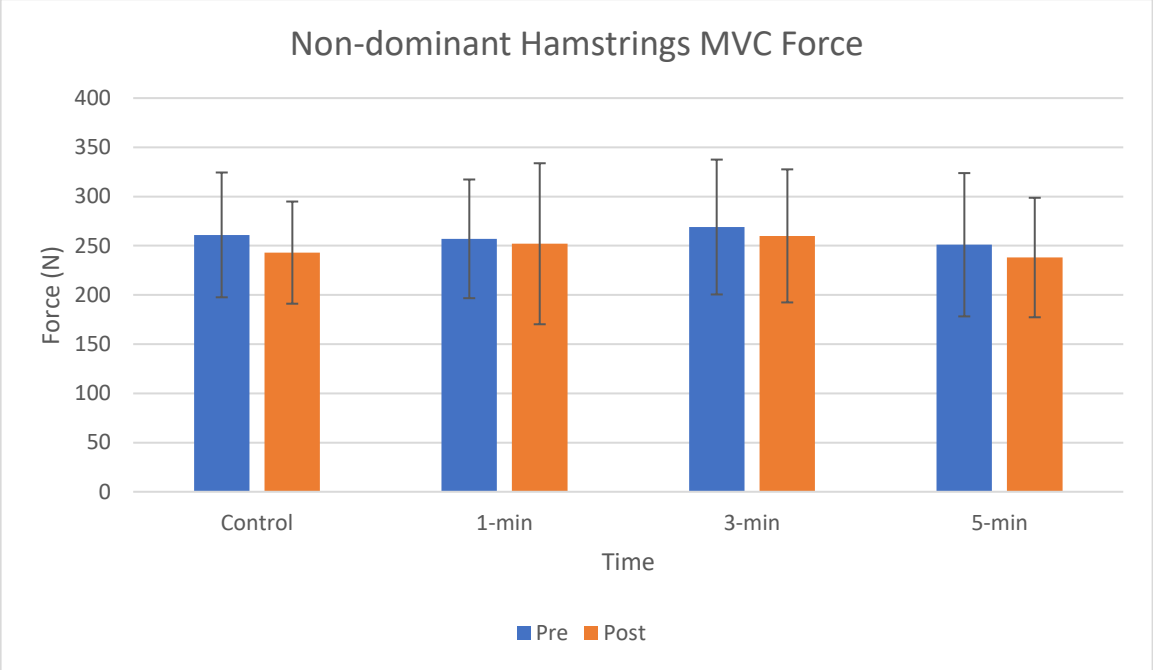
There was an insignificant trivial magnitude interaction ($F_{(1,16)}$ =2.61, p =0.126, d=0.1) for non-dominant quadriceps single MVIC forces. Compared to the pre-test, MVIC forces decreased 1.9%, 3.3% and 5.4% at 1-, 3- and 5-min post-tests respectively. The control group showed a pre- to post-test decrease of 7% (Table 2 and Figure 2).

Table 2.2

Effect of fatigue intervention on the non-dominant knee flexion (hamstrings) MVIC force:

	Pre-MVIC	Post-MVIC	Percent difference (%)	Effect size
Control force (N)	261.2 ±72.8	243 ±60.7	-7	0.1
1-min force (N)	257 ±63.4	252.2 ±51.9	-1.9	0.1
3-min force (N)	269.2 ±60.3	260.2 ±81.8	-3.3	0.1
5-min force (N)	251.8 ±68.5	238.2 ±67.6	-5.4	0.1

