THE EFFECTS OF UNILATERAL DOMINANT KNEE EXTENSORS FATIGUE ON NON-EXERCISED CONTRALATERAL AND IPSILATERAL ELBOW AND PLANTAR FLEXORS

By

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ABSTRACT

The field of non-local muscle fatigue (NLMF) is a relatively young one. However, key factors and trends regarding methodologies and possible mechanisms are starting to be identified. Controlling for factors such as particular muscle groups selected, fatiguing protocols utilized, and participant factors such as age, sex, and training status are starting to illuminate the neurological, biological, biomechanical, and psychological contributions to NLMF effects. To date, this is the first investigation of ipsilateral and contralateral upper and lower body muscle groups following unilateral lower body fatigue that the investigators are aware of. The present study investigated the effects of exercise-induced knee extensor fatigue on force output and electromyography (EMG) activity of both, the ipsilateral and contralateral, non-exercised elbow and plantar flexors. Twelve participants (six females, six males) attended six testing sessions: i) fatigue-ipsilateral plantar flexor (PF), ii) control-ipsilateral PF, iii) fatigue-ipsilateral elbow flexor (EF), iv) control-ipsilateral EF, v) fatigue-contralateral PF, or vi) fatigue-contralateral EF. The non-fatigued muscle groups were assessed with maximal voluntary contractions (MVCs) and normalized electromyographic (EMG) activity prior to and immediately post the intervention as well as during a repeated MVC protocol of twelve repeated MVCs at a work to rest ratio of 5/10 s. Ipsilateral EF MVC strength and endurance decreased following dominant KE fatigue as evidenced by a decrease in both MVC force immediately post-fatigue intervention and FI across the repeated MVC protocol. There were no significant differences in PF force or EMG or EF EMG immediately post-test or during the repeated MVC protocol. This study strengthens current theories which suggest that upper body

muscle groups are more susceptible to NLMF effects following lower body fatigue and postulates that fast twitch (EF) predominant muscles are more susceptible to NLMF effects than are slow twitch (PF) predominant muscles.

KEYWORDS: neuromuscular, cross-over fatigue, non-local muscle fatigue, electromyography, force

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LIST OF ABBREVIATIONS

ANOVA - Analysis of variance
AP – Action Potential
BB – Biceps Brachii
CMEP – Cervico-medullary Motor Evoked Potential
CNS – Central Nervous System
CST – Corticospinal Tract
EF – Elbow Flexors
EMG – Electromyography
ES – Effect Size
FT – Fast Twitch
f100 - the force generated in the initial 100ms of a maximal voluntary contraction MVC
FDI – First Dorsal Interosseus
KE – Knee Extensors
M-wave – Peripheral Nerve Stimulation
MEP – Motor Evoked Potential
MPO – Mean Power Output
MVC – Maximal Voluntary Contraction
NLMF – Non-Local Muscle Fatigue
PP – Peak Power
PF – Plantar Flexors
SICI – Short Interval Intracortical Inhibition
ST – Slow Twitch
TMEP – Thoracic Motor Evoked Potential
TTE- Time To Exhaustion
TMS – Transcranial Magnetic Stimulation
VA – Voluntary Activation
Wpeak – Peak Anaerobic Power

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Review of Literature

A Neuromuscular Physiology Perspective on Non-local Muscle Fatigue

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Introduction

Neuromuscular fatigue is commonly defined as an exercise-induced decrease in maximal force or power production, as well as the inability to maintain force output at a target intensity for a given time (Gandevia, 2001). The observed deficits can be due to factors such as changes occurring within the muscle, as well as changes occurring in the central and/or peripheral nervous systems. Central fatigue has occurred when there is a decrease in the ability of the central nervous system (CNS), the brain and/or spinal cord portion of the previously mentioned pathway, to voluntarily drive muscle activation (Arora, Budden, Byrne, & Behm, 2015). This can be further classified as supraspinal fatigue when the impairment in the ability to produce force originates at the level of the brainstem or higher (Takahashi et al., 2009). Peripheral fatigue has occurred if the reduction in the muscle's ability to generate force is impaired at a location which is distal to the neuromuscular synapse (Arora, Budden, Byrne, & Behm, 2015; Kirkendall, 1990; Ross, Middleton, Shave, George, & Nowicky, 2007). A great deal of neuromuscular fatigue research has investigated the changes occurring in and along the neurological pathway to the working muscle (Bigland-Ritchie, Jones, & Woods, 1979; Komi & Tesch, 1979; Stephens & Taylor, 1972); however, a more recent field of research has explored how localized fatigue can affect corticospinal responsiveness and motor performance in muscles that have not been exercised (Aboodarda, Copithorne, Power, Drinkwater, & Behm, 2015; Bonato et al., 1996; Takahashi et al., 2011). These global responses have been observed to be both inhibitory and excitatory in nature and are known as non-local muscle fatigue (NLMF) and non-local muscle potentiation (NLMP), respectively. In addition, non-local

muscle effects have also been demonstrated with stretching leading to increased range of motion and performance alterations in non-stretched muscles and joints (Behm et al., 2019; Chaouachi et al., 2017).

Altered performance and flexibility of non-fatigued and non-stretched muscle groups and joints provides strong evidence for global neuromuscular responses. However, the evidence for the occurrence and explanation of mechanisms causing these phenomena is currently equivocal. As such, multiple experimental factors are still being examined by researchers such as the muscles groups selected, the fatiguing/testing protocols utilized, as well as participant factors such as age, sex, and training status.

Non-Local Muscle Fatigue

NLMF – Homologous Muscle Groups

When fatigue effects are observed in the non-exercised contralateral homologous muscle group, the phenomenon is known as ‘cross-over fatigue’ and it has been observed in muscle groups of both the lower and upper body in multiple studies (Doix, Lefèvre, & Colson, 2013; Hendy, Chye, & Teo, 2017; Humphry et al., 2004; Kawamoto, Aboodarda, & Behm, 2014; Martin & Rattey, 2007; Todd, Petersen, Taylor, & Gandevia, 2003; Triscott et al., 2008).

Lower body:

The muscle group predominately investigated in crossover fatigue studies of the lower body has been the knee extensors (KEs) and performance deficits in maximal voluntary contraction (MVC) force, time to exhaustion (TTE), as well as voluntary activation (VA) have been observed in the non-exercised contralateral KEs following

various fatiguing protocols (Doix et al., 2013; Hendy et al., 2017; Kawamoto et al., 2014; Martin & Rattey, 2007). For example, following two, 100 second continuous MVCs of the dominant knee extensors, Doix et al. observed a 4.9% decrease in the maximal MVC torque of the non-exercised contralateral KE following the first 100 second MVC and a 10.6% decrease following the second. Voluntary activation was also investigated and though it did decrease approximately 10% in the non-exercised KEs, this finding was not found to be significantly different from the exercised KEs and the change was postulated to likely be due to the testing of the non-exercised KEs and not due to the fatiguing protocol completed by the contralateral homologous muscle group. Similarly, following one, 100 second continuous MVC of the dominant KEs, Martin and Rattey (Martin & Rattey, 2007) observed MVC force decreases in the non-exercised contralateral KEs of 10-13% and 8% in their male and female participants, respectively. However, unlike Doix et al. (Doix et al., 2013), voluntary activation was found to have been significantly ($p < 0.001$ in both cases) reduced for male (to 62.8±11.3%) and female (to 74.7±11.6%) participants; highlighting a discrepancy within the current literature.

Interestingly, these studies both provide evidence suggesting two key factors to consider regarding cross-over fatigue experiments: The factors being that the greater the fatiguing effect on the fatigued muscle group, will impact both he likelihood and the extent of the crossover fatigue effects. The presence of crossover fatigue can be shown by the relationship between the decline in force and the decline in voluntary activation from before (mean of four trials) to during (mean of four trials) fatigue ($r=0.595$, $r^2=0.354$, $p<0.01$) in the Martin and Rattey (Martin & Rattey, 2007)) study. The extent of cross-over

fatigue effects is documented by the decrease of MVC force by 4.9% after the first 100s MVC fatiguing protocol compared to the 10.5% decrease following the second 100s MVC fatiguing protocol as well as the significant correlation ($r = 0.451$; $p=0.05$) between the relative decline in MVC torque and the relative loss in voluntary activation in the Doix et al. (2013) study. Examining the Kawamoto et al. study (2014) further strengthens these theories as non-dominant contralateral KEs were tested following dominant knee extension fatigue under two conditions: 4 sets to task failure of either i) 40% (light) or ii) 70% (heavy) of MVC; where failure was defined as the time it would take the participant to be unable to consistently maintain the prescribed force output following two warnings from the researchers. Crossover fatigue was evident as there was a decrease in MVC, TTE (defined as time to failure), and F100 (the maximal force produced within the first 100 milliseconds of the MVC) of the non-exercised contralateral KEs. Additionally, in all cases, greater deficits were observed for the heavy condition (MVC decrease of 7.1%, TTE decrease of 8%, and F100 decrease of 34.6%) than the light condition (MVC decrease of 4.1%, TTE decrease of 2%, and F100 decrease of 23.7%).

Upper Body:

The muscle group predominately investigated in crossover fatigue studies of the upper body has been the elbow flexors (EFs) and, while similarly to the lower body studies, performance deficits in MVC force, hand grip strength (GS), TTE, and voluntary activation have been observed in the non-exercised contralateral muscle groups following various fatiguing protocols (Humphry et al., 2004; Todd et al., 2003; Triscott et al., 2008). The effects observed when investigating cross-over fatigue within the upper limb tend to be

small, if present at all. Studies that have observed effects, such as the Todd et al. (2003) study, have reported no change in voluntary force production when two, one minute sets of continuous EF MVCs were performed with, either i) one minute of rest between or ii) one minute MVCs with the contralateral EF were performed. However, voluntary activation monitored with transcranial magnetic stimulation (TMS) was 2.9% lower in the second contraction (absolute change, $p<0.05$) despite no alteration in voluntary force production or the EMG responses to TMS. Further adding to the discrepancy between cross-over fatigue effects in the upper body, Humphry et al. (Humphry et al., 2004) similarly observed no changes in MVC, motor evoked potentials (MEPs), simple movement times, or simple reaction times for the non-exercised arm following EF with a 3.5 kg dumbbell at a constant pace until failure. There was, however, a significant ($p<0.05$) decrease in GS for the exercised arm (91.6% of pre-exercise levels) as well as the non-exercised, contralateral, arm (95.4% of pre-exercise levels) observed during the 0-12 minute time period following the exercise protocol. Further, the non-exercised arm GS continued to decrease to 88.0% of pre-exercise levels ($p<0.05$) whereas the difference for the exercised arm became insignificant ($p>0.05$). Similarly, Triscott et al. (Triscott et al., 2008) observed no change in EF MVC force or dexterity task performance, (Roylan 9-hole pegboard test: Smith & Nephew Homecraft Ltd., Nottinghamshire, UK) of the contralateral limb while observing significant changes in MEP and MEP recovery. The variability of observing cross-over fatigue effects within the upper limb was further compounded in this study as the recovery of MEP varied depending on the training status of participants; occurring earlier in endurance athletes (20 min) than in control participants (30 min) and

resistance athletes (> 30 min). Unlike the previously mentioned studies, Post et al. (Post, Bayrak, Kernell, & Zijdewind, 2008) observed a decrease in MVC force when examining the first dorsal interosseus (FDI) muscle during index finger abduction and, contrary to previous studies, the reduction in MVC force was observed whether a maximal or submaximal fatiguing protocol was utilized. Interestingly, this study also examined the effects on recovery for 20 minutes and performance deficits were observed in the contralateral FDI for up to 5 minutes.

