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

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Abstract

Introduction Non-local muscle fatigue (NLMF) refers to a transient decline in the functioning of a non-exercised muscle following the fatigue of a different muscle group. Most studies examining NLMF conducted post-tests immediately after the fatiguing protocols, leaving the duration of these effects uncertain.

Purpose The aim of this study was to investigate the duration of NLMF effects by examining post-test durations of 1-, 3-, and 5-minutes as well as a Control condition,

Methods In this randomized crossover study, 17 recreationally trained participants (four females) were recruited. The study aimed to investigate the acute effects of unilateral knee extensor (KE) muscle fatigue on the contralateral homologous muscle strength, activation, and fatigue resistance (endurance). The participants underwent four sessions, with a minimum 48-hour interval between visits. Each session included testing at one-, three-, or five-minutes post-test, or for a Control condition. Measurements included non-dominant KE muscle force, endurance, and electromyography (EMG) from the vastus lateralis and biceps femoris muscles. The fatigue protocol involved two sets of continuous 100-seconds maximal voluntary isometric contractions (MVIC) performed by the dominant KE, separated by 1-minute of rest.

Results Non-dominant KE MVIC forces showed reductions of 15.81% ($p<0.0001$, $d=0.72$) at 1-min and 8.54% ($p=0.005$, $d=0.30$) at 3-min post-test. The KE MVIC instantaneous strength revealed a significant reduction between 1-min ($p=0.021$, $d=1.33$), and 3-min ($p=0.041$, $d=1.13$) compared with the control. In addition, EMG revealed large magnitude increases with the 1-minute versus control condition ($p=0.03$, $d=1.10$).

Conclusions Recovery duration (recovery time was 5-min) plays a crucial role in the manifestation of NLMF. Moreover, the influence of factors such as familiarity with high-

intensity resistance training loads and the specific muscle group targeted during fatigue protocols were also highlighted.

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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

IEMG - Integral EMG

K+ - Potassium

MAP - Mean Arterial Pressure

MEP - Motor Evoked Potential

MVIC - Maximum Voluntary Isometric 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 perceived exertion

S - Second

SR - Sarcoplasmic Reticulum

TMS - Transcranial Magnetic Stimulation

VL – Vastus lateralis

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Chapter 1: Literature Review

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

1.1 Introduction

Muscle fatigue can impose physical consequences (e.g., force deficits) and is a well-known sensation that many people have experienced. It refers to the reduced ability to exert muscle force or power, even if the activity is not sustained. At the beginning of an activity, one may feel strong and resilient, but as time goes on, the muscles can become tired and weaker. This is what is commonly referred to as muscle fatigue (Bigland-Ritchie & Woods, 1984). Therefore, the feeling of fatigue is not immediately noticeable at the beginning of a physical task, nor is it solely detected when the muscles reach their limit. Instead, fatigue gradually intensifies after the activity has started (Enoka & Duchateau, 2008). Fatigue can arise from various factors, and there isn't a single primary cause for it. It can affect a single muscle, which is called local fatigue, or the entire body, known as global fatigue. Both types can result in temporary reductions in voluntary muscle activation and force production (Behm 2004, Rattey et al., 2006).

NLMF, also known as crossover fatigue, happens when fatigue in one muscle group causes a reduction in force in non-exercised muscle groups that are either similar (homologous) or different (heterologous) to the fatigued muscle group (Halperin et al., 2015a). Despite research on NLMF, there is still uncertainty and conflicting results about the factors that moderate it. Muscle specificity, NLMF protocol, contraction intensity, and sex differences are some of the factors that have been studied, but there has been little research on the duration of NLMF after a contralateral muscle fatiguing intervention. Most studies have conducted NLMF post-tests immediately after fatiguing protocols, but this study will focus on this neglected area to clarify the duration of NLMF impairments. Therefore, further research is needed to fully understand the effects of NLMF.

1.1.1 Fatigue

Muscle fatigue encompasses various aspects and cannot be explained by a single model. While one definition of fatigue is the inability to generate the necessary force for a task, it is not limited to a reduction in externally applied force. For instance, even when holding a submaximal resistance during an isometric contraction, fatigue can occur due to the increased effort required to maintain the contraction and keep the load in position. Simonson and Weiser offer a more comprehensive definition, stating that fatigue is a temporary decrease in work capacity resulting from prior work, regardless of whether the current performance is affected (Simonson & Weiser, 1976). According to Enoka and Duchateau, fatigue can be described as an exercise-induced decline in physical functions, leading to impairments in motor performance accompanied by a sense of tiredness (Enoka & Duchateau, 2008). Enoka and Duchateau further differentiate fatigue into two components: performance fatigability and perceived fatigability. Performance fatigability refers to the decline in performance over time, while perceived fatigability encompasses changes in sensations that impact the individual's experience of fatigue (Enoka & Duchateau, 2016). It is important to note that fatigue involves both qualitative and quantitative measures and can be influenced by psychological factors that affect the entire body, not just the fatigued muscle group. The process of voluntary muscle activation is intricate, beginning from the cerebral cortex and involving action potentials transmitted to the spinal motoneurons and through the neuromuscular junction to the muscle membrane (Enoka & Duchateau, 2016). The action potential reaches the sarcoplasmic reticulum, leading to the release of calcium into the muscle cell, initiating crossbridge kinetics. Due to the complexity of this pathway, fatigue can be categorized into peripheral and central components. There is no singular dominant cause for fatigue, as it depends on the nature

of the task, whether it involves sustained low-intensity or high-intensity activities, which activates specific mechanisms (Enoka & Duchateau, 2016).

1.1.2 Central Fatigue Mechanisms

Prolonged, sustained, maximal voluntary isometric contractions (MVIC) are primarily associated with decreases in force due to central fatigue (Schillings et al., 2003). Central fatigue originates within the central nervous system (CNS) and leads to a decrease in the neural drive to the muscle (Gandevia, 2001). Various sites in the CNS, including the primary motor cortex and the pyramidal system, can experience central fatigue (Bigland-Ritchie, 1981). During high-intensity contractions, fatigue can be rapidly observed, with changes in motoneuron excitability and the involvement of inhibitory mechanisms such as short-interval intracortical inhibition and decreased intracortical facilitation (Bigland-Ritchie et al., 1978). The initial activation of all motor units during activities with high metabolic demand is followed by an immediate decrease in force, indicating the presence of central fatigue (Bigland-Ritchie et al., 1978). Electromyographic (EMG) activity can confirm central fatigue, as there is a decrease in the mean power spectrum frequencies associated with maximal intensity contractions (Kranz et al., 1985). The muscle wisdom hypothesis proposed by Mardsen suggests that a decrease in motor unit discharge during maximal voluntary contractions (MVCs) helps minimize fatigue (Marsden, 1983). Recurrent inhibition, a central process involving Renshaw cells, directly inhibits the excitability of alpha motoneurons and primarily affects nearby homonymous and synergist motor pools (McCURDY & Hamm, 1994; Trank et al., 1999). Recurrent inhibition increases during sustained maximal efforts to prevent excessive force output and contribute to the coordination of motor activity (Maltenfort et al., 1998).

The evidence for fatigue with submaximal intensity contractions may not be as externally evident as with maximal intensity contractions. In the case of submaximal

forces, there is a compromise between the impairments due to fatigue and the neuromuscular facilitation required to sustain the effort (D. G. Behm, 2004a). Initially, it is not necessary to fully activate all the involved muscle fibers (agonist or prime movers and synergists) in order to conserve energy (D. G. Behm, 2004a). However, as time under tension persists, these motor units experience fatigue due to factors such as recurrent inhibition, type III and IV afferent inhibition, and reduced reflex potentiation (D. G. Behm, 2004a). Consequently, non-fatigued, higher threshold fibers are recruited, and existing fibers increase their firing frequency to compensate for the loss of intrinsic force (D. G. Behm, 2004a). In addition to increased recruitment and rate coding, supraspinal strategies such as catch-like properties (resulting in force potentiation) and muscle wisdom contribute to sustaining performance (Behm, 2004). Prolonged full activation of motor units to sustain a load can lead to a decrease in motor unit discharge frequency and eventual de-recruitment (S. Garland et al., 1994; S. J. Garland & Miles, 1997; Person & Kudina, 1972). The crossover or non-local muscle fatigue (NLMF) model highlights the role of central fatigue in this context.

1.1.3 Peripheral Fatigue Mechanisms

Peripheral fatigue refers to the reduction in force production that occurs as a result of changes that take place at or distal to the neuromuscular junction (Enoka & Stuart, 1992). It can be caused by factors such as insufficient blood flow, decreased availability of metabolic substrates, mechanical disruptions (e.g., myofilament crossbridge interactions), and impairment of excitation-contraction (E-C) coupling (Bigland-Ritchie, 1981). Schillings found that peripheral fatigue primarily contributes to the decline in force during the early stages of a 2-minute MVIC of the biceps brachii, resulting in approximately 80% loss of voluntary force (Schillings et al., 2003).

Energetic deficiency plays a significant role in muscle fatigue, as it occurs when the rate of adenosine triphosphate (ATP) consumption exceeds the rate of ATP production during physical activity (Sahlin, 1992). There is a strong correlation between ATP production rate and performance (Sahlin, 1992). The decrease in ATP production combined with high ATP turnover leads to an increase in the breakdown of the adenine nucleotide pool within the muscle cell (Sahlin et al., 1990). Fatigue-related cellular mechanisms can be attributed to both excitation-contraction coupling and the cross-bridge itself. E-C coupling involves the propagation of the action potential through the transverse (T) tubules and the subsequent release of calcium from the sarcoplasmic reticulum, which initiates the interaction of myofilaments and muscle contraction (Fitts, 1996). Fatigue can hinder the propagation of the action potential along the T-tubules, affecting calcium release and resulting in decreased activation of myofibrils and force development (Garcia et al., 1991). Fatigued muscle cells may experience changes in the resting potential of the sarcolemma, shifting from -70mV to -80mV, and a reduction in the spike potential from +20mV to +5mV. This membrane depolarization diminishes the activity of sodium channels. The increase in inorganic phosphate (due to a decrease in phosphocreatine) and hydrogen ions also contribute to fatigue by impairing the ability of myosin to bind to actin and generate high force (Cooke & Pate, 1990). Inorganic phosphate is also believed to be responsible for the initial drop in maximal force (Westerblad & Allen, 1991). As fatigue progresses, the working muscles become more acidic, which further reduces force production by decreasing calcium release from the sarcoplasmic reticulum and the sensitivity of troponin (Stackhouse et al., 2001). This force deficit is more pronounced in fast-twitch (type II) fibers compared to slow-twitch (type I) fibers (Nosek et al., 1987). Additionally, fatigue slows down both relaxation and contraction times by inhibiting the reuptake of calcium by the sarcoplasmic reticulum (Fitts, 1996).