Figure 2.3



2.2.3 Effect of fatigue intervention on the dominant knee extension (quadriceps) MVIC force:

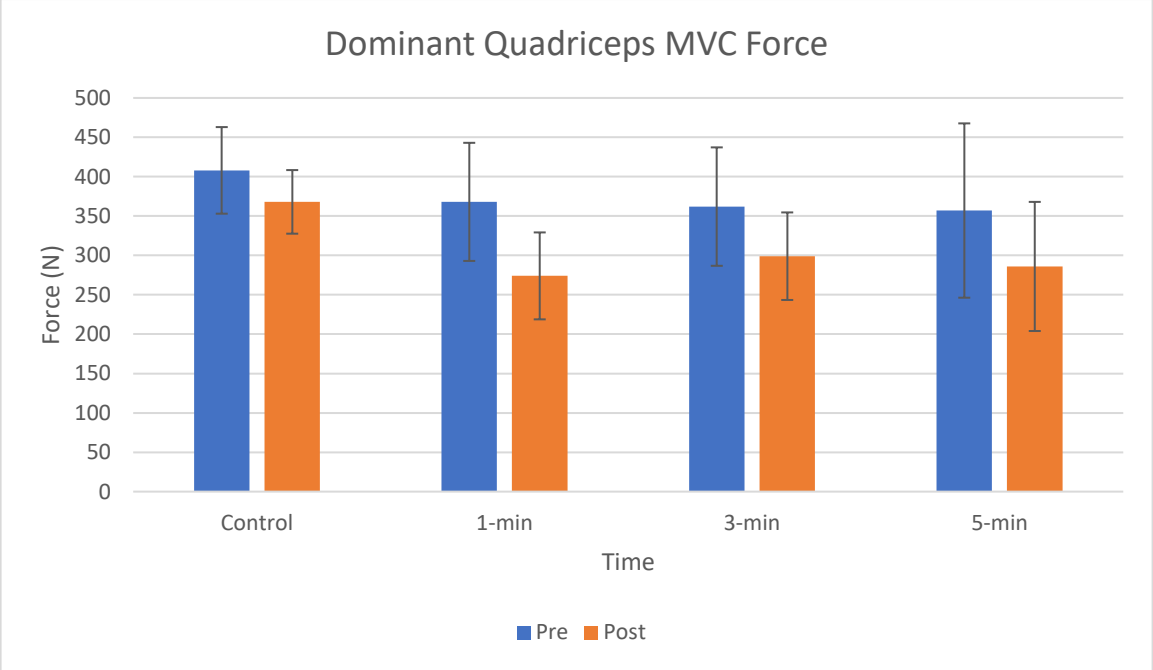
A significant, large magnitude, main effect was found for pre- vs. post-tests ($F_{(1,16)}$ =38.6, p <0.001, d=0.8) decrease in dominant quadriceps MVIC forces but no significant interaction effect (pre vs. post * condition) ($F_{(3,16)}$ =1.38, p = 0.286, d =0.2). Compared to the pre-test, MVIC forces decreased 25.5% at 1-min post-test, increased 17.4% at 3-min, and decreased 19.9% at 5-min post-test. The control group showed a pre- to post-test decrease of 9.8% (Table 3 and Figure 3).

Table 2.4

Effect of fatigue intervention on the dominant knee extension (quadriceps) MVIC force:

	Pre-MVIC	Post-MVIC	Percent difference (%)	Effect size
Control force (N)	408.2 ±110.7	368.4 ±82	-9.8	d= 0.8
1-min force (N)	368.8 ±55	274 ±40.4	-25.5	d= 0.8
3-min force (N)	362.6 ±75	299 ±55.2	+17.4	d= 0.8
5-min force (N)	357.8 ±75.2	286.2 ±55.6	-19.9	d= 0.8

Figure 2.4



The normality and homogeneity of variances within all the EMG collected data were confirmed with the Shapiro–Wilk and Levene's tests, respectively.

2.2.4 Non-dominant quadriceps EMG during the post- tests

A significant, large magnitude, main effect was found for pre vs. post tests ($F_{(1,16)}$ =64.15, p <0.001, d =0.8) decrease in non-dominant quadriceps EMG data but no