Summary

A great deal of inconsistency currently exists within the cross-over fatigue literature. Experimental factors such as muscle group selection, fatigue protocols, and recovery analysis as well as participant factors such as sex and training status contribute to the variability in observed cross-over fatigue effects. The current literature suggests that cross-over fatigue is more prevalent in the lower body than the upper body, higher intensity fatiguing protocols are more likely to elicit cross-over effects with the fatigue intensity being directly related to degree of cross-over effects, and that participant training status can alter the global responses.

NLMF – Heterologous Muscle Groups

Non-local muscle fatigue effects have also been observed in non-exercised heterologous muscle groups. Similar to cross-over fatigue studies, KE and EF muscle groups have been primarily examined and expanding the investigations to include heterologous muscle groups has allowed for investigation of muscle groups, which are both contralateral and ipsilateral to the fatigued muscle group (Aboodarda, Copithorne, Power,

Drinkwater, & Behm, 2014; Grant, Robergs, Baird, & Baker, 2014; Halperin, Aboodarda, & Behm, 2014; Rasmussen et al., 2010).

To date, evidence of global NLMF has been observed primarily when investigating lower body muscle groups following upper body fatigue (Bogdanis, Nevill, & Lakomy, 1994; Johnson, Mills, Brown, & Sharpe, 2014; Kennedy, Hug, Sveistrup, & Guével, 2013; Nordsborg et al., 2003). These studies have observed effects on variables such as peak power (PP), mean power output (MPO), and TTE (Bangsbo, Madsen, Kiens, & Richter, 1996; Bogdanis et al., 1994; Nordsborg et al., 2003), as well as MVC, EMG, and performance in isometric (Aboodarda, Copithorne, et al. 2015; Ciccone, Brown, Coburn, & Galpin, 2014; Grant et al., 2014; Kennedy et al., 2013) and dynamic tasks, such as isoinertial KE (Kawamoto et al., 2014). Similarly, investigations of upper body muscle groups following lower body fatigue have observed effects on variables such as MVC, VA, and dynamic performance tasks (Aboodarda, Šambaher, Millet, & Behm, 2017; Othman et al., 2016; Halperin, Aboodarda, et al., 2014; Rasmussen et al., 2010; Sidhu et al., 2014). Conversely, similar studies have reported an absence of any observed global NLMF effects (Decorte, Lafaix, Millet, Wuyam, & Verges, 2012; Millet, Martin, Lattier, & Ballay, 2003; Place, Lepers, Deley, & Millet, 2004; Ross, Goodall, Stevens, & Harris, 2010; Ross, Middleton, Shave, George, & Nowicky, 2007), while others have reported finding both a presence and an absence of NLMF effects (Bouhlel, Chelly, Gmada, Tabka, & Shephard, 2010; Halperin, Copithorne, & Behm, 2014) depending on particular considerations (e.g. muscle groups selected, age, sex, training status, fatigue protocol).

The conflicts within the current global NLMF literature highlight evidence which suggests two key factors, which should be considered when investigating global NLMF effects; i) variables such as fatigue resistance and endurance appear to be more susceptible to NLMF effects as opposed to single MVC strength evaluations and ii) NLMF effects appear to be more likely to be observed following lower body testing subsequent to upper body fatigue as opposed to the inverse.

i) Variables such as fatigue resistance and endurance appear to be more susceptible to NLMF effects as opposed to single (discrete) MVC strength, evaluations is perhaps best exemplified by the use of two protocols, the Bogdanis (Bogdanis et al., 1994) and the Halperin (Halperin, Aboodarda, et al., 2014) protocols.

Initially utilized in the Bogdanis et al. (1994) study, two, 30 second maximal effort lower body cycling sprints (Wingates) which were interspersed by 6 minutes resulted in a decrease of PP by 5 and 10% ($p<0.01$) in the first and second Wingates, respectively, following 5 minutes of upper arm crank exercise (4.5 min at 80 rev $min.^{1}$ and 30 s all-out cranking at the end of the protocol) against 30% of the individual's arm sprint mean power output (determined on a separate day). Later utilized in the Grant et al. (2014) study, the Bogdanis Wingate Protocol resulted in a decrease of PP by 1 and 5% ($p<0.05$) in the first and second Wingates, respectively, following 3 × 10 repetitions of biceps curls and one set to failure with 70% of 1RM (1 rep maximum: the maximal load that can be successfully completed once) interspersed by 30 s. Interestingly, though both studies saw a decrease in both Wingate tests (and by the same magnitude of 5% for the first), recovery was

considerably different between the two studies. In fact, the recovery effects were opposites as the Bogdanis et al. (1994) study saw a further decrease of performance (from 5 to 10%) between Wingates whereas the Grant et al. (2014) study saw an increase, or recovery, of performance (from 5 to 1%) between Wingates. These results would suggest that despite the Wingate testing protocol, Bogdanis Wingate Protocol, and magnitude of the initial NLMF effect all being similar, (decreased PP by 5%), the observed performance on the second Wingate test was inversely related as a cyclical fatiguing protocol resulted in further decreases in performance and a dynamic exercise fatiguing protocol resulted in the participant's recovering.

Initially utilized in the Halperin, Aboodarda et al. (2014) study, participants performed a MVC of a non-working muscle group (EF in this case) at fifteen different time points: pre-test, immediately post-test, 2 minutes post-test, and then 12 more MVCs with a work to rest ratio of 5/10s, respectively; the Halperin protocol. In the Halperin, et al. (2014) study, KE were fatigued using five sets of submaximal knee extensions to failure (50% of single leg MVC) with one minute of rest between sets and the Halperin protocol was used on unilateral EF. There was no statistically significant difference between pre- and post-test EF MVC. However, during the 12 repeated MVC protocol, the last 5 repetitions were found to be significantly different, [#8 ($p = 0.011$; ES = 0.67; 4.7%), #9 ($p = 0.005$; ES = 0.8; 6.2%), #10 ($p = 0.049$; ES = 0.61; 4.4%), #11 ($p = 0.014$; ES = 0.25; 4.6%) and #12 ($p = 0.029$; ES = 0.57; 5.2%)]. Later utilized in the Halperin, Copithorne, et al. (2014) study on two separate days, the Halperin protocol was used to test

dominant KEs, which were contralateral to non-dominant KE (day 1) or non-dominant EF (day 2). The non-dominant KE or EF were fatigued using two, 100s continuous MVCs. KE MVC was decreased by between 4 and 9% for all MVCs post EF fatiguing protocol ($p \leq 0.05$) and 6-11% post KE fatiguing protocol. Indicating that there was a greater degree of crossover fatigue than there was NLMF as both the lower and upper limits of the range decreases were higher for the contralateral homologous KE muscle group vs the contralateral heterologous EF muscle group.

Comparing the results of the Bogdanis and Halperin protocols, as well as numerous other NLMF studies that utilize a more fatigue or endurance-based testing protocol (Aboodarda et al., 2017; Bangsbo et al., 1996; Nordsborg et al., 2003), to studies which only utilize a single MVC or short and discrete contraction (Decorte et al., 2012; Millet et al., 2003; Ross et al., 2010) provides strong evidence to suggest that selecting a fatigue or endurance-based testing protocol is a key factor, which should be considered when investigating global NLMF effects.

ii) There is an abundance of evidence for a greater likelihood to observe global NLMF effects following lower body testing subsequent to upper body fatigue (Bangsbo et al., 1996; Bogdanis et al., 1994; Ciccone et al., 2014; Grant et al., 2014; Johnson et al., 2014; Kennedy et al., 2013; Nordsborg et al., 2003) as opposed to the inverse (Halperin, Aboodarda, et al., 2014; Rasmussen et al., 2010; Sidhu et al., 2014). However, there are two studies in particular which directly compared the two

scenarios, the Bouhlel et al. (2010) and the Halperin, Copithorne, et al. (2014) studies.

Seeking to examine whether peak anaerobic power of the legs and arms of athletes could be tested in a single session, Bouhlel et al. (2010) was also directly comparing susceptibility to global NLMF of upper vs lower body muscle groups. Six sets of 7 seconds of 'all-out' cycling interspersed by 5 minutes were completed with either the upper or lower body. This protocol was then repeated for the muscle group opposite to the fatigued muscle group and both scenarios were examined. While it was concluded that "a prior sequence of the force–velocity test with either a limited (arm) or a large muscle volume (leg) does not alter the subsequent peak anaerobic power (Wpeak) of trained throwers when using another muscle group", peak power of the lower body was reduced following upper body cycling compared to the converse.

The Halperin, Copithorne et al. (2014) study observed the lower body to be more susceptible to NLMF effects than the upper body as the Halperin protocol resulted in a reduction of non-dominant KE force, VA, and EMG from the first post-intervention MVC to the last ($P \leq 0.05$; effect size (ES) = 0.91–1.15; 2%–8%) following fatigue of the dominant KE and EF. However, non-dominant EF force production, EMG activity, and VA was not affected by the fatiguing tasks performed with either the contralateral EF or KE. Observing NLMF effects in the KE following both contralateral KE and EF fatigue but not in the EF following

contralateral KE may suggest that the lower body is more susceptible NLMF effects regardless of the muscle group being fatigued.

Considering the vast inconsistency in the presentation of NLMF effects, it is still inconclusive if muscle groups of the upper or lower body, as well as muscle groups ipsilateral or contralateral to the working muscle group, are more susceptible to NLMF effects. To date, most studies have a singular independent variable of muscle group fatigued and dependent variable of muscle group tested while few have multiple independent variables. More studies which directly compare NLMF effects following both upper and lower body fatigue such as the Bouhlel et al. (2010) and Halperin et al. (2014) studies are necessary to strengthen our understanding this phenomenon.

Summary

Though a great deal of inconsistency currently exists within the global NLMF literature, the current literature does suggest that global NLMF is more predominant when variables such as fatigue resistance and endurance are examined in the lower body following upper body fatigue. However, more research which directly evaluates the significance of variables such as upper vs lower body muscle groups evaluated, contralateral vs ipsilateral, as well as proximity to the working muscle group is needed in order to properly quantify global NLMF effects.

Mechanisms for NLMF

The exact mechanisms of NLMF and their degree of contribution is not unequivocally known. Thus, a systemic approach which considers neurological,

biochemical, biomechanical, and psychological factors must be employed when investigating possible contributing mechanisms.