1.1.4 Non-local muscle fatigue (NLMF)

NLMF refers to a transient decline in the ability of an unexercised muscle to perform after subjecting a different muscle to a fatigue-inducing protocol. In other word, NLMF is a phenomenon in which a muscle that has not been directly exercised experiences a temporary decrease in performance following the fatigue of a different muscle. For instance, if a person performs a series of strenuous exercises that primarily target their right biceps, their left biceps may still experience temporary weakness or reduced performance due to NLMF. This phenomenon can occur in muscles located on the same side of the body (ipsilateral) as the fatigued muscle or on the opposite side (contralateral) (Halperin, Aboodarda, & Behm, 2014; Kennedy et al., 2013).

The exact mechanisms behind NLMF are not fully understood, but researchers believe that neural and/or biochemical factors may be responsible for affecting the functioning of the non-fatigued muscle. Some have suggested that changes in blood flow, metabolic waste accumulation, or altered neural input to the affected muscle may contribute to NLMF (Amann, 2012; Baker & Davies, 2009; Bangsbo et al., 1996; Gandevia, 2001; Halperin et al., 2015b).

NLMF has important implications for athletes, trainers, and individuals seeking to improve their physical performance. By recognizing the potential for NLMF, people can adjust their training strategies to minimize the risk of injury or overexertion and maximize their gains. Moreover, further research into the mechanisms behind NLMF may lead to new insights into how muscles function and interact with one another.

Crossover fatigue refers to temporary impairments in the performance of a contralateral homologous muscle, which is a muscle that has the same function and location on the opposite side of the body. This term was initially coined by Martin and Rattey and has been further studied by Doix et al. (Doix et al., 2013; Martin & Rattey, 2007). In contrast,

NLMF is a broader term that encompasses impairments in any homologous or heterologous non-exercised muscle (D. G. Behm et al., 2021a; Halperin, Aboodarda, & Behm, 2014; Halperin et al., 2015a). Since the non-fatigued muscle being tested has not undergone any prior activity or fatigue, any impairments observed due to the fatigue of another muscle cannot be attributed to local factors such as changes in intramuscular pH, metabolite accumulation, or disruption of excitation-contraction coupling or crossbridge kinetics. Therefore, it is believed that these NLMF impairments must be due to global or central influences (D. G. Behm et al., 2021a). The extent of NLMF can vary and is influenced by several factors. These factors may include the specific fatigue protocols used, the muscle group that was fatigued, and the techniques used to measure the resulting impairments in performance of the non-fatigued muscle (D. G. Behm et al., 2021a; Halperin et al., 2015a).

1.1.5 Central NLMF mechanisms

Feedback systems, including both spinal and supraspinal mechanisms, contribute to the behavior of working muscles and the maintenance of force output. Fatigue can lead to inhibition within the CNS and a reduction in the neural drive to non-exercised muscles (Gandevia, 2001). Fatiguing protocols that result in the accumulation of metabolic by-products can activate group III and IV muscle afferents, which in turn affect motoneuronal output and inhibit the corticospinal pathway (Amann, 2012; Sidhu et al., 2014). Muscle afferents play a role in determining the fatigue threshold, which represents the level of peripheral fatigue that is not exceeded under normal sensory feedback conditions (Amann et al., 2009, 2013).

The effects of group III and IV muscle afferents on the corticospinal pathway can differ depending on the presence or absence of fatigue. In the absence of fatigue, these afferents can facilitate motor cortical cells and inhibit motoneurons, whereas with fatigue, they inhibit motor cortical cells without significantly affecting motoneurons (Sidhu et al., 2014).

However, recent studies have indicated that group III and IV muscle afferents do not contribute to the effects of NLMF. Kennedy demonstrated that after fatiguing the knee extensors with maximal isometric contractions, group III and IV muscle afferents did not affect the corticomotoneuronal pathway (Kennedy et al., 2013).

Transcranial magnetic stimulation (TMS) is a technique used to assess corticospinal responses by stimulating the motor cortex and measuring motor evoked potentials (MEPs) through surface EMG recordings. MEPs reflect the electrical signals generated by descending motor pathways, and their amplitudes increase during isometric voluntary contractions, indicating increased corticospinal excitability. However, the magnitude of this increase in MEPs depends on the muscle group being tested. Studies have shown that the biceps brachii muscle exhibits greater increases in MEPs compared to distal muscles such as the brachioradialis and adductor pollicis across a range of stimulus intensities (Kischka et al., 1993; J. Taylor et al., 1997). Decreases in force output during fatigue have been associated with reduced MEP amplitudes, suggesting a decrease in descending drive from the motor cortex (J. L. Taylor et al., 2006). During sustained maximal voluntary contractions, MEPs initially increase within the first 15 seconds but then stabilize without further changes (J. Taylor et al., 1997). Furthermore, Šambaher found that fatigue of bilateral knee extensors not only reduced force production in the elbow flexors but also resulted in a significantly lower MEP/CMEP (compound muscle evoked potential) ratio, indicating inhibition of supraspinal excitability (Šambaher et al., 2016).

However, there are contrasting findings in the literature regarding the effects of fatigue on corticospinal excitability. Aboodarda observed significant increases in the MEP/CMEP ratio at 100% MVC following fatigue, suggesting enhanced supraspinal excitability (S. J. Aboodarda et al., 2017). They also reported similar findings in another study investigating the effects of unilateral elbow flexion fatigue on the non-exercised contralateral biceps

brachii, with higher MEP amplitudes during 100% MVC and greater supraspinal motor responses (S. Aboodarda et al., 2016). On the other hand, in another research by Aboodarda, they did not find any changes in neuromuscular function or corticospinal circuits (S. J. Aboodarda et al., 2019).

1.1.6 Biochemical mechanisms of NLMF

During exercise, the depletion of energy substrates and the accumulation of metabolic by-products 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 transported through the cardiovascular system to various parts of the body (Halperin et al., 2015a).

In studies on NLMF, the presence of hydrogen ions and blood lactate has been observed in the non-exercised muscles (Bogdanis et al., 1994). Grant utilized biceps curls as an upper body fatigue protocol before performing two maximal 30-second sprints on a cycle ergometer. The prior upper body exercise significantly affected peak power output, indicating that metabolic by-products had an impact on maximal force production (Grant et al., 2014).

Intense exercise is associated with high levels of lactate, which is correlated with increased acidity within the working muscles (Westerblad & Allen, 1991). Bangsbo suggested that a decrease in muscle pH of 0.2 (from 6.82 to 6.54) does not affect glycogenolytic and glycolytic pathways (Bangsbo et al., 1996). However, acidity levels are not the sole cause of fatigue in high-intensity exercise, as there is also a link between potassium levels in the muscle and fatigue. High-intensity exercise leads to a loss of potassium from the working muscles and an increase in extracellular potassium levels, which can result in a loss of force (Bangsbo et al., 1995). Therefore, fatigue-induced

metabolic disruptions are not confined to the exercising muscle alone but can affect non-local contractile functions globally.

1.1.7 Biomechanical mechanisms of NLMF

Core stability has gained significant attention in sports strength and conditioning as a crucial factor for athletes to optimize their performance (D. G. Behm et al., 2010). From an anatomical perspective, the core refers to the axial skeleton and all the associated soft tissues that are attached either to the axial or appendicular skeleton (D. G. Behm et al., 2010). Developing core muscles not only aids in the prevention of lower back injuries but also has the potential to enhance overall performance (D. G. Behm & Anderson, 2006). However, a meta-analysis conducted by Behm et al. (2015) revealed that unstable resistance training has limited effects on power and balance compared to stable resistance training.

It is important to note that core muscles can serve to facilitate force generation and transfer throughout the kinetic chain or provide resistance against motion (D. G. Behm et al., 2010; Kibler et al., 2006). Core muscles do not work in isolation but rather establish connections between the upper and lower body muscles, ensuring minimal energy dissipation (Shinkle et al., 2012). Upper body exercises, such as bilateral shoulder extensions, have been shown to highly activate trunk muscles, with significantly higher EMG amplitudes observed in the rectus abdominis and external oblique compared to trunk flexion exercises (Tarnanen et al., 2008).

When a fatigue protocol is applied, resulting in the exhaustion of stabilizer muscles, their ability to stabilize the body becomes compromised, thus impacting the kinetic chain of movement and leading to a decrease in force production of non-exercised muscles. This can be considered as another potential indirect cause of non-local muscle fatigue (Halperin et al., 2015a).

1.1.8 Psychological mechanisms of NLMF

The psychological aspect of the fatiguing protocol plays a significant role, as psychological states, and feelings such as anger or fatigue are mental representations of the physiological changes induced by physical activity, whether maximal or submaximal. These changes in neural networks are believed to involve the prefrontal cortex as a primary region in the brain. Perceived fatigability, which is associated with changes in sensations regulating the individual's well-being during the task, facilitates these psychological effects (Enoka & Duchateau, 2016). Perceived fatigability can be assessed both at rest and during the task, and participants may naturally desire to stop as the task becomes uncomfortable (Halperin et al., 2015a). For instance, when a prolonged fatiguing protocol (e.g., 100-second MVC) is followed by the same intensity using a non-exercised muscle, participants may already be mentally fatigued, impacting their focus and concentration, thereby impairing physical performance and resulting in lower activation of the non-exercised muscle (Marcora et al., 2009).

The presence of pre-induced fatigue from one task can increase the feedback from group III/IV muscle afferents in the non-exercised limb, even when the work rate remains the same (Amann et al., 2013). Studies with known endpoints, such as a predetermined duration or distance of the task, have shown higher force and EMG outputs (Billaut et al., 2011). On the other hand, the absence of a pacing plan based on the knowledge of the endpoint throughout the task, as seen in protocols with unknown durations, can limit performance when participants are asked to maintain MVC for the entire duration of the test. This absence of pacing can decrease motivation for optimal performance (Mauger et al., 2009; St Gibson et al., 2006).