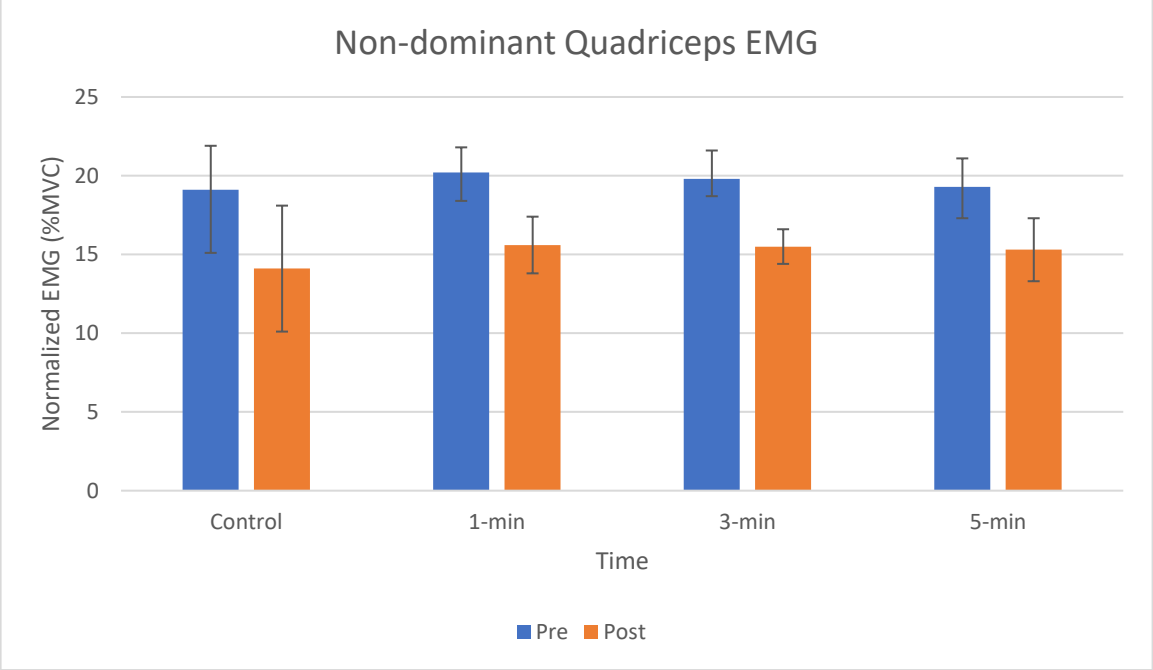
significant interaction effect (pre vs post * condition) ($F_{(3,16)}$ =0.132, p =0.94, d =0.02). Compared to the pre-test, EMG means decreased 22.8%, 21.7% and 20.7% at 1-, 3- and 5-min post-tests respectively. The control group showed a pre- to post-test decrease of 26.2% (Table 4 and Figure 4).

Table 2.4

Effect of fatigue intervention on the non-dominant quadriceps EMG:

Normalized EMG Condition	Pre (%MVIC)	Post (%MVIC)	Percent difference (%)	Effect size
Control	19.1 ±2	14.1 ±2	-26.2	d= 0.8
1-min	20.2 ±3	15.6 ±4	-22.8	d= 0.8
3-min	19.8 ±20	15.5 ±20	-21.7	d= 0.8
5-min	19.3 ±2	15.3 ±2	-20.7	d= 0.8

Figure 2.5



2.2.5 Non-dominant hamstrings EMG during the post-tests

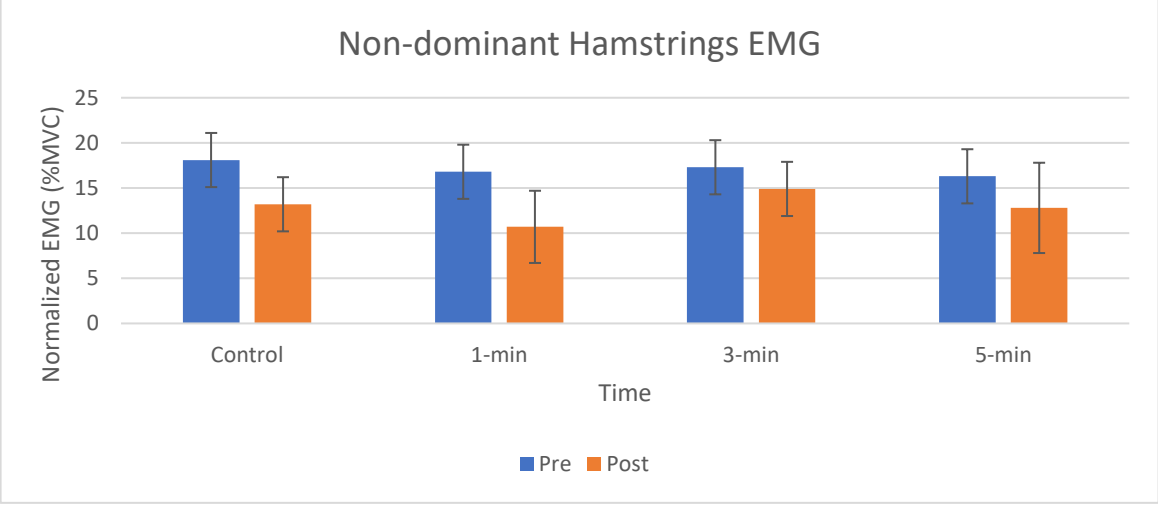
A significant, moderate magnitude, main effect was found for pre- vs. post-tests ($F_{(1,16)}$ =21.74, p <0.001, d =0.6) decrease in non-dominant hamstrings EMG data but no significant interaction effect (pre vs post * condition) ($F_{(3,16)}$ =0.79, p = 0.516, d =0.1). Compared to the pre-test, EMG means decreased 36.3%, 13.9% and 21.5% at 1-, 3- and 5-min post-tests respectively. The control group showed a pre- to post-test decrease of 27.1% (Table 5 and Figure 5).