Neurological

Investigations of the neurological components of NLMF utilize the interpretation of muscle EMG recordings following combinations of various evoked stimulations along specific locations to isolate and determine the degree of involvement for each segment. While TMS is utilized to elicit a MEP of the entire neural and muscle action potential (AP) pathways, from the motor cortex, corticospinal tract (CST), and peripheral nerve, transmastoid and peripheral nerve stimulations provide cervico-medullary motor evoked potentials (CMEPs) and compound muscle action potentials (M-waves), which allow for more specific interpretation of supraspinal and peripheral involvement, respectively. (Gandevia, 2001; McNeil, Butler, Taylor, & Gandevia, 2013; McNeil, Giesebrecht, Gandevia, & Taylor, 2011; Taylor & Gandevia, 2004; Taylor, Butler, Allen, & Gandevia, 1996)

To date, studies have found both inhibitory (Aboodarda et al., 2015; Bonato et al., 1996; Takahashi et al., 2011; Takahashi et al., 2009) and excitatory (Aboodarda, Šambaher, & Behm, 2016; Brasil-Neto, Araújo, & Carneiro, 1999; Hess, Mills, & Murray, 1986; Samii, Caños, Ikoma, Wassermann, & Hallett, 1997) responses along the AP pathway to non-exercised muscle groups following fatigue. Examining the effect of spinal and peripheral, thoracic motor evoked potentials (TMEPs) and femoral nerve M-waves, respectively, stimulations along with MVCs and EMG of the non-exercised, non-dominant KE following fatigue of the EF (both bilateral as well as ipsilateral – dominant), the

Aboodarda et. al (2015) study was able to postulate that supraspinal motor output must have been reduced. Investigation of the specific changes at the supraspinal level of the CST were observed by Takahashi et al. (2009, 2011) when they examined short interval intracortical inhibition (SICI), which is an assessment of excitability of intracortical inhibitory neural tracks, during testing of 3 muscles (FDI, biceps brachii (BB), and quadriceps femoris) following three bouts of leg press (5 minutes at 50% of MVC). During the testing of FDI and BB, SICI was in such a way that matched the time course of MEP decreases that allowed them to postulate that an increased tonic level of inter-hemispheric or transcallosal inhibition could be a contributing factor. Furthermore, also at the supraspinal level, facilitation of the CST measured during examination of non-exercised muscles groups has been attributed to the spread of excitatory signals between the two cortical hemispheres (Carroll, Herbert, Munn, Lee, & Gandevia, 2006; Carson et al., 2004; Hortobágyi, Taylor, Petersen, Russell, & Gandevia, 2003). It is still inconclusive whether NLMF is induced by excitatory or inhibitory mechanisms at the supraspinal or spinal level of the CST. Additionally, there is extensive evidence showing that MEP increases after 2 min to 5 hours fatiguing isometric and cycling tasks (Aboodarda, Fan, Coates, & Millet, 2019; Aboodarda et al., 2020; Aboodarda, Zhang, Sharara, Cline, & Millet, 2019). Therefore, there is no conclusive relationship between TMS responses and exercise performance.

Biochemical

Investigations of the biochemical components of NLMF have measured the metabolic environments of specific muscle groups (Amann et al., 2013; Halperin,

Aboodarda, et al., 2014; Kennedy, Fitzpatrick, Gandevia, & Taylor, 2015; Martin & Rattey, 2007) as well as the cerebrum (Nybo & Rasmussen, 2007; Rasmussen et al., 2010; Shibuya, Kuboyama, & Yamada, 2016).

Observing an increase in blood lactate levels of the non-working contralateral limb, the Halperin et. al (2014) study suggested that increased lactate from the working muscle is distributed throughout the body and thus could affect the metabolic environment of non-working muscle groups globally by increasing the pH, adversely affecting enzymatic activity and myofilament functioning. Additionally, alterations in the metabolic environment of the working muscle have been shown to activate group III and IV muscle afferents (Amann, 2011, 2012; Amann et al., 2013) which, through a feedback loop, could inhibit the CNS and thus affect performance globally (Sidhu et al., 2014). However, when Kennedy et. al (2015) utilized blood occlusion to determine the degree to which group III and IV afferents contribute to NLMF, no differences were found. This finding led them to conclude that group III and IV afferents do not in fact contribute to NLMF effects.

At the supraspinal level of the CST, recent investigations suggest that changes in cerebral blood flow and oxygenation could also be a contributing factor when observing NLMF effects (Nybo & Rasmussen, 2007; Rasmussen et al., 2010; Shibuya et al., 2016). The Nybo & Rasmussen (2007) study demonstrated that a decrease in cerebral oxygenation occurring during intense exercise could also lead to subsequent NLMF. On the other hand, the increased ipsilateral cortical blood flow would illustrate the interconnectivity of the working and contralateral muscle motor areas. Shibuya et al. (2016) observed a significant ($p < 0.05$) increase in oxygenation values of the cortical hemisphere ipsilateral to the

working muscle group. Considering the fact that increased neural activity in a given cortical region increases local blood flow (Fox & Raichle, 1986; Fox, Raichle, Mintun, & Dence, 1988), we are able to infer that the ipsilateral hemisphere could be contributing to the observance of NLMF effects. Of note is that their study used 30–60% of MVC to induce fatigue while the previously mentioned studies had used 100% MVC, highlighting biochemical factors are to be considered regarding NLMF research and further investigation regarding their contribution is warranted.

Biomechanical

Investigations of the biomechanical components of NLMF have highlighted how non-working muscle groups can contribute to the performance of working muscle groups by means of factors such as stabilization and mechanical energy transference and thus have the potential to influence NLMF effects (Baker & Davies, 2009; Bogdanis et al., 1994; Danneels et al., 2001; Grant et al., 2014). For example, a 20% reduction of power production during 30 seconds of lower body cycling was observed when the lower body cycling was performed without gripping the handlebar for stability in the Baker & Davies (2009) study. Similarly, high levels of activation in the muscles groups of the trunk (abdominal and lower back) have been reported during upper (Tarnanen et al., 2008) and lower body (Danneels et al., 2001) movements due to the trunk muscles acting in a stabilizing role to allow for efficient proximal to distal transfer of mechanical energy (Kibler, Press, & Sciascia, 2006).

Psychological

Maintaining contractions to the point of fatigue is uncomfortable, sometimes painful, and necessitates focus and concentration (cognitive demand) to maintain the force and activation. Mentally fatiguing tasks have been shown to impede subsequent physical performance especially with repeated or continuous activities (Marcora, Staiano, & Manning, 2009; Pageaux, Lepers, Dietz, & Marcora, 2014; Pageaux, Marcora, & Lepers, 2013). This mental energy deficit is a global experience as performance deficits are demonstrated in non-exercised muscles following fatigue of a contralateral muscle that requires sustained focus/concentration to maintain the forces (Israel Halperin, Chapman, & Behm, 2015). Mentally fatiguing actions lead individuals to perceive a subsequent task to be more demanding or stressful, resulting in an earlier cessation of the activity (Pageaux et al., 2013, Pageaux et al., 2014, Marcora et al., 2009). Unlike many prior definitions, Enoka and Duchateau (Enoka & Duchateau, 2016) highlight the psychological role of perception in their definition of fatigue. Their concept of fatigue emphasizes two major attributes: (1) performance fatigability – the decline in an objective measure of performance over a discrete period of time; and (2) perceived fatigability changes in the sensations that regulate the integrity of the performer. They suggest that fatigue is a disabling system and perceived fatigability derives from the rate of change in sensations that regulate performance integrity based on the maintenance of homeostasis and the psychological state. Inherently, it would be expected that the role of the psychological state (perception) would not be limited to just an exercised muscle but would have global repercussions. Whereas, higher perceived exertion of non-exercised, knee extensors at

exercise onset was reported after completing a contralateral fatiguing protocol by Amann et al. (Amann et al., 2013) ; Elmer et al. (Elmer et al., 2013) reported only marginal, non-significant increases in perceived exertion with no significant NLMF effect. Although Pageaux et al. (Pageaux et al., 2013) and Rozand et al. (Rozand, Pageaux, Marcora, Papaxanthis, & Lepers, 2014) found that single knee extensors MVCs were unaltered by a previous mentally fatiguing task, Pageaux et al. (2013) found that a subsequent knee extensors submaximal isometric time to exhaustion test was decreased after the mentally fatiguing task. Pageaux's results substantiate the proposition of larger effects with time to exhaustion tests compared to single, discrete MVCs.

Summary

Neurological, biochemical, and biomechanical mechanisms are likely all contributing to observed NLMF effects to varying degrees during any particular circumstance. To date, the majority of mechanism isolation has been conducted with the objective of determining at what level of the CST a change may have occurred that explains the observation of NLMF effects. Each of these mechanisms offer a unique perspective to potential explanations and as we contrinue to expand our understanding of them, our insight into NLMF continues to grow.

Critical Evaluation of Methodologies

As outlined above, there is currently a great deal of variability within NLMF literature and differing choices regarding experimental methodologies is often stated as an explanation. Factors such as what type of fatiguing and testing protocols are used (Arora et al., 2015; Humphry et al., 2004), which muscles are selected for testing, as well as participant specific

factors such as age (Watanabe, Kanehisa, & Yoshitake, 2017), sex (Martin & Rattey, 2007), and training status (Triscott et al., 2008) have been cited as possible contributing factors to the presence or absence of NLMF effects.

Fatigue Protocol Factors

Isometric

Based on the current literature, it appears that NLMF effects are likely to be observed when an isometric protocol has been used to fatigue a lower body muscle group (Doix et al., 2013; Halperin, Aboodarda, et al., 2014; Martin & Rattey, 2007) as no studies which have utilized this method have reported an absence of NLMF effects. However, when a muscle groups of the upper body were fatigued using an isometric fatiguing protocols, studies have reported both a presence (Post et al., 2008; Todd et al., 2003) and absence of NLMF effects (Arora et al., 2015; Kennedy et al., 2015; Paillard, Chaubet, Maitre, Dumitrescu, & Borel, 2010; Zijdewind, Zwarts, & Kernell, 1998).

Dynamic

Inversely, when a dynamic protocol has been used to fatigue an upper body muscle group, to date, both studies have reported NLMF effects (Humphry et al., 2004; Triscott et al., 2008). However, dynamic fatiguing protocols used to fatigue muscle groups of the lower body have reported both a presence (Amann et al., 2013; Grabiner & Owings, 1999; Kawamoto et al., 2014) and absence (Regueme, Barthèlemy, & Nicol, 2007) of NLMF effects.

Cyclical

Lastly, cyclical fatiguing protocols, despite having been the least utilized method of fatiguing protocol within current NLMF literature, have provided some of the most consistent results. NLMF effects have been observed in studies which have utilized bilateral upper body cycling fatiguing protocols (Baker & Davies, 2009; Bogdanis et al., 1994; Bouhlel et al., 2010) while studies which have utilized unilateral and bilateral lower body cycling fatiguing protocols have reported an absence of NLMF effects (Bouhlel et al., 2010; Elmer, Amann, McDaniel, Martin, & Martin, 2013). Interestingly, the Boulhel et. al (2010) study directly compared the effects of both scenarios creating a strong piece of evidence to suggest that the lower body is more susceptible to NLMF effects than the lower body is. To date, unilateral cycling of the lower body has not reported any crossover or NLMF effects and unilateral cycling of the upper body has not been investigated for crossover or NLMF effects.