Pacing strategies help delay the development of fatigue and alleviate discomfort. Previous experiences can also influence participants' decision-making regarding pacing or

sustaining effort levels for longer durations. Stone demonstrated that performance feedback influenced average power output in trained cyclists during time trials (Stone et al., 2012). Therefore, mental fatigue can have negative effects on motivation and force output. Participants may perceive greater exertion, especially during prolonged submaximal fatiguing protocols.

NLMF effects primarily arise from neural and psychological factors (Halperin et al., 2015a). The psychological element, including experiencing discomfort or pain during longer fatiguing protocols, can affect both the fatigued and non-exercised muscles (Halperin et al., 2015a). Hamilton and Behm investigated the presence of NLMF in protocols with known versus unknown testing endpoints and found that unknown endpoints resulted in lower force and muscle activity (Hamilton & Behm, 2017). Conversely, known endpoints provided participants with greater motivation to overcome performance decrements due to fatigue (Hagger et al., 2010). Therefore, having knowledge of the test endpoint can influence the effects of NLMF.

1.2 Factors affecting NLMF.

1.2.1 Effect of fatiguing protocol intensity on NLMF

The magnitude of NLMF is significantly influenced by the intensity of muscle contractions, with higher intensities having a greater impact compared to lower intensities (Kennedy et al., 2013). In a study by Kennedy et al. (2013) focusing on upper body muscle fatigue protocols (specifically the forearm), NLMF effects were observed in the lower body muscles (plantar flexors) when measuring MVIC and voluntary activation post-intervention.

To further investigate this, Kawamoto et al., (2014) examined the effects of fatiguing dynamic knee extensions on the non-dominant limb at two different intensities, namely 70% and 40% of MVC. The participants performed four sets of knee extensions until

failure, with one-minute recovery intervals. Both intensity conditions resulted in significant decrements in F100 (force produced in the first 100 ms of an MVIC) and MVIC peak force. Notably, the higher intensity condition (70% MVIC) exhibited larger magnitude decrements compared to the lower intensity condition (40% MVIC). These findings align with previous studies (Doix et al., 2013; Halperin et al., 2015a; Hamilton & Behm, 2017), collectively suggesting that high intensity fatiguing protocols, particularly when combined with high volume (e.g., two bouts of 100 s MVIC), can induce NLMF.

1.2.2 Muscle specificity

NLMF exhibits muscle-specific characteristics, with varying levels of force decrement observed among different muscle groups in response to fatiguing protocols. The majority of research indicates that lower body muscle groups experience greater NLMF effects compared to the upper body (Halperin et al., 2015a). This notion was supported by Alcaraz et al., (2008), who investigated heavy loading circuit training involving maximum effort bench presses (6-repetition maximum) with both passive and active recovery (leg and ankle extensions). The study found that neither condition significantly affected bar speed or the number of repetitions. However, impairments in the number of repetitions until failure were observed when participants performed upper body exercises (bench press and bench pull) as active recovery between back squat sets (Ciccone et al., 2014).

These findings suggest that lower body muscles, particularly the quadriceps (a commonly examined lower body muscle group), are more susceptible to NLMF compared to upper body muscles. This can be attributed to the larger mass and higher proportion of fast-twitch fibers in lower body muscles (Miller et al., 1993a). Such functions necessitate the full activation of neural drive. However, due to fatigue in the lower body muscles, the nervous system's ability to fully activate a high volume of motor units is hindered compared to upper body muscles (Galea et al., 1991). Consequently, fatiguing lower body

muscles intensifies the perception of effort, impacting the rate of perceived exertion (RPE). Research has shown that RPE is higher during back squats compared to bench presses, even when performed at the same intensity, volume, and rest intervals (Mayo et al., 2014), indicating a greater NLMF effect when lower body muscles are fatigued.

1.2.3 Sex differences

The specific effects of non-local muscle fatigue (NLMF) between sexes are not yet well-established, and there is a scarcity of studies comparing males and females in this regard. Martin & Rattey (2007) demonstrated that both sexes experienced NLMF; however, males exhibited greater central fatigue, resulting in a 13% decrease in MVIC compared to an 8% impairment in females (MVIC assessed before and after a 100-second MVIC task). Further research is necessary to determine if NLMF is sex specific. Notably, females represent only a small portion (approximately 8%) of participants in NLMF studies, as indicated by the meta-analysis conducted by (D. G. Behm et al., 2021a).

Physiologically, females possess less muscle mass, which can influence oxygen demand and perfusion. Consequently, the reduced muscle mass leads to lower absolute force production, intramuscular pressures, and blood flow occlusion during tasks performed at the same relative intensity compared to males (Hunter, 2009). Additionally, females exhibit less decrement in maximal force during sustained submaximal isometric contractions (20-70% of MVC) across several muscles tested (Hunter et al., 2006). In terms of energy metabolism, males rely more on efficient glycolytic pathways, while females exhibit a decreased reliance on carbohydrate metabolism, higher rates of fat oxidation, and a lower respiratory exchange ratio during endurance exercises (Tarnopolsky, 1998). Research also suggests that estrogen possesses glycogen-sparing properties, indicating that females may have greater fatigue resistance during longer duration activities (Tarnopolsky, 1998). However, with only one study comparing NLMF responses between sexes, it

remains unclear whether the generally greater fatigue resistance observed in females translates to differential NLMF responses.

1.2.4 NLMF testing protocols.

The magnitude of NLMF can vary depending on the type of testing protocols employed. Most studies utilize either 1-3 single post-fatigue MVICs with ample rest intervals or submaximal exercise until exhaustion. Doix et al. (2013) discovered that a unilateral fatigue protocol consisting of two bouts of 100-second knee extensions resulted in a reduction of MVIC (approximately 10%) in both the exercised and non-exercised muscles. Conversely, (Halperin, Copithorne, & Behm, 2014) observed a decrease in force production (around 8%) in the rested knee extensors following the completion of 12 MVICs with 5 seconds of work and 10 seconds of rest between each repetition. Halperin (2015) summarized that time to exhaustion and repetitive MVIC fatiguing protocols tend to have a greater impact on NLMF due to the additional stress imposed on various systems (neural, biochemical, and psychological) compared to a single contraction. In a meta-analysis by Behm et al. (2021), it was concluded that NLMF was more pronounced (moderate effect size magnitude) when a post-test fatigue protocol was employed, rather than a single or discrete strength measurement (overall trivial magnitude effects). Time to exhaustion and repetitive MVIC fatiguing protocols result in a greater accumulation of metabolic by-products such as hydrogen ions, blood lactate, and potassium in the fatigued muscles (Halperin et al., 2015a). These by-products can be disseminated throughout the body via the cardiovascular system, affecting the performance and contractile ability of resting muscles (Bangsbo et al., 1995, 1996). Elevated levels of hydrogen ions hinder force production by inhibiting ATP cleavage, while decreasing pH and increasing inorganic phosphate (Pi) during fatigue reduce myofibrillar calcium ion (Ca^{2+}) sensitivity and tension (Fitts, 2008).

Additionally, the activation of type III and IV muscle afferents inhibits central motor drive in both the exercised and non-exercised muscles (Amann, 2011, 2012; Amann et al., 2013; Sidhu et al., 2014). However, further studies are necessary to ascertain the precise roles and effects of group III/IV muscle afferents. Sidhu et al. (2014) investigated the roles of group III/IV muscle afferents and demonstrated that feedback from these afferents originating from lower body muscles led to supraspinal fatigue in upper body muscles during a cycling to exhaustion test. On the other hand, Kennedy et al. (2015) examined muscle afferent activity and found no crossover fatigue in the contralateral knee extensors following a sustained two-minute unilateral MVIC, and no NLMF was observed. Consistent with these findings, other studies consistently reported similar results (Halperin, Aboodarda, & Behm, 2014; Halperin, Copithorne, & Behm, 2014; Kawamoto et al., 2014), suggesting that the longer the duration of the fatigue protocol used, the more significant the NLMF effects measured compared to single maximal voluntary isometric contractions (D. G. Behm et al., 2021a; Halperin et al., 2015a).

1.2.5 NLMF Post-test durations

The search for crossover fatigue studies yielded 37 relevant articles, of which 21 studies reported significant NLMF effects, characterized by a significant reduction in EMG activity and force in the non-exercised muscle group. Among the reviewed NLMF studies, 95% conducted the post-test assessment within the first minute following the fatiguing protocol. Only 11% examined NLMF effects at different time intervals (1, 5, and 10 minutes), while one study specifically tested at 3 minutes post-fatigue protocol. Therefore, further research is necessary to determine the duration of NLMF effects.

Many studies have shown that physiological and neurological fatigue effects on the exercised muscles persist for extended periods following the post-test assessment. For instance, Arora et al. (2015) observed significant reductions of 44.8% in peak force and

39.9% in F100 (force produced in the first 100 ms of an MVIC) 10 minutes after the fatiguing protocol. Prieske et al. (2017) reported a decrease in neuromuscular efficiency ranging from 4% to 24% at a test velocity of 60°/s for up to 5 minutes post-test. Humphry et al. (2004) found a 26% decrease in MEP in fatigued biceps brachii muscles up to 9 minutes post-test, with MEP values remaining relatively stable for 30 minutes, before increasing to 58% after 60 minutes, although still significantly lower than pre-test values. These findings indicate that fatigue effects in the exercised limb can persist for up to 30 minutes post-fatigue. However, limited information is available regarding the duration of NLMF effects, highlighting the need for further investigation.

1.3 Conclusions

Despite the overall trivial NLMF effects reported in the recent meta-analysis conducted by Behm et al. (2021) regarding single or discrete strength measures, a significant number of studies did observe NLMF effects. Among these studies, certain conditions were found to elicit more noticeable NLMF effects. Specifically, fatiguing the lower body muscles tends to result in greater NLMF compared to the upper body, likely due to the higher sensation of effort and increased rating of perceived exertion (RPE) associated with lower body fatigue. Indirectly, NLMF can also occur when stabilizer muscles are fatigued, as diminished stabilization can decrease force production in non-exercised muscles.