Table 2.5

Effect of fatigue intervention on the non-dominant hamstrings EMG:

Normalized EMG Condition	Pre (%MVIC)	Post (%EMG)	Percent difference (%)	Effect size
Control	18.1 ±3	13.2 ±5	-27.1	d= 0.6
1-min	16.8 ±3	10.7 ±3	-36.3	d= 0.6
3-min	16.3 ±3	14.9 ±4	-13.9	d= 0.6
5-min	16.3 ±3	12.8 ±3	-21.5	d= 0.6

Figure 2.6



2.2.6 Dominant quadriceps EMG during the post-tests

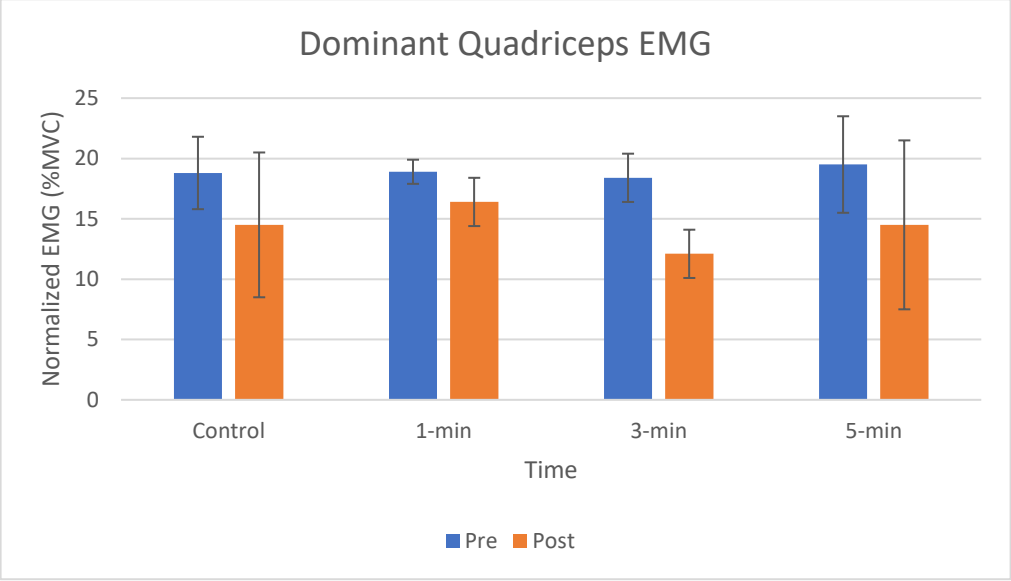
A significant, large magnitude, main effect was found for pre- vs. post-tests ($F_{(1,16)}$ =72.07, p <0.001, d=0.8) decrease in dominant quadriceps EMG but no significant interaction effect (pre vs post * condition) ($F_{(3,16)}$ =2.58, p = 0.09, d =0.3). Compared to the pre-test, EMG means decreased 13.2%, 34.2% and 23% at 1-, 3- and 5-min post-tests respectively. The control group showed a pre- to post-test decrease of 20.3% (Table 6 and Figure 6).

Table 2.6

Effect of fatigue intervention on the dominant quadriceps EMG:

Normalized EMG Condition	Pre (%MVIC)	Post (%MVIC)	Percent difference (%)	Effect size
Control	18.8 ±4	14.5 ±7	-20.3	d= 0.8
1-min	18.9 ±3	16.4 ±6	-13.2	d= 0.8
3-min	18.4 ±1	12.1 ±2	-34.2	d= 0.8
5-min	19.5 ±2	14.5 ±2	-23	d= 0.8

Figure 2.7



2.2.7 Fatigue Index

The one-way ANOVA results for both MVIC force ($F_{3,16}$= 0.399, p =0.755) and EMG ($F_{3,16}$= 0.458, p =0.715) fatigue index suggest that time conditions (1-, 3- , 5-min and control) did not differ significantly.