Summary

Within the current literature, there appears to be the highest degree of consistency, and therefore opportunity to analyze NLMF effects, when investigations utilize isometric fatigue of the lower body and dynamic or cyclical fatigue of the upper body.

Participant Factors

Age

Directly comparing two age groups, the Watanabe et al. (2017) study reported crossover fatigue effects on the right-hand following left-hand index finger abduction in both groups of adult men; young (21.8 ± 2.4 years) and old (69.9 ± 5.3 years). However,

EMG activity of the right hand in the old adult age group was 44.1% larger compared with young adults (ES = 0.07, $P < 0.05$). They postulated that the observed age differences were due to functional changes in the corpus callosum, resulting in decreases in interhemispheric inhibition.

Though not comparing two age groups directly, Ben Othman et al. (2016) conducted possibly the only known study to investigate NLMF effects in youth. Forty-two young males (aged 10 - 13 years old) were assigned to one of three different groups based on method of unilateral KE fatiguing protocol: isometric, isokinetic, or control. The results led the researchers to conclude that youth may be more susceptible to NLMF effects as multiple statistically significant crossover and NLMF effects were observed with neural and metabolic mechanisms highlighted as possible explanations for the differences.

Sex

The contribution of sex differences to NLMF effects has also been directly compared. In the Martin and Rattey (2007) study, both groups (male and female) displayed crossover fatigue effects which presented as a decrease in the contralateral KE MVC following a 100s unilateral isometric MVC. However, the crossover effects were greater in males (13%) vs females (8%). Additionally, the decrease in central activation by 9% in males and only 3% in females is a possible explanation for why this difference between groups was observed. The concept of females being more resistant to NLMF effects is further strengthened by evidence which suggests they are more resistant to fatigue effects in working muscle groups as well and not only non-working muscle groups (Doix et al., 2013).

Training Status

The effect of participant training status on NLMF effects has been scarcely investigated directly, with only a single study comparing trained vs. untrained populations. The trained group included two specific training backgrounds, endurance and resistance trained athletes, while the untrained (control) group consisted of non-athletic moderately active individuals. Of note is that the study contained both male and female participants. However, only 3 of them were females (2 athlete-endurance group, 1 untrained). EF crossover fatigue was investigated using a unilateral TTE EF fatiguing protocol. MEPs of all three groups were depressed in the contralateral non-working EF. However, no difference in the depression was found between the groups. MEP recovery however did differ between all three groups with the athlete-endurance group recovering fastest (20 minutes), followed by the control group (30 minutes), and last was the athlete-resistance group (43 minutes). Additionally, TTE of the contralateral non-working EF was reduced significantly for control and athlete-endurance groups while there was no change for the athlete-endurance group. These findings, though limited, suggest that endurance trained athletes may be more resistant to NLMF effects than other training status populations.

Summary

Based on very limited research to date, when considering participant factors such as age, sex, and training status, it would appear that young and old male populations who are not athletes who are resistance trained are more likely to be susceptible to NLMF effects. However, given the limited number of investigations which directly consider these factors,

more investigations are needed in order to obtain a more exact understanding of their contributions.

Conclusion

Despite the profusion of inconsistency within current NLMF literature, several trends are starting to become prevalent. Key factors and trends are being identified and considering the investigations completed to date we can gather important considerations regarding the most appropriate experimental designs for NLMF research. Muscle groups selections should be made with the fatiguing protocol in mind as there appears to be the highest degree of consistency with NLMF effects when investigations utilize isometric fatigue of the lower body and dynamic or cyclical fatigue of the upper body. Regardless of the type of exercise used to induce fatigue in a working muscle group, the effort from participants should be maximal and sustained and the effects measured should be monitored beyond immediately following the fatigue intervention. As neurological, biochemical, and biomechanical mechanisms have been reported as contributing factors for observed NLMF effects, all factors should continue to be investigated. Particular to the investigation of neurological components, a comprehensive approach which allows the analysis to separate supraspinal, spinal, and peripheral involvement should be employed. Additionally, confounding participant factors such as age, sex, and training status have been investigated and to date, young and old male populations who are not athletes who are resistance trained are more likely to be susceptible to NLMF effects.

By quantifying, or even simply being aware of, an isolated working muscle group's indirect, and possibly undesired, contributions to the performance of a non-working muscle

group, training and rehabilitation professionals will be able to design and implement more effective programs that offer improved development or recovery options.

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RESEARCH OBJECTIVES

1. To determine if unilateral fatigue of dominant leg knee extensors has an effect on the ipsilateral and contralateral elbow flexors and plantar flexors.

HYPOTHESIS

The researchers hypothesize that unilateral dominant knee extension fatigue will induce non-local muscle fatigue effects in both the ipsilateral and contralateral elbow and plantar flexors. It is also hypothesized that the ipsilateral plantar flexors will be more susceptible to the non-local effects as they share more of the same neurological pathway than the other muscle groups.

RESEARCH MANUSCRIPT

The effects of unilateral dominant knee extensors fatigue on non-exercised contralateral and ipsilateral elbow and plantar flexors

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Abstract

The present study investigated the effects of exercise-induced knee extensor (KE) fatigue on force output and electromyography (EMG) activity of both, the ipsilateral and contralateral, non-exercised elbow (EF) and plantar flexors (PF). Twelve participants (six females, six males) attended six randomized testing sessions where either PF or EF which were ipsilateral or contralateral to dominant KE were tested following a fatigue (2x100s maximal voluntary contractions [MVC] with dominant KE) or control (resting for 150 seconds) condition. MVCs of the tested muscle group were completed prior to and immediately post-intervention. Additionally, following 1 minute of rest, 12 MVCs at a work-to-rest ratio of 5:10s then completed. Condition x time interaction showed that immediately post-fatigue, ipsilateral EF MVC force was significantly lower (6.6%, $p=0.04$, $d=0.18$) than pre-fatigue with no significant time-related changes in the contralateral or control conditions. Main effect for condition demonstrated that ipsilateral EF MVC force was significantly lower (8.7%, $p=0.03$, $d=1.04$) than control while the contralateral condition was not significantly different than the control or ipsilateral conditions. EF MVC force during the repeated MVC protocol was significantly or near significantly lower ($p<0.01$) for all 12 repetitions during the ipsilateral condition when compared to the respective repetitions of the control and contralateral conditions. Additionally, EF ipsilateral repetitions 2-13 were significantly lower than their respective PF ipsilateral repetitions and also significantly lower than the PF control and contralateral repetitions 3-13. There were no significant differences in PF force or EMG or EF EMG immediately post-test or during the repeated MVC protocol. The results of this study suggest that NLMF

effects are muscle specific and highlight that prior lower body fatigue could hinder subsequent upper body performance and thus is an important consideration for rehabilitation, training, and performance programs.

Key Words: quadriceps; plantar flexors; elbow flexors; crossover fatigue; force; electromyography;

Introduction

Central fatigue is defined as a decrease in the ability of the central nervous system (CNS); the brain and/or spinal cord, to voluntarily drive muscle activation (Gandevia, 2001). This can be further classified as supraspinal fatigue when the impairment in the ability to produce force originates at the level of the brainstem or higher (Gandevia, 2001). Spinal level-related fatigue would be ascribed to inhibition in the ability to fully or consistently maintain activation (depolarization) and discharge frequency of the spinal motor neurons (Gandevia, 2001). Peripheral fatigue has occurred if the reduction in the muscle's ability to generate force is impaired at a location, which is distal to the spinal cord (Arora et al., 2015; Kirkendall, 1990; Ross et al., 2007).

Extensive research on neuromuscular fatigue has investigated the changes occurring in, and along the neurological pathway to the working muscle (Bigland-Ritchie, Jones, & Woods, 1979; Komi & Tesch, 1979; Stephens & Taylor, 1972) but a more recent field of research has explored how localized fatigue can induce fatigue in muscles that have not been exercised (Halperin, Aboodarda, et al., 2014; Halperin, David Copithorne, et al., 2014; Kennedy et al., 2013). These global effects have been classified as non-local muscle fatigue (Halperin et al., 2015). For example, non-exercised contralateral knee extensors (KEs) have exhibited decreases in the rate of force development (F100: the force generated in the initial 100ms of a maximal voluntary contraction (MVC)) of 23.7% and 34.6% following light (50% of MVC) and moderate (70% of MVC) fatiguing protocols of the dominant KEs, respectively (Kawamoto et al., 2014). Additionally, Kennedy et al. (2013) demonstrated that sustained bilateral isometric handgrip contractions (100% and 30% of

MVC) caused a decrease in unilateral (right leg) plantar flexor (PF) force (77-92.4% of pre-fatigue MVC, for 100% and 30%, respectively) and voluntary activation (VA) (84.3-97.7% of pre-fatigue VA for 100% and 30%, respectively), indicating that NLMF effects were not limited to homologous muscle groups. Furthermore, Halperin, Copithorne, & Behm (2014) suggested that NLMF effects are muscle specific. They showed that non-dominant KE force, electromyography (EMG), and VA all decreased ($p \leq 0.05$; effect size (ES) = 0.91–1.15; 2%–8%) regardless of whether the dominant KEs or elbow flexors (EFs) were fatigued, whereas no differences were found for the non-dominant EF regardless of whether dominant KEs or EFs were fatigued ($p \geq 0.33$; $ES \leq 0.2$; ≤3.0%), suggesting that the KE are susceptible but the EF were less susceptible to NLMF effects.

However, a similar investigation of EF observed NLMF effects in EF following KE fatigue (Halperin, Aboodarda, et al., 2014). In fact, substantial conflict currently exists within NLMF literature as multiple studies have reported varying degrees as well as a total absence of NLMF effects (Decorte, Lafaix, Millet, Wuyam, & Verges, 2012; Millet et al., 2003; Ross et al., 2007). Despite this, the current literature suggests that global NLMF is more predominant when certain variables are considered. Experimental and participant factors have been shown to influence NLMF effects.

To date, evidence of global NLMF has been observed primarily when investigating lower body muscle groups following upper body fatigue (Bogdanis et al., 1994; Johnson et al., 2014; Kennedy et al., 2013; Nordsborg et al., 2003), which according to Halperin et al. (2015) may be related to differences in muscle volume, ability to fully activate, and reflex connectivity. Further, employing extended and maximal fatiguing and testing protocols has also led to

greater incidences and degree of NLMF effects (Kawamoto et al., 2014; Martin & Rattey, 2007). Hence, variables, such as fatigue resistance and endurance appear to be more susceptible to NLMF effects as opposed to single MVC strength evaluations (Bogdanis et al., 1994; Halperin, Aboodarda, et al., 2014). Additionally, participant factors such as age (Watanabe et al., 2017), sex (Martin & Rattey, 2007), and training status (Triscott et al., 2008) have reported that young and old male populations who are not athletes but are resistance trained are more likely to be susceptible to NLMF effects, though the sample size for investigation of these variables is very limited to date.