The duration of the fatigue intervention appears to be a determining factor in the magnitude of NLMF effects. Studies employing longer fatigue protocols generally report more significant NLMF effects compared to studies using a single MVIC. Furthermore, the presence of unknown testing endpoints, which create uncertainty for participants, tends to result in lower force and muscle activity, potentially influencing NLMF. Conversely, known endpoint conditions, where participants are aware of the testing endpoint, often

provide greater motivation to overcome any performance decrements, potentially minimizing NLMF effects.

However, the impact of sex on NLMF remains unclear due to limited available studies. It is uncertain whether the greater fatigue resistance observed in females translates into differential NLMF responses. Additionally, the majority of NLMF post-tests have been conducted within the first minute or immediately following the completion of the fatiguing protocols, focusing on identifying the presence of NLMF using the factors and protocols mentioned previously.

1.4 Objectives

The objective of the present study was to examine the duration of NLMF effects by testing produced force and EMG at different time conditions (1, 3, and 5min) to investigate the duration of possible effects. In pursuit of our research objectives, we executed MVIC assessments on the knee extensor and flexor muscles of the non-dominant lower limb. Additionally, a comprehensive analysis of EMG data obtained from the vastus lateralis and biceps femoris muscles was conducted.

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 was performed using the G*Power 3.1.9.2 software package, based on force measures from relevant studies conducted by (D. G. Behm et al., 2016; Chaouachi et al., 2017; Whitten et al., 2021). The analysis aimed to achieve an alpha level of 0.05, effect size of 0.5, and a statistical power of 0.8 using the F-

test family. The results of the analysis suggested that having between 8 to 13 participants per group would be sufficient to attain adequate statistical power in the study.

For this study, 17 recreationally trained participants were recruited. Among them, four were females with an average height of 159.1 ± 2.9 cm, body mass of 62.7 ± 7 kg, and age of 26.6 ± 9.8 years. The remaining participant was male with a height of 177.45 cm ± 2.43, body mass of 81.51 ± 9.86 kg, and age of 30.54 ± 5.52 years. Fourteen (14) participants identified as right-leg dominant, while three participants identified as left-leg dominant based on their preference and accuracy in kicking a ball.

Before the testing session, each participant completed several preliminary procedures. They filled out the Physical Activity Readiness Questionnaire Plus (PAR-Q+ 2020) to assess their readiness for physical activity. They also read and signed an informed consent form as well.

Exclusion criteria for this study was a history of quadriceps muscle or knee joint injury, as well as any neurological conditions. Participants were instructed to abstain from engaging in intense physical activity and refrain from consuming alcohol, caffeine, or nicotine for the 24 hours leading up to their scheduled lab visit.

The research protocol for this study was approved by the Health Research Ethics Authority of the Memorial University of Newfoundland under the protocol number #20210760-HK.

2.1.2 Experimental design

To examine the acute effects of unilateral knee extensors muscle fatigue on the strength, activation, and endurance of the contralateral homologous muscle, a randomized crossover study design was implemented by using proper website. Prior to the study, participants underwent a familiarization session to become acquainted with the testing procedures and equipment. The study consisted of five separate sessions (one familiarization session and

4 experimental testing sessions), each separated by a minimum of 48 hours, including a control condition. The experimental conditions were presented in a random order and involved testing at pre-test as well as one, three, and five-minutes post-test, as well as a Control condition where participants rested for 260 seconds before performing a post-test at one minute following the control period of inactivity. Measurements of force output, instantaneous strength (force produced in the first 100 ms of MVIC: F100), endurance, and electromyography (EMG) activity of the vastus lateralis were collected for the non-dominant knee extensors. During the endurance test, participants performed a series of 12 isometric maximal voluntary contractions (MVIC) of the non-dominant knee extensors, with each contraction lasting five seconds and followed by a 10-second recovery period between repetitions (figure 1).

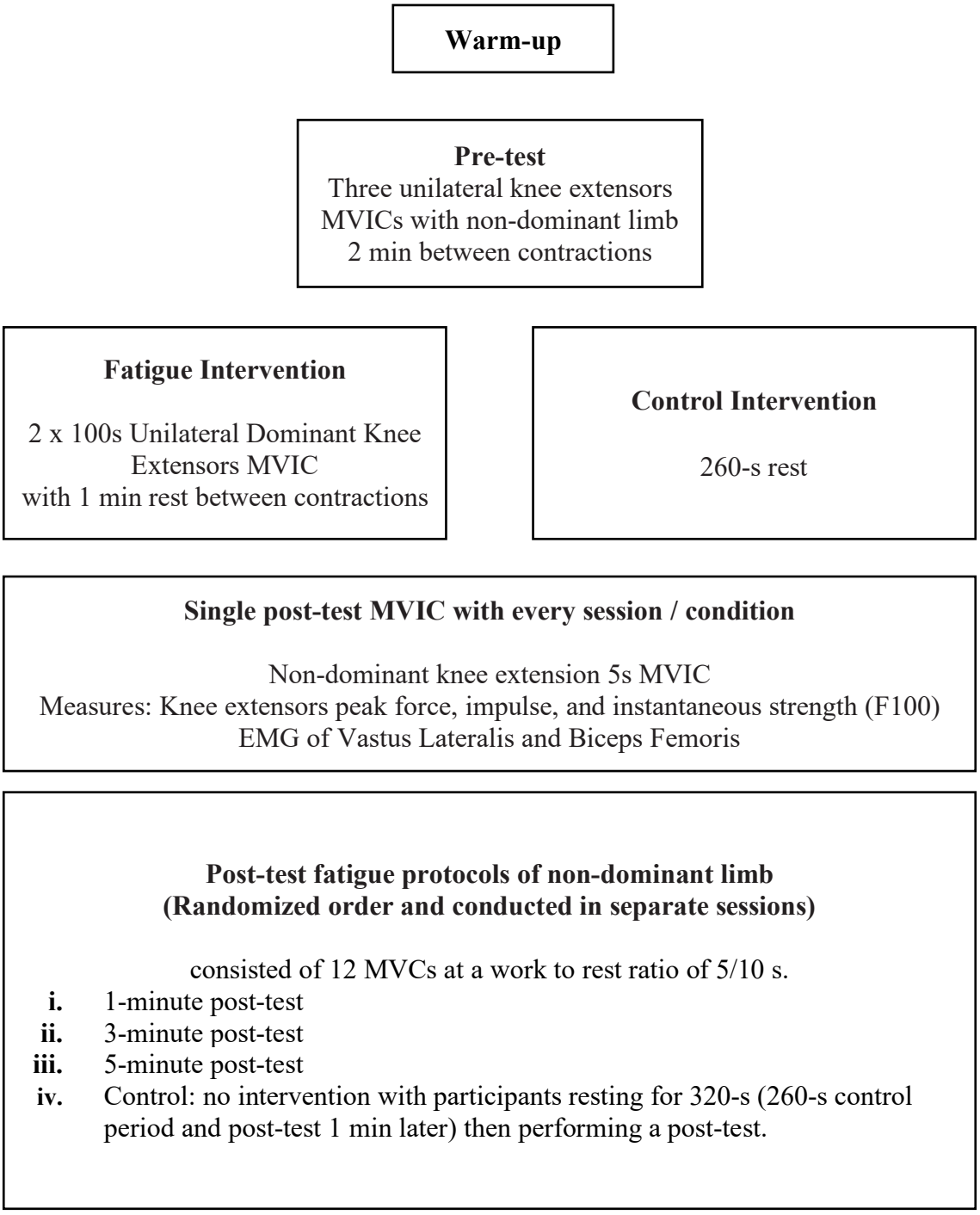


Figure 1 Experimental Design

2.1.3 Protocol

2.1.3.1 Electromyography (EMG)

At the beginning of each testing session, surface electromyography (EMG) electrodes were applied to the vastus lateralis (VL) and biceps femoris (BF) muscles of both legs. For

electrode placement, self-adhesive Ag/AgCl electrodes (MeditraceTM 130 ECG conductive adhesive electrodes) were utilized based on established protocols from previous studies (Hermens et al., 2000; Kawamoto et al., 2014; Paddock & Behm, 2009). The electrodes for the VL were positioned at 66% of the distance between the anterior superior iliac spine and the lateral side of the patella. The mid-point between the gluteal fold and popliteal space was used for the BF. The electrodes were spaced 2 cm apart (center to center) and aligned parallel to the direction of the muscle fibers. To ensure minimal skin resistance, the area was prepared by shaving, lightly abrasing with sandpaper, and cleansing with an isopropyl alcohol swab. Additionally, a ground electrode was positioned on the lateral femoral epicondyle.

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.

An integral EMG (IEMG) was used over the peak MVIC force (0.5-s prior to and after the peak force). IEMG values were determined using a window width of 100-ms. Once IEMG was calculated the mean amplitude 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

A specific warm-up protocol was conducted for the MVICs, which involved three 5-second contractions at approximately 50% of the MVIC intensity, followed by two 5-second contractions at approximately 75% intensity. Following a general warm-up of lower body cycling on a Monark cycle ergometer for 5-minutes at a cadence of 70 rpm (70 Watts), the participants proceeded to perform a pre-test involving MVICs for knee flexion and extension. The order of muscle testing was randomized. For each muscle, two MVICs consisting of knee flexion or extension were performed, each lasting 5-seconds, with a 2-minute rest period between MVICs. Participants were instructed to exert maximum effort and contract the target muscles as forcefully and quickly as possible throughout the 5-second duration. The MVIC with the highest peak force was selected for further analysis. In cases where the second MVIC exceeded the first by 10% or more, an additional MVIC was performed. To minimize upper body involvement, a five-point harness was secured around the waist and shoulders of the participants, and they were instructed to cross their arms over their chest. An ankle cuff was placed on the participant's ankle, which was connected to strain gauges (Omega engineering Inc., LCCA 250, Don Mills, Ontario) via a non-extensible chain. The strain gauges and chains were attached either to the chair (for VL MVICs) or to the wall (for BF MVICs). The chair was positioned at a distance from the wall that ensured the chain remained taut without any slack.