2.3 Discussion

The major finding was the lack of significant NLMF-induced single (discrete) MVIC force decrements at any post-test duration. While a few statistically significant decreases were identified, there were also similar impairments in the control condition. Thus, the testing presumably influenced the responses. Hence, in agreement with the Behm et al. (2021) meta-analytical review, there was no demonstrable effect of unilateral dominant quadriceps fatigue on contralateral quadriceps or hamstrings single MVIC force or EMG activity. The second major finding was the lack of NLMF force or EMG changes with the fatigue test (fatigue index), which was not in accord with the recent Behm et al. (2021) meta-analysis.

Although similar methodologies were used in previous studies (Doix et al. 2013; Halperin et al. 2015; Hamilton and Behm 2017), that reported NLMF with single discrete MVICs, there was no significant NLMF force impairment in the present study. The lack of significant NLMF with single MVIC forces might be due to the lack of statistical power given the low sample size (n=5). While an increased sample size would increase statistical power and diminish the chances of type II errors (false negatives), there was no indication of any near significant trends for single MVIC NLMF. Control conditions induced similar deficits as the experimental conditions. Hence, these single MVIC force

and EMG results do agree with the Behm et al. (2021) meta-analysis (39 NLMF studies with 303 participants and sample sizes ranging from 6 to 45 participants), which reported that following unilateral fatigue interventions, there were overall trivial NLMF effects.

The proposed experimental design for this study was supposed to be optimal for eliciting NLMF according to Halperin et al. (2015). According to Halperin and colleagues (2015) NLMF effects mainly exist due to neural and psychological factors So taking that postulation into consideration while choosing the fatigue intervention, high intensity fatiguing protocols have been shown to lead to NLMF effects especially when combined with high volume of exercise (Halperin et al. 2015). Hence, the fatigue protocol consisted of two sets of 100s maximal voluntary isometric contractions with 1-min rest. In addition, this protocol was similar to that used by previous studies that reported NLMF effects (Doix et al. 2013; Halperin et al. 2015; Hamilton and Behm 2017).

On the other hand, longer duration fatigue protocols have been also shown to affect the psychological element (i.e., mental energy deficit) when experiencing discomfort, leading to mental fatigue (diminished focus and concentration affecting neuromuscular activation) affecting both fatigued and non-exercised muscles (Halperin et al. 2015). The participants in this study were mainly recreationally trained with no extensive resistance training experience. Due to a lack of experience with high intensity resistance training loads, the participants might not have fully activated their muscles (i.e., 100% MVIC) for such a long intervention duration (2x100s). Hence the possibility of submaximal intensity contractions may not have induced a sufficient mental energy deficit diminishing the possibility of NLMF effects.

In addition, participants were also made aware of the exact endpoint of the fatigue protocol (12 repetitions of 5-s each with 1-s recovery), which typically produce higher forces and EMG outputs than unknown endpoints (Billaut et al. 2011, Hamilton and Behm 2017). Mauger et al. (2009) showed that an unknown endpoint limits performance when participants are asked to maintain a high intensity MVIC for an unknown duration. Unknown end point can also decrease motivation for optimum performance (St Clair Gibson et al. 2006). Nonetheless, even with a known endpoint in the present study, NLMF with a fatigue resistance test was still not evident.

As recommended by Halperin et al. (2015) and others (Alcaraz et al. 2008) to optimize the chance for NLMF, the knee extensors (with VL EMG) were fatigued and tested in this study. The quadriceps have a larger muscle mass and higher number of fast twitch fibres (Miller et al. 1993) accelerating the onset of fatigue and increasing the difficulty to fully activate this muscle group (Behm et al. 2002). Also, RPE is reported to be higher with lower body muscles compared to upper body muscles as it promotes a higher sensation of the effort (Mayo et al. 2014). This prior evidence supported the idea that NLMF can be considered muscle specific and testing lower body muscles (VL in this study) would show higher NLMF effects. Once again, this recommended muscle group did not elicit NLMF in the present study. As suggested previously if the participants failed to fully activate the quadriceps during the fatigue intervention due to their lack of resistance training history and recreationally trained state the possibility of NLMF-induced effects would be diminished.