As such, the goal of the present study was to further investigate muscle specificity and quantify NLMF effects by directly comparing the effects of lower body muscle group (KE) fatigue on heterologous ipsilateral and contralateral muscle groups of the upper (EF) and lower (PF) body while utilizing maximal and repeated contraction fatiguing and testing protocols. Secondary to this, factors such as sex and training status were evaluated to strengthen our understanding of their contribution to NLMF effects. It was hypothesized that non-working muscle groups (PF and EF), which were ipsilateral to the working muscle group (KE) would have greater NLMF effects than non-working muscle groups which were contralateral to the working muscle group and that based on the prior literature reporting greater lower limb NLMF susceptibility (Halperin, Copithorne, et al., 2014) that ipsilateral PF would have greater NLMF than ipsilateral EF.

Methods

Participants

Based on prior repeated measures (within) NLMF force data (Halperin et al. 2014, Kawamoto et al. 2015, Doix et al. 2013, Bogdanis et al. 1994), an "a priori" statistical power analysis (G*Power: Dusseldorf Germany) indicated that 4-8 participants would be needed to achieve an alpha of 0.05 with a power of 0.8. Initially, 8 males and 7 females were recruited as participants, but 2 males and 1 female did not complete all data collection trials. Hence, six male (27.3 ± 2 years, 186.0 ± 2 cm, 91 ± 4 kg) and six female (23 ± 1.6 years, 168.2 ± 6 cm, 60 ± 4 kg) participants volunteered for this study. Participants were either recreationally active (2 male, 4 female), defined as participating in self-directed exercise programs or recreational sport activities at least 3 times weekly for the past 5 years, or competitive athletes (4 males, 2 females), defined as participating in a provincial, national, or varsity competitive sports program for the past 5 years (Triscott et al., 2008). Each participant was verbally informed of the procedures and risks associated with the study and then if they agreed, they signed the consent form. Participants were requested to avoid training a day before the testing days. Ethical approval for the study was granted by the institutional Health Research Ethics Board (ICEHR No. 20170541-HK).

Experimental Design

Participants attended the laboratory on six different occasions and performed one of six conditions in a randomized fashion:

1. Fatigue - Ipsilateral PF

   Dominant KE were fatigued and the ipsilateral PF were tested

2. Control - Ipsilateral PF

   Dominant KE were rested and the ipsilateral PF were tested

3. Fatigue - Ipsilateral EF

   Dominant KE were fatigued and the ipsilateral EF were tested

4. Control - Ipsilateral EF

   Dominant KE were rested and the ipsilateral EF were tested

5. Fatigue - Contralateral PF

   Dominant KE were fatigued and the contralateral PF were tested

6. Fatigue - Contralateral EF

   Dominant KE were fatigued and the contralateral EF were tested

Participants were familiarized with the equipment and testing procedures during the first testing day. Each experimental session began with a general warm up on a cycle ergometer (Monark Inc., Sweden) for five minutes at a cadence of 70 rpm at 1 kilopond. This was followed by two, five second isometric maximal voluntary contractions (MVCs) of the dominant knee extensors (KE), identified as the leg used to kick a ball, with one minute of rest between each MVC. Depending on the randomly selected condition for the particular day, each participant then performed a specific warm-up for their appropriate PF or EF muscle group which consisted of ten isometric contractions at approximately 50% of their perceived maximum with a work to rest ratio of 2:2s.

Following the warm-ups and pre-test MVCs, participants performed either the fatiguing or control protocol. In order to limit the number of sessions required, the control sessions were only conducted on the ipsilateral side with the expectation that the response of a non-

exercised muscle would be similar regardless if ipsilateral or contralateral conditions were tested.

Intervention

For the fatiguing protocol, participants completed two, 100s MVCs with the dominant KE with 30s of rest after the first 100s and for the control protocol, participants were seated and resting for 230s, the time it took to complete the fatiguing protocol (Halperin, Aboodarda, et al., 2014). Participants were constantly motivated during the fatiguing protocol by two experimenters and reminded to keep their upper body as relaxed as possible during the protocol. Biceps brachii EMG activity was monitored throughout the protocol and with any evidence of activation, participants were reminded to relax their arms. For the control protocol, participants sat in a rested position for 230 seconds, the amount of time it took to complete the fatigue protocol.

Testing

Immediately after each protocol was completed, participants performed a unilateral isometric KE MVC with the dominant limb. An ipsilateral or contralateral EF or PF MVC were performed within 30 seconds of the intervention. One minute after the post-test EF or PF MVC, they performed a repeated MVC protocol of the same muscle group consisting of 12 MVCs at a work-to-rest ratio of 5:10 s (Israel Halperin, Saied J. Aboodarda, et al., 2014).

Dependent Variables

Maximal Voluntary Contraction (MVC) Force

To measure KE force, participants were seated on a chair with their knees flexed at 90° and their arms crossed such that each hand held the shoulder strap on the opposite side while their elbows rested on their torso. The ankle of the testing leg was inserted into a padded strap attached by a carabiner to a load cell (strain gauge: Omega Engineering Inc., LCCA 500 pounds; sensitivity = 3 mV/V, OEI, Canada) that measured the KE force during the isometric MVC (Figure 1). To measure EF force, participants were seated in the same chair. Their testing arm was supported with the elbow flexed at 90° while their other hand held the opposite shoulder strap of a harness which kept them from rising out of the seat. The testing arm was inserted into a padded strap which was connected to a similar load cell by a carabiner which measured the EF force during the isometric MVC. To measure PF force, the participants were seated with their hips, knees, and ankles flexed at 90° and their lower leg was secured in an isometric boot apparatus (Figure 2: constructed by Technical Services Division of Memorial University of Newfoundland) equipped with strain gauges (Omega Engineering Inc. LCCA 250, Don Mills, ON, Canada). All force data were sampled at a rate of 2,000 Hz using a Biopac data collection system (Biopac Systems Inc. DA 100 Holliston, MA). Force data was digitally filtered by the software with a linear phase Blackman -61 dB band-pass filter between 10-500 Hz, amplified (bi-polar differential amplifier, input impedance = 2MΩ, common mode rejection ratio > 110 dB min (50/60 Hz), gain x 1000, noise > 5 µV), and analog-to-digitally converted (12 bit). Data were recorded and analyzed with a commercially designed software program (Acq-Knowledge III, Biopac Systems Inc. Holliston, MA). The peak force and instantaneous

strength (F100: the force generated in the first 100ms) were normalized to pre-test values for each participant and all data were reported as percentage of pre-test values.

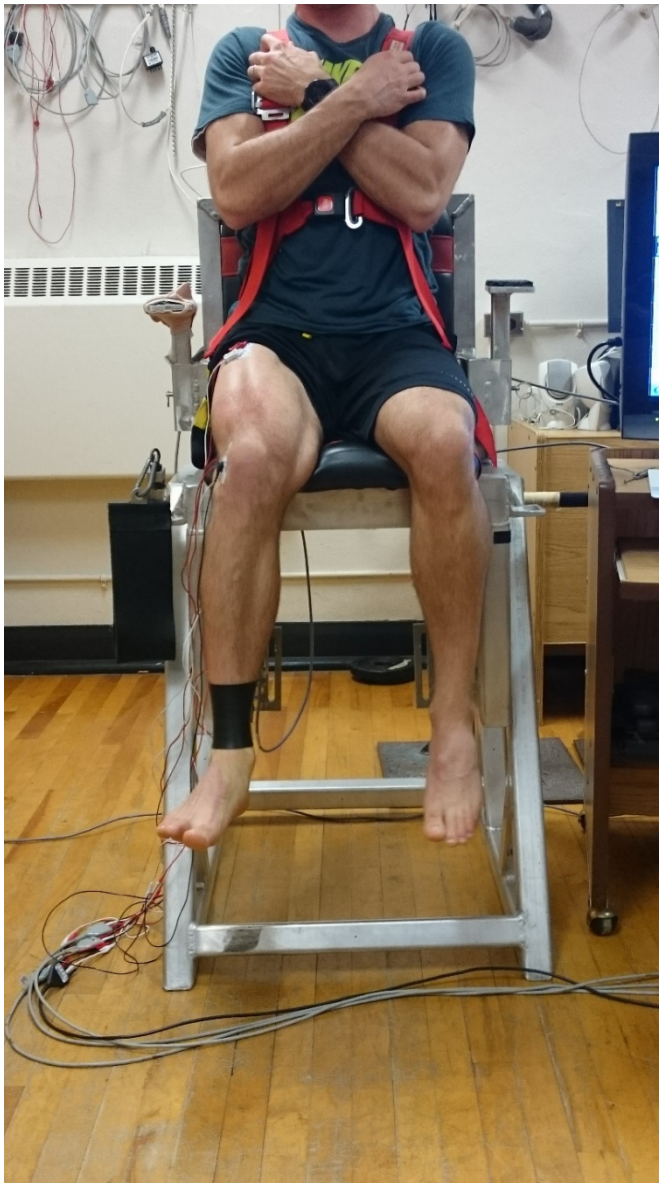

Figure 1 - Chair for the collection of EF and KE MVC force data.

Figure 2 - Boot apparatus for the collection of PF MVC data.

Electromyography (EMG)

Skin preparation included shaving hair with reusable razors and cleansing the area with isopropyl alcohol swabs. Then, self-adhesive, 3.2 cm diameter Ag/AgCl bipolar surface electrodes (Meditrace TM 130 ECG conductive adhesive electrodes) with an edge-to-edge inter-electrode spacing of 20 mm were placed on six muscles in accordance with the SENIAM recommendations (Hermens et al., 1999). EMG activity was collected from the rectus femoris (midway between the anterior superior iliac spine to the superior edge of the patella), biceps femoris (midway between ischial tuberosity and the lateral epicondyle), biceps brachii and triceps brachii (midway between the acromion process and lateral epicondyle of humerus), gastrocnemius (midway between the popliteal space and the gastrocnemius-soleus intersection), and soleus (1/3 of the distance from the gastrocnemius-soleus intersection to the calcaneus and 1 cm lateral). The reference electrode was placed over the fibular head. An inter-electrode impedance of <5 kOhms was obtained prior to recording to ensure an adequate signal-to-noise ratio. All EMG signals were recorded (Biopac System Inc., DA 100: analog-digital converter MP150WSW; Holliston, Massachusetts) with a sampling rate of 2000 Hz using a commercially designed software program (AcqKnowledge III, Biopac System Inc.). EMG activity was digitally filtered by the software with a linear phase Blackman -61 dB band-pass filter between 10-500 Hz, amplified (bi-polar differential amplifier, input impedance = 2MΩ, common mode rejection ratio > 110 dB min (50/60 Hz), gain x 1000, noise > 5 μV), and analog-to-digitally converted (12 bit). The root mean square (RMS) of the EMG signals were processed over

each 50 samples and monitored over a 1 second period encompassing the peak MVIC force (500 ms before and after the peak force).

Fatigue Index (FI)

Fatigue index was calculated by obtaining the average force values of repetitions 11 and 12 of the repeated MVC protocol and dividing this value by the average force values of repetitions 1 and 2 to give an indication of how much fatigue had occurred across all MVC repetitions of the repeated MVC protocol.