2.1.3.3 Unilateral Fatigue Intervention

Following the 5-second duration MVIC pre-tests, participants either underwent a fatigue protocol or a rest period lasting 260 seconds (Control), depending on the

experimental condition. The fatigue protocol used in this study has been demonstrated to induce NLMF in the contralateral knee extensors in previous research (Doix et al., 2013; Halperin, Copithorne, & Behm, 2014). Using the same setup as the pre-MVIC testing, the dominant leg performed continuous knee extension MVICs for two sets, each lasting 100 seconds, with a 1-minute rest period between sets. Throughout the fatigue protocol, participants were instructed to keep the contralateral leg relaxed during leg contractions, and the EMG activity of the contralateral leg was monitored to ensure it remained below 5% of the MVIC EMG level. Data for both legs were recorded during the fatigue protocol for later analysis. A fatigue index was calculated by dividing the mean values of the last two MVICs by the mean values of the first two MVICs for both force and EMG measurements, providing an endurance outcome measure.

2.1.3.4 Post-test Single MVIC Force Measures

For the post-tests, a single 5-second MVIC was performed after the fatigue protocol based on the specific condition (1-minute, 3-minute, 5-minute, or control). The sequence of MVICs started with dominant leg knee extension, followed by non-dominant leg knee extension, and finally non-dominant leg knee flexion. Each MVIC was executed for a duration of 5-seconds, and the transition between MVICs was rapid (i.e., less than 30-seconds). Peak force, impulse (work multiplied by time), and instantaneous strength (F100) were measured for each knee flexion and extension MVIC of both legs during the post-tests.

2.1.3.5 Post-test Fatigue Measures

To examine the presence of NLMF effects, a post-test fatigue protocol was conducted involving the non-exercised knee extensors. This protocol consisted of 12 MVICs performed with a work-to-rest ratio of 5 seconds to 10 seconds (D. G. Behm et al., 2021a;

Halperin, Copithorne, & Behm, 2014). Each testing session had a different time point for the post-test (1-minute, 3-minute, and 5-minute). In the control session, participants followed the same pre-test protocol but instead of performing the fatigue protocol, they rested for 260 seconds. After the rest period, a post-test was conducted at 1 minute following the control inactivity period.

The purpose of the 12 MVICs during the post-test was to calculate a fatigue index that could indicate possible significant difference in forces or EMG activity in the non-exercised muscle group, possibly reflecting the presence of NLMF effects. The fatigue index was calculated by dividing the mean values of the last two MVICs by the mean values of the first two MVICs for both force and EMG measurements. This analysis allowed for the detection of potential changes in force and EMG activity during the endurance test in the non-exercised muscle group, indicative of NLMF effects.

2.1.4 Statistical Analysis

The statistical analyses were conducted using SPSS software (Version 27). Intraclass correlation coefficients (ICC) were calculated to assess the reliability of MVIC force, VL, and BF EMG measurements in the non-dominant limb. Normality tests (Kolmogorov-Smirnov) and tests for the assumption of sphericity were performed for all dependent variables. If the assumptions of normality and sphericity were met, two-way repeated measures ANOVA tests were used to analyze the effects of the fatiguing protocol on pre- and post-test measurements (at 1-, 3-, and 5-minutes). The factors included in the ANOVA were time (2 levels) and "post-testing condition" (Control, 1 min, 3 min, and 5 min). These analyses were conducted for both MVIC force, instantaneous strength (the force produced in the first 100 milliseconds of the MVIC) and EMG measurements in the non-exercised leg.

Furthermore, a one-way repeated measures ANOVA was used to analyze the effect of post-testing conditions (Control, 1 min, 3 min, and 5 min) on the fatigue index. This analysis was specifically applied to the non-exercised leg. If significant main effects were observed, post-hoc tests with Bonferroni correction were conducted to compare different conditions and time points. The threshold for statistical significance was set at $p < 0.05$.

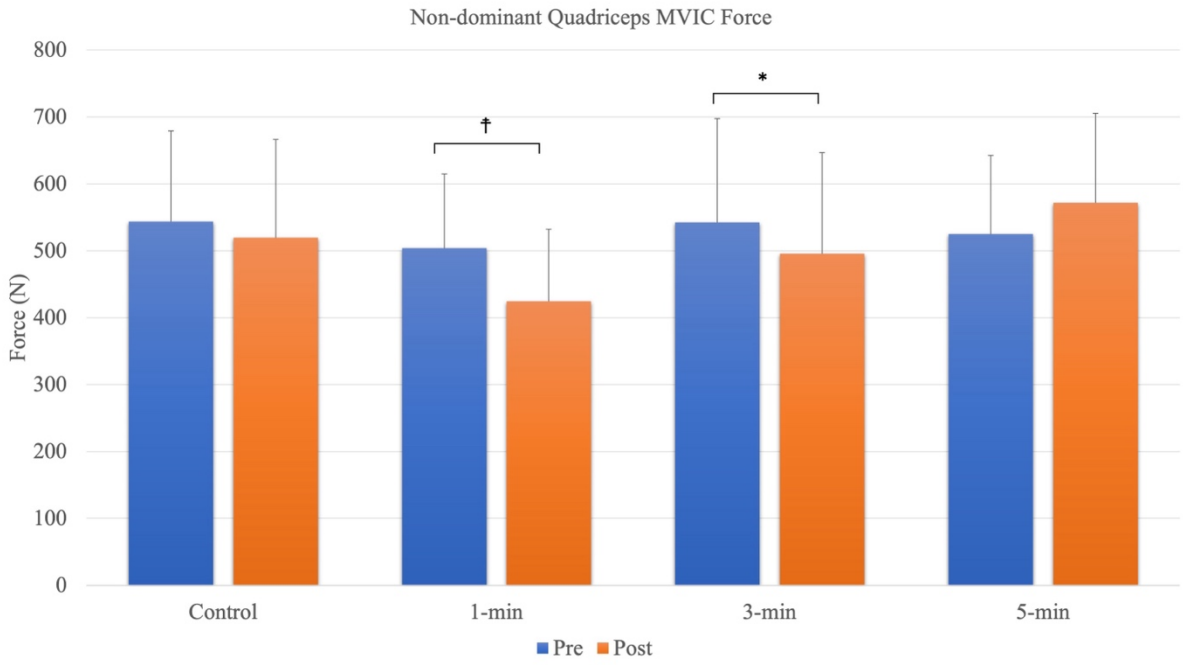
To assess the magnitude of the observed effects, Cohen's d effect sizes were calculated, following Cohen's guidelines (1988). Effect sizes less than 0.2 were considered trivial, effect sizes between 0.2 and less than 0.5 were classified as small, effect sizes between 0.5 and less than 0.8 were considered medium, and effect sizes of 0.8 or greater were considered large. The reported data are presented as means ± standard deviation (SD).

2.2 Results

2.2.1 Non-dominant knee extensors MVIC:

For non-dominant knee extensors MVIC the results showed significant interactions between condition and time ($F_{1,64}$ =9.17, $p<0.0001$, $p\eta2=0.30$) and a significant main effect for times ($F_{1,64}$ =8.36, $p=0.005$, $p\eta2=0.12$).

Compared to the pre-test, MVIC forces showed moderate magnitude decrease of 15.81% ($p<0.0001$, $d=0.72$) at 1-min post-test, and a small magnitude 8.54% ($p=0.005$, $d=0.30$) decrement at 3-min. The 5-min group showed a trivial magnitude, non-significant ($p=0.076$, $d=0.15$) pre- to post-test increase of 8.98% (Figure 2).

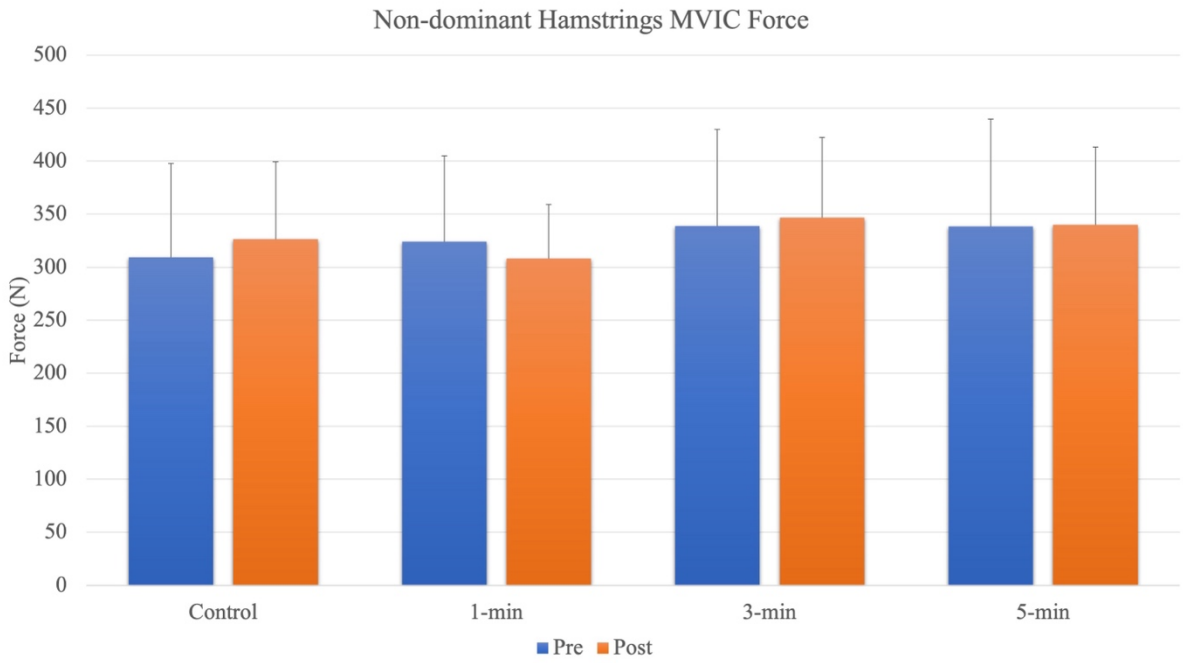


	Pre-MVIC	Post-MVIC	Percent difference (%)
Control force (N)	543.47 ±135.54	519.82 ±146.85	-4.35 (p=0.13)
1-min force (N)	504.03 ±111.10	424.31 ±108.21	-15.81 (p<0.0001)
3-min force (N)	542.31 ±155.38	495.97 ±150.82	-8.54 (p=0.005)
5-min force (N)	524.83 ±117.9	571.97 ±133.32	+8.98 (p=0.076)

Figure 2 Non-dominant quadriceps MVIC force

2.2.2 Non-dominant knee flexors MVIC force:

The analysis of the knee flexion MVIC force did not reveal any significant interactions between the experimental conditions and time ($F_{1,64}$=0.91, p=0.442, pη2=0.041) (Figure 3). Furthermore, there were no significant differences found in the main effects across the various conditions ($F_{1,64}$=0.13, p=0.718, pη2=0.002).