Few studies tested for NLMF later than 1min and very few actually reported significant effects. Prieske et al. (2016) tested unilateral fatigue at different movement velocities using

an isokinetic dynamometer and found that slower movement velocities (60º/s) showed decrease in torque production in the non-exercised knee extensors up to 5min. However, Arora et al. (2015) reported the absence of NLMF after examining the effect of fatiguing unilateral knee extensor on the contralateral non-exercised leg's force and activation after 10min from finishing the low intensity fatigue protocol (15 isometric knee extensions at 30% of peak MVIC force, each lasted for 16 s followed by 4 s recovery). Yet, most of NLMF studies performed the post-test immediately after the fatigue intervention. In this experimental design, the shortest time condition was 1-min after the fatigue intervention. Central neuromuscular fatigue recovery typically happens within 1-2 minutes (Carroll et al. 2017). The minimum of 1-min before the post-test might have been enough time allowing participants to recover. Sustained MVIC forces can drop progressively by 50% within 1-2 minutes (2x100s in this study). A rapid recovery during the first 15-30s is also influenced by rapid muscle reperfusion (Carroll et al. 2017).

Although all these previous factors were put into consideration when considering the experimental plan, we still failed to elicit NLMF effects with either single MVICs or fatigue endurance test. Beside not having enough participants, there might be another factor leading to these insignificant results such as sex differences. Unlike previous studies, 4 out of the 5 participants were females. While in previous NLMF studies, females represented only around 8% of total participants with 13 studies reporting females in their studies and only 3 compared males to females (Behm et al. 2021). This is a gap in NLMF research that can be examined in future projects. Studies with female participants should consider sex differences, as females (the majority of participants in this study) physiologically have greater muscle endurance (Hunter 2009) and might have

been more resistant to the fatigue endurance test. Females have less muscle mass which produces less absolute force when compared to males performing the same physical test which leads to less muscle oxygen demand and less mechanical compression of the local vasculature (Hunter 2009). One of the key points is that females show less reduction during sustained MVIC (Hunter et al. 2006).

An influential variable when dealing with female participants is the menstrual cycle hormonal fluctuations especially oestrogen. Throughout the menstrual cycle there is variability in strength and fatiguability (Phillips et al. 1993a). Also the ingestion of contraceptive pills can play a role. Highest levels of oestrogen are seen just before ovulation (Phillips et al. 1993a). It is suggested that this peak in oestrogen is responsible for the muscle strength increase in this phase (Sarwar et al. 1996). During mid-cycle quadriceps muscles were found stronger and more fatigable, while women taking contraceptive pills were not affected (Sarwar et al. 1996). More studies with female participants are required to get more details about the correlation between strength and ovulation and the mechanism responsible for all these changes. These variations are more than just changes in levels of estradiol and progesterone. Menstrual cycles were not taken into consideration in this experiment and thus the variable effects of the cycle on strength and endurance may have contributed to the lack of significant results.

2.4 Limitations

Starting from the sudden COVID breakout suspending the data collection and ending with data from only 5 participants instead of the projected 16. Those participants were only recreationally trained which might have affected the intensity of the fatigue

intervention not being able to fully contract the quadriceps to the maximal ability. Four out of the five participants were females which added more variability and lack of heterogeneity to the lack of statistical power that already existed. The menstrual cycle was not taken into consideration in addition to the physiological ability of females to resist fatigue compared to males may have increased the variability in the data. Is a different approach for the post-tests needed for future experimental design? As Halperin et al. (2015), Behm et al. (2021) and this study agreed on the lack of significant NLMF-induced single MVIC force decrements, single (discrete) MVICs should not be tested (the control condition had similar deficits as the experimental conditions) and move directly to the endurance fatigue post-test as the time between single and multiple MVICs might be long enough for some significant recovery and diminution of NLMF effects.

2.5 Conclusion

The results of this study suggest that following a fatiguing protocol, when testing non-exercised muscles there was a lack of significant NLMF-induced single MVIC force decrements at any post-test duration. Thus, higher statistical power (i.e., increased sample size) and more studies are needed to clarify if NLMF endurance deficits can be replicated in other studies and what is the size of the NLMF effects at different post-testing durations? Many factors too can be put into consideration in the future for the possible mechanisms, NLMF effects on endurance outcomes and sex differences in addition to examining population differences (such as training background, young and older population).

2.6 References

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