Statistical Analysis

Statistical analyses were completed using the SPSS software (Version 26.0, SPSS, Inc. Chicago, IL). The assumption of sphericity (Mauchly's) and normality (Kolmogorov-Smirnov (K-S)) were tested for all dependent variables and if a violation was noted, the corrected values for non-sphericity with Greenhouse-Geisser were reported. As no significant sex or trained state differences were detected, all participant data was integrated. To investigate the efficacy of the fatiguing protocol, the dominant KE fatigue protocol was analyzed with a 1-way repeated measures ANOVA (data was normalized by dividing the post-test into the pre-test MVCs). To investigate the effect of unilateral, dominant limb, quadriceps fatigue on ipsilateral and contralateral EF and PF discrete (single) MVC responses, a 1-way repeated measures ANOVA was used to examine normalized differences (normalized to pre-test values) in peak force, F100 and EMG during a single post-intervention MVC. A 2-way repeated measures ANOVA (3 conditions x 13 contractions) was utilized to examine the distinct or separate (EF and PF) muscle effects of unilateral quadriceps fatigue on repeated ipsilateral and contralateral EF and PF fatigue

contraction force responses. To compare relative differences in EF and PF fatigue responses to a unilateral quadriceps fatigue intervention, EF and PF MVC values during the fatigue protocol were normalized to a pre-test MVC and analyzed with a 3-way ANOVA (2 muscles x 3 conditions x 13 contractions). In the event of significant main effects or interactions, planned pairwise comparisons were made using the Bonferroni method to test for differences among mean value time points. The level of significance was set at $p < 0.05$ and all results are expressed as mean ± SD. Partial eta^2 (η_p^2) values were also provided for main effects and interactions with >0.02, >0.13, and >0.26 representing small, moderate and large magnitude differences. Effect size (d) magnitude of change were calculated for post-hoc interactions and reported as trivial (<0.2), small (0.2-0.49), medium (0.5-0.79) or large (≥0.8) effect sizes (d) (Cohen, 1992). Inter-session reliability responses were assessed with Cronbach's alpha intraclass correlation coefficient (ICC) for all muscles and tests.

Results

Reliability

ICC reliability scores were excellent for EF MVC force (0.97) and generally ranged from fair to moderate correlations for EF F100 (0.79), triceps brachii EMG (0.40), biceps brachii EMG (0.59) as well as for PF MVC force (0.73), PF F100 (0.48), soleus EMG (0.73), and gastrocnemius EMG (0.77).

Post-Quadriceps Fatigue: Knee Extensor (KE) MVC Force

After the intervention, KE MVC force decreased for all fatiguing conditions and no changes occurred under the control conditions (Table 1).

Table 1 - Mean Relative Change in Knee Extension Force Values

	PF IPSI	PF CONTROL	EF IPSI	EF CONTROL	PF CONTRA	EF CONTRA
Pre-test	59.92 ± 13.49	58.76 ± 16.63	57.67 ± 14.29	59.69 ± 15.06	57.39 ± 14.94	58.38 ± 13.26
Post-test	41.32 ± 6.56	55.15 ± 16.74	41.38 ± 10.37	58.25 ± 13.28	43.31 ± 10.22	39.88 ± 6.59
% Change	29.27*	4.738	27.31*	1.64	23.75*	30.53*
p	0.009	1.00	0.006	1.00	0.007	0.005
d	1.75	0.75	4.52	0.35	3.81	6.12

** Indicates significantly altered from pre intervention.*

Post-Quadriceps Fatigue: Elbow Flexor (EF) MVC Force and EMG

A significant condition x time interaction ($F_{(2,24)}$=3.81, p=0.04, η_p^2: 0.241) revealed a 6.6% (d=0.18) pre- to post-test ipsilateral EF MVC force decrease with no significant changes in the contralateral or control conditions (Table 2). A main effect for conditions ($F_{(2,24)}$=3.35, p=0.05, η_p^2: 0.219) demonstrated that the relative (normalized) post-fatigue ipsilateral EF MVC (93.3%±10.5) was 8.7% significantly (p=0.03, d=1.04) lower than the control (102.3%±6.7) condition. The contralateral (101.9%±12.4) condition was not significantly different than the control or ipsilateral conditions.

There were no significant EF F100, biceps brachii EMG, or triceps brachii EMG pre- to post-test differences.

There was a significant anticipatory (pacing) response between the single post-test MVC and the first repetition of the fatigue protocol. A main effect for time ($F_{(1,12)}$=4.99, p=0.045, η_p^2: 0.294) found a 6.7% (d=0.17) decrement with the first MVC of the fatigue protocol. There was a near significant condition effect (p=0.064) with 8.9% and 4.9% lower anticipatory forces with the ipsilateral (29.04±9.7 kg) and contralateral (30.3 ±11.1 kg) EF

conditions versus control (31.9±10.6 kg). There was no significant condition x time interaction effect.

Post-Quadriceps Fatigue: Plantar Flexor (PF) MVC Peak Force and EMG

A near significant ($F_{(1,12)}$=3.8, p=0.09, η_p^2: 0.031) effect for time suggested an overall post-intervention PF MVC decrease of 4.8% (d=0.13) for all conditions combined. There were no significant relative (normalized to pre-test) post-test differences between PF MVC force conditions or PF F100, soleus EMG, or gastrocnemius EMG pre- to post-test differences. There was no significant anticipatory (pacing) responses between the single post-test MVC and the first repetition of the fatigue protocol.

Table 2 - Absolute post-test single MVC force outputs.

	Ipsilateral Pre-Test	Ipsilateral Post-Test	Contralateral Pre-Test	Contralateral Post-Test	Control Pre-Test	Control Post-Test
EF	32.3±11.9	30.1±11.8*	30.1±10.7	31.3±13.3	32.04±12.7	33.01±13.9
PF	159.2±50.7	146.3±44.4	171.1±64.5	165.6±57.6	137.0±57.1	132.7±69.1

**Asterisk indicates a significant difference between elbow flexors ipsilateral pre- to posttest values. EF: elbow flexors, PF: plantar flexors.*

Post-Quadriceps Fatigue: EF and PF Fatigue Index

A significant main effect for muscle type ($F_{(1,12)}$=11.21, p=0.006, η_p^2: 0.483) was evident with 12.6% higher fatigue index for the EF (0.845±0.13) versus the PF (0.967±0.18). A significant muscle type x condition interaction ($F_{(2,24)}$=4.08, p=0.03, η_p^2: 0.254) demonstrated 9.5% and 20.3% greater fatigue indexes for the ipsilateral (p=0.04, d=0.75) and contralateral (p=0.006, d=1.5) EF over the PF respectively (Table 3).

Table 3 - Fatigue Index. Asterisks indicate significant differences between the elbow flexors and plantar flexors for each identified condition (i.e. ipsilateral vs. ipsilateral and contralateral vs. contralateral

Conditions	Fatigue Index
Elbow flexor ipsilateral	0.857±0.11*
Elbow flexor contralateral	0.821±0.09*
Elbow flexor control	0.856±0.07
Plantar flexor ipsilateral	0.944±0.13
Plantar flexor contralateral	1.03±0.21
Plantar flexor control	0.922±0.09

Post-Quadriceps Fatigue: PF vs. EF Fatigue Repetitions

A main effect for repetitions ($F_{(13,156)}$=17.29, p<0.0001, η_p^2: 0.590) indicated a decrease in force output with increasing number of MVC repetitions. Generally, there were significantly lower forces when comparing repetitions 1-4 to repetitions 8-13. A significant muscle type x conditions x repetitions interaction ($F_{(65,780)}$=2.96, p<0.01, η_p^2: 0.198) demonstrated that EF ipsilateral repetitions 1-12 were significantly or near significantly lower than their respective EF control and contralateral repetitions (Figure 1). Furthermore, EF ipsilateral repetitions 2-13 were significantly lower than their respective PF ipsilateral repetitions and also significantly lower than the PF control and contralateral repetitions 3-13 (Figure 1).

Figure 1 - Force values for pre and post intervention and RMVC protocol

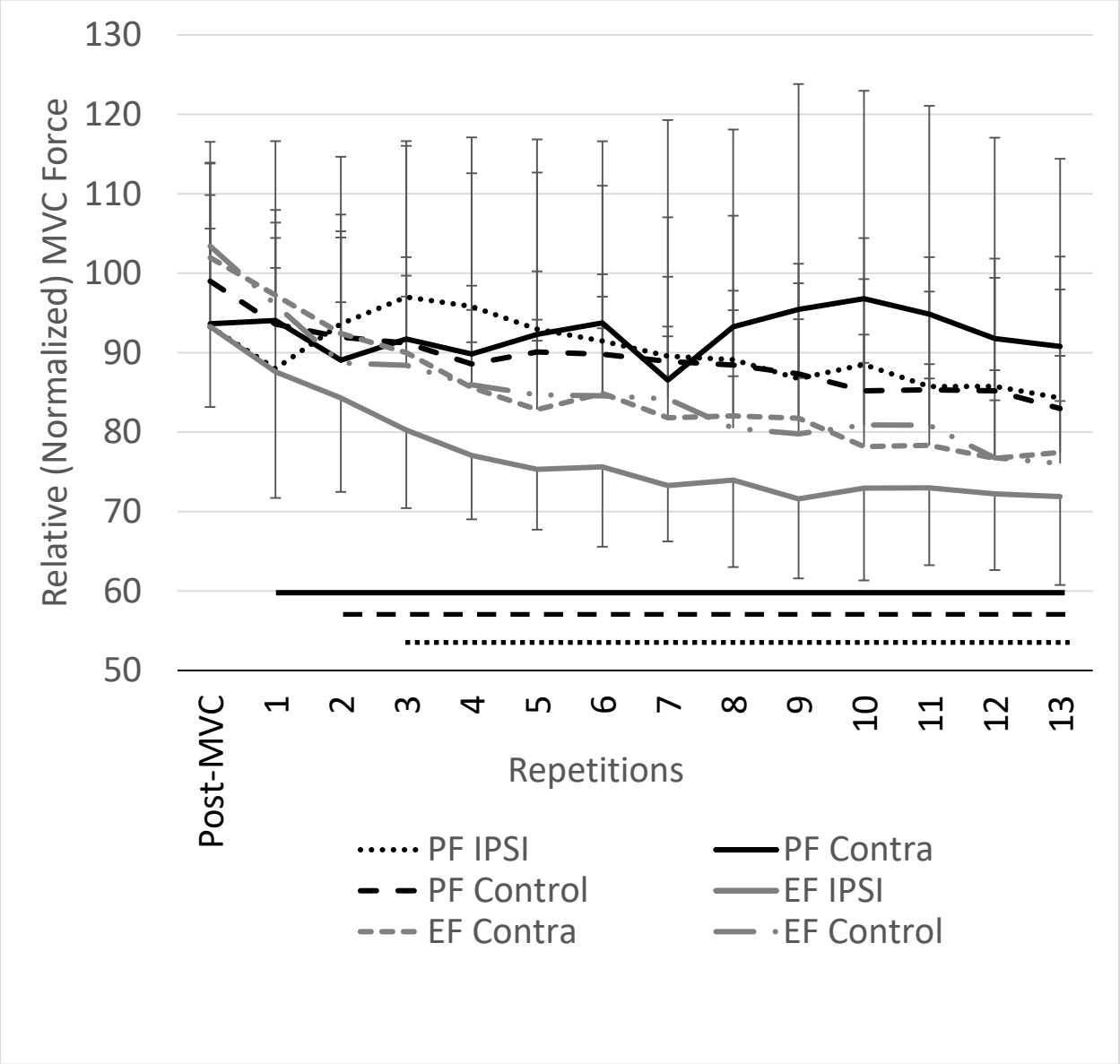

Figure 3: Elbow flexors (EF) and plantar flexors (PF) fatigue protocol, post-unilateral quadriceps fatigue. Solid black line illustrates significant and near significant differences between EF ipsilateral fatigue versus EF contralateral and control conditions. The dashed line represents that EF ipsilateral repetitions 2-13 were significantly lower than their respective PF ipsilateral repetitions. The dotted line indicates that EF ipsilateral repetitions were significantly lower than the PF control and contralateral repetitions 3-13.