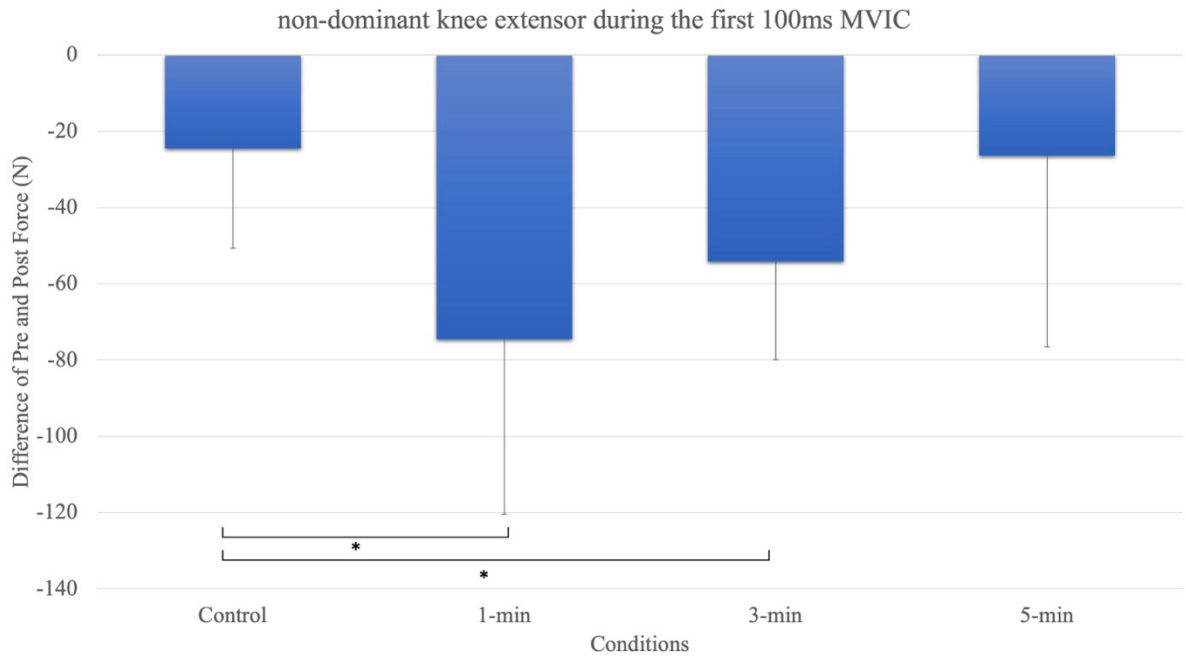


	Pre-MVIC	Post-MVIC	Percent difference (%)
Control force (N)	309.39 ±88.57	326.25 ±72.99	5.44
1-min force (N)	323.94 ±81.2	308.21 ±50.88	- 4.85
3-min force (N)	338.98 ±90.77	346.73 ±75.76	2.28
5-min force (N)	338.49 ±101.43	340.05 ±73.1	0.46

Figure 3 Non-dominant hamstrings MVIC force

2.2.3 Non-dominant knee extensors Instantaneous Strength

The analysis of knee extension MVIC instantaneous strength revealed a significant main effect among the experimental conditions, ($F_{3,48}$=5.43, p=0.006, pη2=0.25). Significantly, large magnitude, greater decreases were specifically observed between the 1-minute (p=0.021, d=1.33), as well as between the 3-minute conditions (p=0.041, d=1.13) and the control conditions (Figure 4). However, no significant differences were detected among the other conditions (p>0.05).

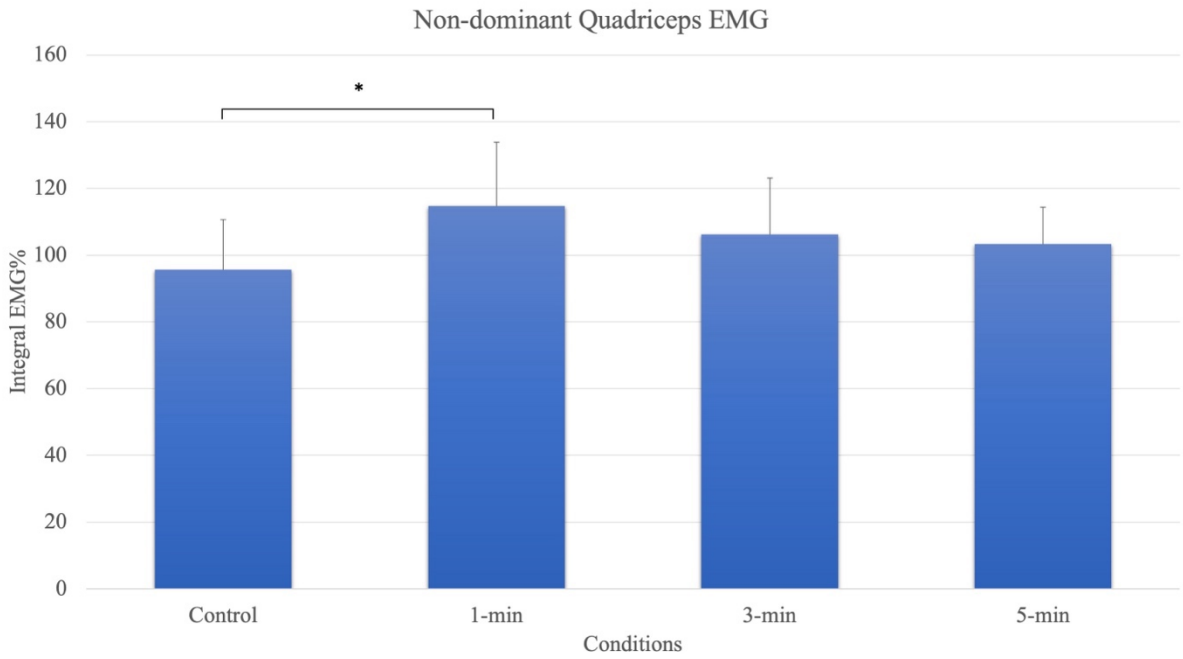


	The difference between Pre- and Post-test	Std. Deviation
Control force (N)	-24.45	26.16
1-min force (N)	-74.44	45.96
3-min force (N)	-54.08	25.83
5-min force (N)	-26.36	50.14

Figure 4 Non-dominant knee extensor (quadriceps) MVIC force during the first 100ms MVIC. Asterisks indicate significant differences of p=0.021 and p=0.041 for 1-min and 3-min versus control respectively.

2.2.4 Non-dominant Vastus Lateralis EMG

The analysis of the normalized EMG data in the Integral of EMG values between pre- and post-tests for the vastus lateralis muscle yielded significant main effect differences among the experimental conditions, ($F_{3,14} = 5.13$, $p = 0.013$, $p\eta 2 = 0.52$). Post hoc analysis revealed that large magnitude increases were specifically observed between the 1-minute and control conditions ($p=0.03$, $d=1.10$) (Figure 5). However, no significant differences were found among the other conditions ($p > 0.05$).

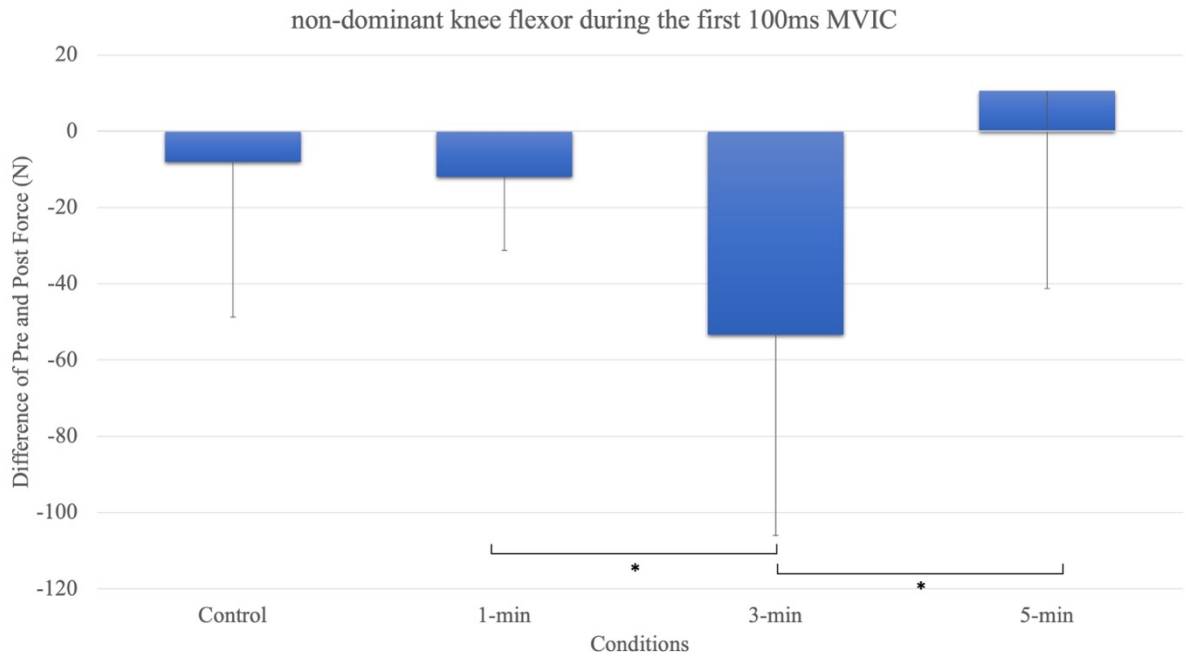


Normalized EMG Condition	The difference percentage between Pre- and Post-test	Std. Deviation
Control force	95.72	14.95
1-min force	114.72	19.13
3-min force	106.24	16.93
5-min force	103.41	11.04

Figure 5 Non-dominant quadriceps normalized EMG. Asterisk indicates significance of p=0.03.

2.2.5 Non-dominant knee flexors Instantaneous Strength

MVIC knee flexors instantaneous strength analysis revealed significant main effect differences among the experimental conditions, ($F_{3,14}$=3.37, p=0.049, pη2=0.42). Post hoc analysis further revealed large magnitude decreases were observed between the 1-minute and 3-minute conditions (p=0.045, d=1.04), as well as between the 3-minute and 5-minute conditions (p=0.046, d=1.22) (Figure 6). However, no significant differences were found among the other conditions (p > 0.05).

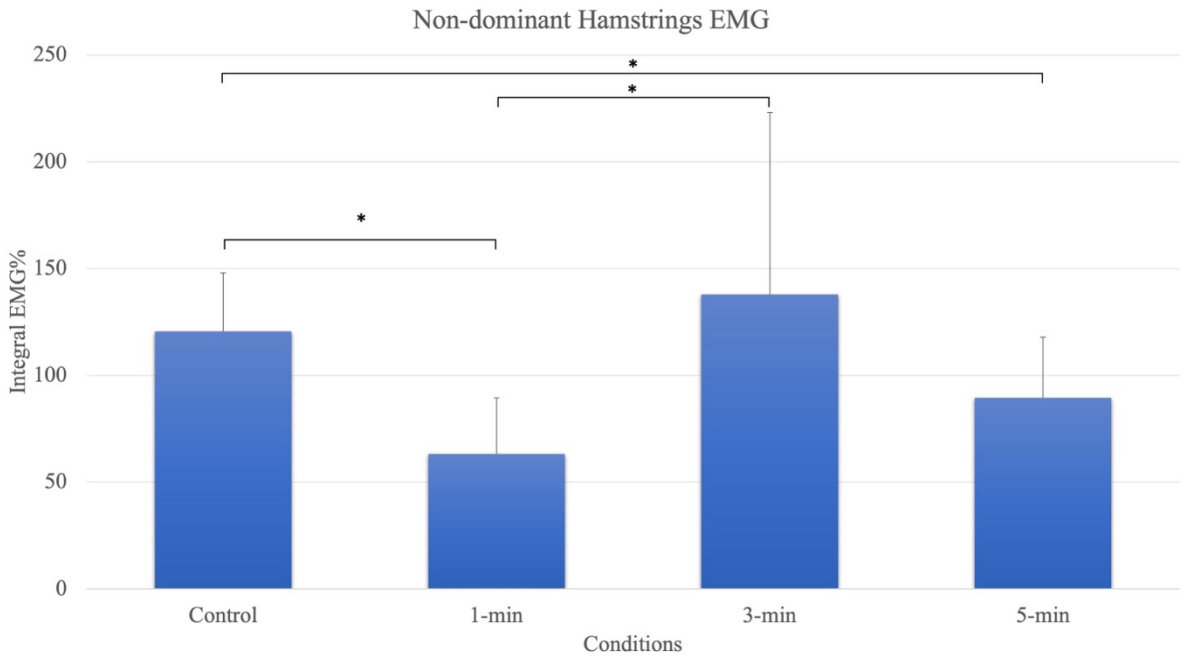


	The difference between Pre- and Post-test	Std. Deviation
Control force (N)	-8.03	40.66
1-min force (N)	-11.87	19.37
3-min force (N)	-53.34	52.71
5-min force (N)	10.63	51.85

Figure 6 Non-dominant knee flexor (hamstrings) MVIC force during the first 100ms MVIC. Asterisks indicate significant differences of p=0.045 and p=0.046 between the 1- and 3-min recoveries and the 3- and 5-min recoveries respectively.

2.2.6 Non-dominant Biceps Femoris EMG

Pre- vs. post-tests biceps femoris EMG analysis revealed significant main effect differences among the experimental conditions, ($F_{3,14}$ =16.86, p=0.001, pη2=0.78). Post hoc analysis further revealed large magnitude increases between the 1-minute and 3-minute conditions (p=0.015, d=1.18), between the 1-minute and control condition (p=0.001, d=2.14), as well as between the 5-minute and control condition (p=0.018, d=1.11) (Figure 7). However, no significant differences were found among the other conditions (p>0.05).



Normalized EMG Condition	The difference percentage between Pre- and Post-test	Std. Deviation
Control force	120.63	27.34
1-min force	63.06	26.32
3-min force	137.85	85.15
5-min force	89.39	28.53

Figure 7 Non-dominant quadriceps normalized EMG. Asterisks indicates significant differences ranging from p=0.015 to p=0.001.

2.2.7 Fatigue Index

The fatigue index results for knee extensors MVIC showed significant interactions between conditions ($F_{4,13}$=4.44, p=0.018, pη2=0.58). The results showed significant large magnitude fatigue index differences between 5-min (p=0.005, d=7.32) and control group (p=0.029, d=5.29).

The analysis of the normalized EMG Integral data between pre- and post-tests for the vastus lateralis muscle yielded significant main effect differences among the experimental conditions, ($F_{4,13}$=48.97, p<0.001, pη2=0.93). Post hoc analysis revealed significant fatigue index differences between 1-min (p<0.001, d=9.43), 3-min (p<0.001, d=8.05), 5-min (p<0.001, d=8.59) and control (p=0.047, d=5.91).

The analysis of knee extension MVIC instantaneous strength fatigue index revealed a significant main effect among the experimental conditions, ($F_{4,13}$=8.65, p=0.001, pη2=0.72). Significantly, large magnitude, greater decreases were observed between the experimental and control conditions (p=0.005, d=5.35).

2.3 Discussion

The primary outcome of this study revealed a significant impairment in quadriceps NLMF-induced single MVIC force decrements, specifically at 1-minute and 3-minute recovery intervals. However, no significant differences were observed at the 5-minute recovery interval or in the control condition. The second prominent finding of this study pertains to the fact that, the analysis of hamstrings MVIC, instantaneous strength, and EMG activity did not reveal any consistent and meaningful patterns. While there were some statistically significant differences observed in instantaneous strength and EMG activity, especially during the 3-minute recovery period, these differences did not follow a logical or predictable pattern. These findings highlight the complex nature of NLMF effects on the hamstrings, where the anticipated changes in muscle performance and EMG activity were not consistently observed across post-test durations. The third significant finding showed that the fatigue index revealed no significant difference between the 1-minute and 3-minute groups in the MVIC fatigue test. Furthermore, no difference was found with the 1-minute recovery of the MVIC instantaneous strength fatigue index. However, the EMG fatigue index results demonstrated a difference between all groups, although this difference did not provide conclusive evidence.

The purpose of this study was to investigate the presence of non-local muscle fatigue (NLMF) and assess the impact of various recovery durations on NLMF. A number of original research studies have reported NLMF (Doix et al., 2013; Halperin, Copithorne, & Behm, 2014; Halperin et al., 2015a; Hamilton & Behm, 2017; Kawamoto et al., 2014;

Kennedy et al., 2013; Martin & Rattey, 2007), but there is scant research that examined the duration of NLMF recovery. The findings of this study indicate that the presence of NLMF with single MVICs can be demonstrated within recovery times of 1- and 3-minutes, while no significant NLMF was observed within a 5-minute recovery period. These results suggest that the recovery duration plays a crucial role in the manifestation of NLMF and highlights the importance of considering the optimal recovery period when assessing and interpreting NLMF phenomena. The present study contributes to the growing body of literature exploring the interplay between unilateral muscle fatigue and its impact on contralateral muscle function, highlighting the specificity of these effects within the quadriceps muscles.

As mentioned, the antagonist (hamstrings) muscle did not follow a logical or predictable pattern. Carolan & Cafarelli (1992) investigated the effects of isometric resistance training on co-activation adaptations observing that after 8 weeks of static resistance training, hamstrings co-activation during knee extension MVIC significantly decreased, while knee extension MVIC force showed a significant increase. This present outcome might be attributed to the principle of movement specificity, (Behm & Sale, 1993). The fatigue intervention utilized in this study involved knee extension, and it is plausible that different joint movements or contractions of heterologous muscles might not exhibit a comparable degree of neuromuscular responses.

The proposed experimental design for this study aimed to optimize the elicitation of NLMF based on previous research by Halperin, who suggested that NLMF effects are primarily influenced by neural and psychological factors. To account for this postulation, a high intensity fatiguing protocol combined with a high volume of exercise was chosen, as such protocols have been shown to induce NLMF effects (Halperin et al., 2015a). The fatigue intervention comprised two sets of 100 seconds of maximal voluntary isometric

contractions, separated by 1 minute of rest, which closely resembled protocols used in prior studies reporting NLMF effects (Doix et al., 2013; Halperin et al., 2015a; Hamilton & Behm, 2017).

These findings align with previous original research (Doix et al., 2013; Halperin, Copithorne, & Behm, 2014; Halperin et al., 2015a; Hamilton & Behm, 2017; Kawamoto et al., 2014; Kennedy et al., 2013; Martin & Rattey, 2007) providing supporting evidence for the influence of unilateral dominant quadriceps fatigue on contralateral quadriceps single or discrete MVIC force, instantaneous strength, and EMG activity. However, in the Behm et al. (2021b) meta-analysis, their overall findings did not provide strong support for the existence of a general NLMF effect on individual MVICs. When examining specific types of performance outcomes, particularly related to endurance-based measures such as time to task failure, there may be a discernible effect, which aligns with the endurance-based protocol used in this study. It is worth noting that the meta-analysis did not differentiate between slow and fast twitch predominant muscles, which can have significant implications for both fatigue protocol design and NLMF responses. Further exploration of the influence of muscle fiber type on NLMF is warranted.

Despite the utilization of similar methodologies by Anvar et al. (2022), which focused on plantar flexor muscles, no significant impairment in NLMF single MVIC force was observed in that study. In line with recommendations from Halperin et al. (2015b) and other researchers (Alcaraz et al., 2008) to enhance the likelihood of NLMF, this study targeted the knee extensors for fatigue induction and assessment. The quadriceps muscles, which constitute a larger muscle mass and possess a higher proportion of fast-twitch fibers (Miller et al., 1993b), exhibit an accelerated onset of fatigue. compared to plantar flexion in a seated, flexed knee position. In this position, the gastrocnemius is disadvantaged, resulting in greater reliance on the soleus muscle, which is characterized by a

predominance of slow-twitch fibers (Campbell et al., 1979; Costill et al., 1976; Monster et al., 1978). According to Henneman's size principle (Henneman et al., 1965), type I (slow twitch) motor units with smaller somas have lower recruitment thresholds. Therefore, considering that muscle inactivation may increase with fatigue (Behm, 2004b), the decrease in the central nervous system's capacity to fully activate the muscle may not be as significant of a concern with the lower threshold slow-twitch predominant motor units of the soleus muscle.