Discussion

The most important finding in the present study was the substantially greater fatigue-induced ipsilateral EF single and repeated MVC deficits following unilateral fatigue of the dominant KE. However, there were no corresponding significant changes in EMG activity. The significant decrease in MVC force in anticipation (pacing strategy) of performing multiple MVCs was not affected by the conditions (i.e. ipsilateral, contralateral, or control). In addition, the EF experienced significantly greater fatigue than the PF.

This study's findings are in accordance with several other investigations of upper body muscle groups following lower body fatigue (Aboodarda et al., 2017; Othman et al., 2016; Halperin, Aboodarda, et al., 2014; Rasmussen et al., 2010; Sidhu et al., 2014; Šambaher, Aboodarda, & Behm, 2016). In fact, the 6.6% decrease in ipsilateral EF MVC immediately following KE fatigue is consistent with the 10.7% (Othman et al., 2016), 5% (Halperin, Saied J. Aboodarda, et al., 2014), and 6.1% (Šambaher et al., 2016) values previously reported in similar investigations. However, both the Othman et al. (2016) and Šambaher et al. (2016) studies employed dynamic bilateral KE to induce fatigue whereas Halperin, Aboodarda et al. (2014) employed the same protocol as the present study. Additionally, both Halperin, Aboodarda et al. (2014) and Šambaher et al. (2016) studies also found endurance deficits with a repeated MVC protocol, similar to the results of this study.

However, contradictory to the present study's findings, Halperin, Copithorne, & Behm (2014) suggested that NLMF effects are muscle specific and that, while the KE are susceptible to NLMF effects, the EF are less susceptible. They showed that non-dominant KE force, EMG, and VA all decreased ($P \leq 0.05$; effect size (ES) = 0.91–1.15; 2%–8%)

regardless of whether the dominant KEs or elbow flexors (EFs) were fatigued, whereas no differences were found for the non-dominant EF regardless of whether dominant KEs or EFs were fatigued ($P \geq 0.33$; $ES \leq 0.2$; $\leq 3.0\%$). Interestingly, this study found ipsilateral EF were susceptible to NLMF effects but contralateral EF were not and this could explain the rationale behind the difference in findings; perhaps NLMF is not only muscle specific, but also side specific. Additionally, contradictory to the Bogdanis et al. (1994) and the Halperin, Aboodarda, et al. (2014) studies, which indicated that fatigue resistance and local muscular endurance performance tasks appear to be more susceptible to NLMF effects than strength, the present study observed single MVC strength evaluations were indeed affected as evidenced by a decrease in ipsilateral EF MVC force immediately post-dominant KE fatigue. A possible explanation for the discrepancy between the findings of the present study and the findings of the Bogdanis et al. (1994) study is that an isometric fatiguing protocol was utilized versus a cyclical. Furthermore, the discrepancy between the current study and the Halperin, Aboodarda, et al. (2014) study could also be due to differing fatiguing protocols utilized as KE were fatigued using five sets of submaximal knee extensions to failure (50% of single leg MVC) with one minute of rest between sets. However, isometric (Doix et al., 2013; Halperin, Aboodarda, et al., 2014; Martin & Rattey, 2007; Post et al., 2008; Todd et al., 2003), cyclical (Baker & Davies, 2009; Bogdanis et al., 1994; Bouhlel et al., 2010), and dynamic (Amann et al., 2013; Grabiner & Owings, 1999; Humphry et al., 2004; Kawamoto et al., 2014; Triscott et al., 2008) fatiguing protocols have all resulted in NLMF effects and thus more research is needed in order to fully understand the degree to which each method of fatigue affects NLMF responses.

It is speculated that the greater NLMF for ipsilateral versus contralateral EF may be related to the closer spatial geography of cortical and spinal motor neurons of the ipsilateral versus contralateral motor neurons (i.e. motor homunculus). Contralateral muscle inhibition from the cortex would necessitate a transit across the corpus callosum and a descent to the target muscle groups. At the spinal level, while fatigue-induced afferent inhibitory influences from type II, III and IV afferents (i.e. Golgi tendon organs, nociceptors, metaboreceptors) would attenuate the excitation of target motor neurons (Taylor & Gandevia, 2008), it could be expected with the extensive neuronal interconnectivity that neighbouring motor neurons ipsilaterally inferior and superior to the area could also be more substantially inhibited. The present results suggest that ipsilateral motor neuron interconnectivity may induce a greater extent of inhibition than contralateral interconnectivity. However, unilateral activation of a muscle group, such as the dominant KE in this study, has been reported to lead to transcallosal inhibition inhibiting the contralateral motor cortex, suppressing activation of the contralateral muscle groups (Meyer, Roricht, Grafin von Einsiedel, Kruggel, & Weindl, 1995), the greater ipsilateral effects in the present study suggest the dispersal of inhibitory effects may be greater when motor neurons are located in the same cortical hemisphere.

Additionally, we suggest that there are a number of possible mechanisms for EF displaying greater NLMF effects than PF. Again, spatial geography may play a role, but it is unlikely as the location of the PF in relation to the quadriceps neurons at both the sensory and motor cortex may be closer than EF neurons (Cheney, Fetz, & Mewes, 1991). However, the distance from the quadriceps neurons to their superior (EF) and inferior (PF)

locations respectively may not be substantially disparate to induce a significantly different effect. Hence, we might not expect significantly greater inhibitory influences upon the EF motor neurons. However, their descending pathways provide some divergence. Whereas both sets of neurons can descend through the lateral corticospinal tract, PF also receive innervation through the medial reticulospinal tract (Peterson, Pitts, & Fukushima, 1979), which facilitates ipsilateral lower motor neurons and innervates postural muscles and limb extensors. On the other hand, in addition to the lateral corticospinal tract pathway, EF pathways descend the rubrospinal tract which mainly activate the upper-limb flexor muscles (Lawrence & Kuypers, 1968). Thirdly, the PF would be influenced by different patterns of reflex actions such as the central pattern generator for locomotion (Kern, Semmler, & Enoka, 2001) and thus their respective spinal reflex connectivity will differ (Duysens & Van de Crommert, 1998; MacKay-Lyons, 2002).

A 12.6% greater fatigue index was observed in the current study for repeated MVC's in the EF compared to the PF, suggesting the effects of NLMF on the EF progressed with additional maximal efforts. This is consistent with Halperin, Aboodarda, et al. (2014), who used quadriceps fatigue to elicit NLMF in only the final five repetitions of a repeated MVC protocol for the contralateral EF; suggesting a muscle's capacity to resist fatigue may be compromised to a greater extent than its ability to perform a single maximal effort.

The most likely factor contributing to the noted differences in fatigability is the variation of fibre composition in the observed muscles. The soleus muscle is primarily composed of type I fibers (Edgerton, Smith, & Simpson, 1975; Johnson et al., 2014). Similarly, the gastrocnemius has been shown to contain predominantly slow twitch

oxidative (type I) compared to fast twitch oxidative glycolytic and fast twitch glycolytic (type II) fibers (Edgerton et al, 1975). In contrast, the biceps brachii contains a higher density of type II fibres (Jennekens, Tomlinson, & Walton, 1971; Johnson, Polgar, Weightman, & Appleton, 1973). Type I fibers are well adapted to prolonged activity and thus are fatigue-resistant (Edström & Kugelberg, 1968) compared to the more fatigable type II fibres. The rectus femoris, part of the fatigued quadriceps group in the present study, is principally composed of type II fibres (Jennekens et al., 1971; Johnson et al., 1973). The relative similarity in muscle fibre composition, and thus fatigability, of the biceps brachii to the rectus femoris may dictate a greater NLMF response in the EF compared to the PF. It is possible that NLMF occurs more readily in type II (fatigable) than in type I (fatigue resistant) fibres – suggesting that a muscle's fibre composition, or predominant fibre type, may determine its susceptibility to NLMF.

In the absence of fatigue to a non-local muscle, the PF are prone to an initial reduction in peak force with an ensuing plateau during repeated maximal outputs (Iguchi & Shields, 2012; Kawakami, Amemiya, Kanehisa, Ikegawa, & Fukunaga, 2000). Furthermore, 100 repeated PF MVCs determined that significantly less force, as well as less fatigue, was produced in a seated 90 degree knee flexed position than a straight legged position (Kawakami et al., 2000); in fact the seated position, primarily activating the soleus, did not elicit significant fatigue during the initial 40 repetitions. The straight-legged position, predominantly activating the gastrocnemius, produced much higher relative torque while also demonstrating an initial significant decline and ensuing taper of force deficits following the 30th repetition. This is in line with the present study which employed

a seated, knee flexed, position for PF MVCs, isolating mainly soleus fibres, and failed to elicit significant fatigue during 12 repetitions. It is speculated that given the significantly greater proportion of type I fibres in the soleus compared to the gastrocnemius (Edgerton et al., 1975; Johnson et al., 1973) provides a possible explanation for the long-term fatigue resistant properties of these fibres. In contrast, fatigue of the EF (high relative concentration of type II fibres) has been shown to progress in the second half of repeated MVC protocols. Indeed, EF peak force and biceps brachii EMG was significantly lower in later repetitions for trained females (Halperin, Aboodarda, Basset, & Behm, 2014), adolescent females (Reid et al., 2017), and trained males (Halperin, Aboodarda, Basset, Byrne, & Behm, 2014) during various repeated MVC protocols. This may further explain the contribution of varying muscle fibre types in the patterns of fatigue elicited in the present study using a fatigued non-local muscle.

Granted, each of the above studies demonstrating EF fatigue with repeated MVC protocols also observed pacing strategies where a) force produced during the first repetition of a repeated MVC protocol was significantly less than maximal pre-test force, and b) when subjects were aware it was their final MVC they consistently produced greater force than the preceding repetitions. This suggests that the fatigue elicited in these studies may be at least partially attributed to a subconscious pacing strategy in addition to possible changes to the muscle or central drive. In the present study, evidence of an anticipatory pacing response in the EF is seen when comparing the post-test MVC peak force to the first repetition of the repeated MVC protocol. Near significant deficits to maximal force were observed in the ipsilateral (8.9%) and contralateral (4.9%) EF compared to the control

condition. This suggests that the anticipatory response may be strengthened following fatigue to a non-local muscle. Conversely, the PF did not demonstrate this anticipatory response suggesting that type I and type II muscle fibres respond differently to pacing. This is consistent with the notion that type 1 fibres can accommodate prolonged activation and are more fatigue-resistant, and is supported by previous studies which did not report pacing responses following 45 (Iguchi & Shields, 2012) and 100 (Kawakami et al., 2000) repeated PF MVCs.