Only a limited number of studies have examined NLMF beyond a 1-minute recovery period, and very few have reported significant effects. For instance, Prieske et al. (2017) investigated unilateral fatigue at various movement velocities using an isokinetic dynamometer, revealing decreased torque production in the non-exercised knee extensors for up to 5 minutes following fatigue induction at slower movement velocities (60º/s). However, Arora reported the absence of NLMF when examining the impact of low-intensity fatiguing unilateral knee extensor exercise on force and activation in the contralateral non-exercised leg after a 10-minute recovery period following the fatigue protocol (consisting of 15 isometric knee extensions at 30% of peak MVIC force, each lasting 16 seconds with 4 seconds of recovery) (Arora et al., 2015). It is worth noting that most studies assessing NLMF have typically conducted post-tests immediately after the fatigue intervention. In this particular study, the shortest recovery time condition was 1 minute following the fatigue intervention. Central neuromuscular fatigue recovery typically occurs within 1-2 minutes (Carroll et al., 2017). Thus, the minimum 1-minute recovery time before the post-test may have allowed participants sufficient time to recover. Sustained MVIC forces can progressively decrease by 50% within 1-2 minutes (as observed in the 2 sets of 100 seconds in this study), with initial rapid recovery influenced by rapid muscle reperfusion (Carroll et al., 2017). Consistent with the present research, the

findings regarding MVIC and MVIC instantaneous strength demonstrate that the reduction in post-test compared to pre-test is more pronounced in the 1-minute recovery time condition, followed by the 3-minute recovery time condition, while no significant differences were observed with the 5-minute recovery time condition.

Two potential mechanisms may explain the findings of this study. Firstly, it is plausible that various metabolites including potassium, hydrogen, lactate, and heat shock proteins are dispersed to non-exercised muscles through the cardiovascular system during and after fatiguing protocols (Halperin et al. 2015), potentially impairing their contractile capacity (Henneman et al., 1965). Secondly, it is possible that certain fatiguing protocols result in heightened activation of stabilizer muscles, which in turn impairs their ability to stabilize during testing of the non-exercised muscle groups (Halperin et al. 2015, Baker & Davies, 2009). Consequently, this can lead to reductions in muscle force and the observation of indirect NLMF.

Fatigue interventions of longer duration have also been demonstrated to impact the psychological aspect, specifically resulting in a mental energy deficit when experiencing discomfort. This can lead to mental fatigue, which is characterized by reduced focus and concentration, subsequently affecting neuromuscular activation in both fatigued and non-exercised muscles (Halperin et al., 2015b). In Steele's study, "perception of effort" is defined as the individual's perception of the required effort to accomplish a specific task or set of tasks, determined by comparing the current task demands to the perceived capacity to meet those demands, without exceeding the perceived current capacity. Steele formulated the perception of effort (EP) for an individual (i) at a given time (t) as EP (i, t, CP, DP), where CP (i, t, xC) and DP (i, t, xD) represent the perception of capacity (CP) and perception of demands (DP), respectively, with xC and xD denoting the magnitudes of these factors (Steele, 2020). Applying Steele's definition and formula to our study,

where a severe fatigue protocol was performed on the dominant quadriceps, it is plausible that the preceding unilateral work may have heightened the perception of effort involved in the subsequent task, potentially contributing to the occurrence of NLMF.

In addition, it is worth noting that the participants in this study were primarily individuals with recreational training backgrounds and limited experience with resistance training. Their lack of familiarity with high-intensity resistance training loads may have influenced their ability to fully activate their muscles, achieving 100% MVIC throughout the extended intervention duration of 2 sets of 100 seconds. Consequently, the potential for submaximal intensity contractions might not have induced a significant mental energy deficit, limiting the likelihood of observing NLMF effects.

Moreover, the participants in this study were not provided with specific information regarding the exact endpoint of the fatigue protocol, which consisted of 12 repetitions lasting 5 seconds each with 1-second recovery intervals. This deliberate omission of endpoint knowledge is known to elicit lower forces and EMG outputs compared to protocols with known endpoints, as reported by Billaut et al. (2011) and Hamilton and Behm (2017). Mauger et al. (2009) demonstrated that an unknown endpoint imposes limitations on performance when participants are required to sustain a high-intensity MVIC for an unknown duration. Moreover, unknown endpoints have been shown to diminish motivation for optimal performance, as documented by St Gibson et al. (2006). In the study conducted by Halperin et al. (2014), it was observed that female participants exhibited distinct pacing strategies depending on their expectations regarding the number of maximal voluntary contractions (MVCs) they were required to perform. Specifically, in the deception condition, where subjects were informed of performing fewer MVCs, significantly greater forces were applied during the initial six MVCs when compared to both the unknown condition and the control condition. Furthermore, another Halperin et

al. (2014) investigation involved participants performing a fatiguing protocol with the same maximal intent. In this scenario, subjects demonstrated higher force production during the deception condition when compared to the unknown condition from the initial contraction onward. These findings suggest that information regarding the number of expected MVICs can significantly influence pacing strategies and force production patterns during fatiguing tasks in female individuals. Consequently, the absence of an endpoint in the fatigue protocol employed in this study likely resulted in reduced motivation to fully activate all motor neurons, thus contributing to a greater decline in fatigue protocol outcomes compared to post-test NLMF assessments.

2.4 Limitation

One of the challenges encountered in this study was the recruitment of an equal number of female and male participants. Despite conducting an initial "a priori" statistical power analysis, which indicated that a sample size of 8 to 13 participants would be sufficient to achieve adequate statistical power, it is worth noting that a larger number of participants, particularly males, could have potentially enhanced the statistical power of the study and allowed for a more comprehensive examination of potential sex differences.

It is important to acknowledge that certain factors were not considered in this study, such as the influence of the menstrual cycle on physiological responses. Moreover, the inherent ability of females to resist fatigue compared to males could have introduced additional variability in the female data (Hicks et al., 2001; Hunter, 2009). It is noteworthy, however, that the female cohort consisted of only four participants, which limits the generalizability of the findings pertaining to this specific group.

Given the considerations, future studies in this area could benefit from a more concerted effort to recruit a larger and balanced representation of both female and male participants. This would enable a more robust analysis of potential sex differences and provide a more

comprehensive understanding of the topic under investigation. Additionally, incorporating the menstrual cycle as a relevant variable in the study design could further elucidate any impact it may have on the observed outcomes and potentially enhance the overall validity and reliability of the findings.

2.5 Conclusions:

In conclusion, this study aimed to investigate the presence and effects of NLMF in the context of different recovery durations. The findings of this study, both supports a number of previous individual studies but contradicts a recent meta-analysis. It was observed that quadriceps NLMF effects were evident within recovery times of 1- and 3-minutes, whereas no significant NLMF was observed after a 5-minute recovery period. There was also no consistent evidence for contralateral hamstrings NLMF. The results align with some previous studies, suggesting that recovery duration plays a crucial role in the manifestation of NLMF. The fatigue experienced in the contralateral muscle after focused unilateral training has important implications for planning workouts. This phenomenon affects exercise timing and rest between sets or exercises that target similar muscle groups bilaterally. For sufficient recovery from this type of training, it is suggested to wait around 3 minutes. Moreover, the influence of factors such as familiarity with high-intensity resistance training loads, perception of effort, and the specific muscle group targeted during fatigue protocols were also highlighted. Overall, these findings contribute to the growing body of knowledge on NLMF, emphasizing the importance of considering recovery duration and specific muscle characteristics when investigating and interpreting NLMF phenomena. Further research is warranted to explore the underlying mechanisms and potential implications of NLMF across a range of experimental conditions.

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Appendix:

Appendix 1- Ethics Letter Approval

MEMORIAL UNIVERSITY

Interdisciplinary Committee on Ethics in Human Research (ICEHR)

St. John's, NL Canada A1C 5S7
Tel: 709 864-2561 icehr@mun.ca
www.mun.ca/research/ethics/humans/icehr

ICEHR Number:	**20210760-HK**
Approval Period:	November 12, 2020 – November 30, 2021
Funding Source:	
Responsible Faculty:	Dr. David Behm School of Human Kinetics and Recreation
Title of Project:	*An analysis of the duration of non-local muscle fatigue effects*

November 12, 2020

Mr. Mohamed Mamdouh Ibrahim Mahmoud
School of Human Kinetics and Recreation
Memorial University of Newfoundland

Dear Mr. Mahmoud:

Thank you for your correspondence addressing the issues raised by the Interdisciplinary Committee on Ethics in Human Research (ICEHR) concerning the above-named research project. ICEHR has re-examined the proposal with the clarification and revisions submitted, and is satisfied that the concerns raised by the Committee have been adequately addressed. In accordance with the *Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans (TCPS2)*, the project has been granted *full ethics clearance* to November 30, 2021. ICEHR approval applies to the ethical acceptability of the research, as per Article 6.3 of the *TCPS2*. Researchers are responsible for adherence to any other relevant University policies and/or funded or non-funded agreements that may be associated with the project.

The *TCPS2* **requires** that you submit an Annual Update to ICEHR before November 30, 2021. If you plan to continue the project, you need to request renewal of your ethics clearance and include a brief summary on the progress of your research. When the project no longer involves contact with human participants, is completed and/or terminated, you are required to provide an annual update with a brief final summary and your file will be closed. If you need to make changes during the project which may raise ethical concerns, you must submit an Amendment Request with a description of these changes for the Committee's consideration prior to implementation. If funding is obtained subsequent to approval, you must submit a Funding and/or Partner Change Request to ICEHR before this clearance can be linked to your award.

All post-approval event forms noted above can be submitted from your Researcher Portal account by clicking the *Applications: Post-Review* link on your Portal homepage. We wish you success with your research.

Yours sincerely,

Kelly Blidook, Ph.D.
Vice-Chair, Interdisciplinary Committee on
Ethics in Human Research

KB/bc

cc: Supervisor – Dr. David Behm, School of Human Kinetics and Recreation