Regarding the anticipatory pacing response, it is important to consider the discrepancy in peak force during post-test and first repeated MVC repetition seen with ipsilateral and contralateral EF. These initial repetitions of the repeated MVC protocol directly impact the fatigue index – calculated as the ratio of peak force elicited by the final two versus the first two MVC repetitions. Despite evidence of anticipatory response in the first repetition, the fatigue index for the ipsilateral (0.857) and contralateral (0.821) EF indicate significant NLMF occurred following fatigue of the quadriceps. It can be postulated that, had the initial pacing strategies been avoided (resulting in greater peak force during the first MVC repetition), the fatigue index for the ipsilateral and contralateral EF would be even lower (greater fatigue). This suggests that the data likely underestimates the extent of NLMF elicited in the present study. Perhaps a more accurate representation would be seen when the fatigue index is calculated using the ratio of peak force during the final two repetitions versus only the post-intervention MVC, thus eliminating the skew created by the anticipated first MVC. Since a pacing response was not identified for the PF

conditions, this correction would further distinguish the NLMF effects prompted in the EF versus the PF or, more specifically, in type II versus type I muscle fibres.

Limitations

A methodological limitation to this study is exposed when considering the post-intervention MVC of the non-local muscle. While EF and PF testing were performed within 30s following the intervention, PF MVCs were typically delayed accommodating transferring the subject to the PF testing device. This delay may have been sufficient to partially negate any fatigue-induced deficits to PF peak force – PF fatigue has been shown to recover approximately 85% following as little as 1-minute rest (Iguchi & Shields, 2012). Therefore, it is possible that NLMF in the PF was underestimated in the present study. Nevertheless, based on prior justification for the lack of PF fatigue in this study, it is likely that the 30-60-second delay was negligible and did not conceal significant fatigue effects.

Additionally, as mentioned above, the evident pacing strategy would have a direct impact on the fatigue index result. Had there been no pacing strategy present, there would have been greater fatigue.

Further, participants of heterogenous sexes increases variability of results and thus makes it more difficult to observe statistical significance.

Finally, a major limitation of the present study was the inability to distinguish between central and peripheral fatigue since investigative tools such as transcranial magnetic stimulation (TMS) and interpolated twitch technique (ITT) were not employed. Consequently, it is suggested that similar future studies identify more clearly the locus of fatigue.

Conclusion

Following dominant KE fatigue, NLMF effects were found in EFs ipsilateral to the fatigued KEs but not in EFs which were contralateral or in PF which were ipsilateral or contralateral to the fatigued KEs. Ipsilateral EFs displayed single MVC as well as a repeated MVC protocol performance deficits. The results of this study suggest that NLMF effects are muscle specific and could be influenced by the motoneuron location in the cerebral hemisphere, and muscle fibre type. Both of the aforementioned factors may influence the degree to which each muscle group is affected by NLMF. Prior lower body fatigue hindering subsequent upper body performance could be an important consideration for rehabilitation, training, and performance programs. For example, superset training with squats and biceps curls may not maximize the potential of the EFs due to NLMF; whereas squats followed by seated heel raises may provide an efficient superset while avoiding NLMF in the soleus.

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APPENDICES

Appendix A: Ethics Application Approval

Ethics Office
Suite 200, Eastern Trust Building
95 Bonaventure Avenue
St. John's, NL
A1B 2X5

July 29, 2016

30a Merrymeeting Road
St. John's, NL
A1C 2V8
Canada

Dear Mr. Whitten:

Researcher Portal File # 20170541
Reference # 2016.203

RE: "The effects of unilateral dominant knee extensors fatigue on non-exercised and ipsilateral elbow and plantar flexors"

Your application received an expedited review by a sub-committee of the Health Research Ethics Board (HREB). ***Full approval*** of this research study is granted for one year effective **July 29, 2016**.

This is your ethics approval only. Organizational approval may also be required. It is your responsibility to seek the necessary organizational approval from the Regional Health Authority (RHA) or other organization as appropriate. You can refer to the HREA website for further guidance on organizational approvals.

This is to confirm that the HREB reviewed and approved or acknowledged the following documents (as indicated):

- Application, approved
- Budget, approved
- Recruitment poster, approved
- Script for social media, approved
- Revised consent form, approved
- ParQ form, appoved

MARK THE DATE

This approval will lapse on July 29, 2017 . It is your responsibility to ensure that the Ethics Renewal form is submitted prior to the renewal date; you may not receive a reminder. The Ethics Renewal form can be found on the Researcher Portal as an Event form.

If you do not return the completed Ethics Renewal form prior to date of renewal:

- ***You will no longer have ethics approval***
- *You will be required to stop research activity immediately*
- *You may not be permitted to restart the study until you reapply for and receive approval to undertake the study again*
- *Lapse in ethics approval* ***may result in interruption or termination of funding***

You are solely responsible for providing a copy of this letter, along with your approved HREB application form; **to Research Grant and Contract Services** should your research depend on funding administered through that office.

Modifications of the protocol/consent are not permitted without prior approval from the HREB. **Implementing changes without HREB approval may result in your ethics approval being revoked, meaning your research must stop**. Request for modification to the protocol/consent must be outlined on an amendment form (available on the Researcher Portal website as an Event form) and submitted to the HREB for review.

The HREB operates according to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2), the Health Research Ethics Authority Act (HREA Act) and applicable laws and regulations.

You are responsible for the ethical conduct of this research, notwithstanding the approval of the HREB.

We wish you every success with your study.

Sincerely,

Patricia Grainger

Ms. Patricia Grainger (Acting -Chair, Non-Clinical Trials Health Research Ethics Board)

CC: D Behm

appendix A attachment: PAR-Q.

Physical Activity Readiness
Questionnaire - PAR-Q
(revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO		
☐	☐	1.	**Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	2.	**Do you feel pain in your chest when you do physical activity?**
☐	☐	3.	**In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4.	**Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5.	**Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6.	**Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7.	**Do you know of any other reason why you should not do physical activity?**

If you answered YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

→

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

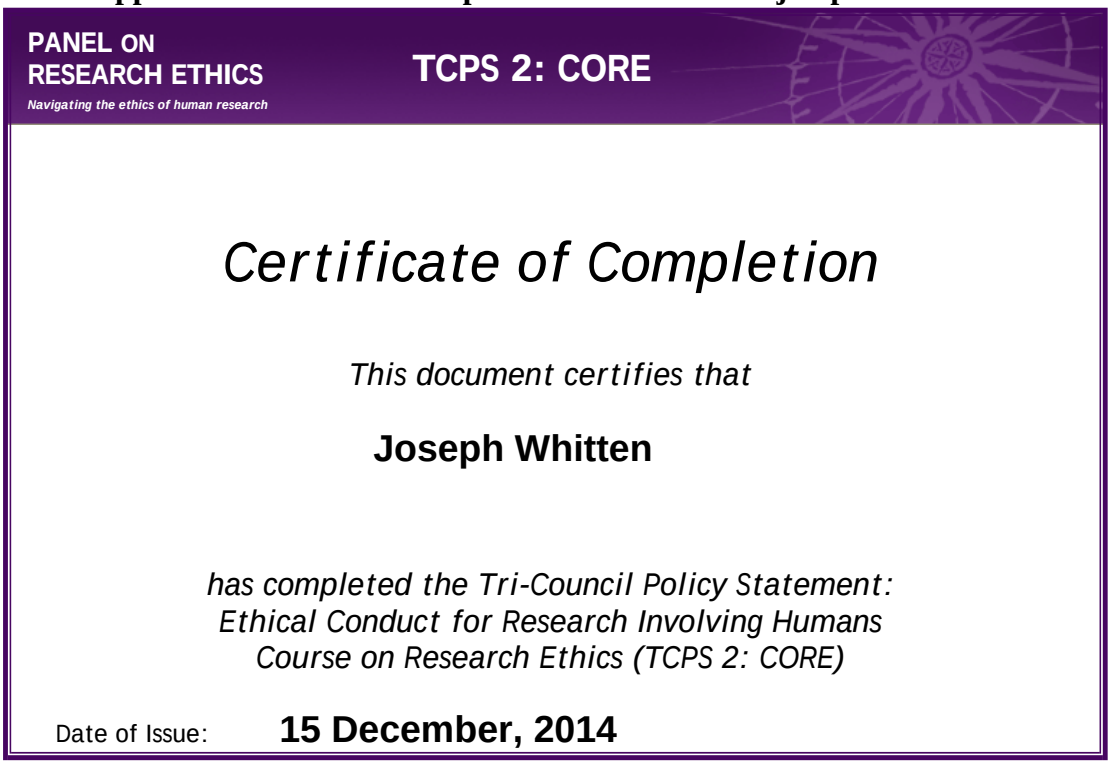
"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority) _____ WITNESS _____

appendix A attachment: tcps2 core certificate for joseph whitten.



PANEL ON RESEARCH ETHICS

Navigating the ethics of human research

TCPS 2: CORE

Certificate of Completion

This document certifies that

Joseph Whitten

has completed the Tri-Council Policy Statement:
Ethical Conduct for Research Involving Humans
Course on Research Ethics (TCPS 2: CORE)

Date of Issue: **15 December, 2014**

appendix A attachment: consent to take part in research form.

Name:_____ Date: _____

Height: _____ Weight: _ ¼ distance _____ Sex: M F

General warm-up: 70 ☐ RPM for 5 min

Pretest

Specific warm-up for EF or PF: 10 Iso at 50% ☐ perceived max 2/2

EF/PF MVCs: 5s/2min

	Trial 1	Trial 2
File		
Force		

Specific warm-up for KE: 10 Unilateral Iso KE at ~50% of ☐ perceived max 2/2

KE MVCs

	Trial 1	Trial 2
File		
Force		

Intervention

Unilateral KE MVC for 100s x 2 w/

First Set	Second Set

30s rest

Rest ☐ for 230s

Post Test

MVCs

	KE Immediately	EF or PF Immediately	EF or PF 1 min Post
File			
Force			

Repeated MVCs of EF or PF 5s/10s

	1	2	3	4	5	6	7	8	9	10	11	12
File												

appendix A attachment: recruitment poster

School of HKR Current Research

MEMORIAL UNIVERSITY

Neuromusclar Physiology Study Seeking Participants!

The effects of upper thigh fatigue on non-exercised arms and calves

- Are you healthy, physically active, and interested in becomming part of current research at Memorial?
- The School of HKR currently needs participants for a study that will evaluate the effects of localized fatigue on non-working muscles!

Taking part in this study will involve:

- A warm-up which involves cycling followed by Maximal Voluntary Contractions of your knee extensors and elbow and plantar flexors
- 1 hour of your time on 4 seperate days (4 hours total)

joe.whitten@mun.ca (709) 764-0539

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