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Research article

Unilateral Quadriceps Fatigue Induces Greater Impairments of Ipsilateral versus Contralateral Elbow Flexors and Plantar Flexors Performance in Physically Active Young Adults

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Abstract

Non-local muscle fatigue (NLMF) studies have examined crossover impairments of maximal voluntary force output in non-exercised, contralateral muscles as well as comparing upper and lower limb muscles. Since prior studies primarily investigated contralateral muscles, the purpose of this study was to compare NLMF effects on elbow flexors (EF) and plantar flexors (PF) force and activation (electromyography: EMG). Secondly, possible differences when testing ipsilateral or contralateral muscles with a single or repeated isometric maximum voluntary contractions (MVC) were also investigated. Twelve participants (six males: (27.3 ± 2.5 years, 186.0 ± 2.2 cm, 91.0 ± 4.1 kg; six females: 23.0 ± 1.6 years, 168.2 ± 6.7 cm, 60.0 ± 4.3 kg) attended six randomized sessions where ipsilateral or contralateral PF or EF MVC force and EMG activity (root mean square) were tested following a dominant knee extensors (KE) fatigue intervention (2×100s MVC) or equivalent rest (control). Testing involving a single MVC (5s) was completed by the ipsilateral or contralateral PF or EF prior to and immediately post-interventions. One minute after the post-intervention single MVC, a 12×5s MVCs fatigue test was completed. Two-way repeated measures ANOVAs revealed that ipsilateral EF post-fatigue force was lower (-6.6%, $p = 0.04$, $d = 0.18$) than pre-fatigue with no significant changes in the contralateral or control conditions. EF demonstrated greater fatigue indexes for the ipsilateral (9.5%, $p = 0.04$, $d = 0.75$) and contralateral (20.3%, $p < 0.01$, $d = 1.50$) EF over the PF, respectively. There were no significant differences in PF force, EMG or EF EMG post-test or during the MVCs fatigue test. The results suggest that NLMF effects are side and muscle specific where prior KE fatigue could hinder subsequent ipsilateral upper body performance and thus is an important consideration for rehabilitation, recreation and athletic programs.

Key words: Quadriceps, plantar flexors, elbow flexors, crossover fatigue, force, electromyography.

Introduction

A relatively recent field of fatigue research has explored how localized fatigue can impair force output in muscles that have not been directly exercised (Halperin et al., 2014a; 2014b; 2015; Kennedy et al., 2013). This global effect of fatigue has been classified as crossover (Doix et al., 2018; Martin and Rattey, 2007; Rattey et al., 2006) or non-local muscle fatigue (NLMF) (Halperin et al., 2015). NLMF refers to deficits of maximal force output in any contralateral or ipsilateral, homologous or heterologous, non-exercised muscles (Halperin et al., 2015, Miller et al., 2019, Ye et al., 2018), whereas crossover fatigue is a subgroup of NLMF and specifically describes the impairment of a contralateral, homologous, non-exercised muscle (Doix et al., 2018; Halperin et al., 2015; Martin and Rattey, 2007). Contrary to these concepts however, numerous studies failed to show NLMF effects (Aboodarda et al., 2019; Andrews et al., 2016; Doix et al., 2018; Grabiner and Owings, 1999; Hamilton and Behm, 2017; Kennedy et al., 2015; Morgan et al., 2019; Prieske et al., 2017). Indeed, there are a number of inconsistencies and gaps in the NLMF literature.

A review by Halperin et al. (2015) reported that the incidence or extent of NLMF may be muscle specific, with NLMF effects more likely to occur when testing lower limb muscle groups such as the quadriceps. In the majority of NLMF studies, the fatigue intervention involved the homologous contralateral KE. However, Halperin et al. (2014a) showed that non-dominant KE force, integrated electromyography (EMG) signal, and voluntary activation (VA) measured with the interpolated twitch technique decreased (effect size (ES) = 0.91-1.15) regardless of whether the dominant KE or elbow flexors (EF) were fatigued (intervention). In contrast, no differences were found for the non-dominant EF suggesting that the KE were more susceptible to NLMF effects than EF. However, there are some crossover studies that have illustrated moderate magnitude impairments when testing the contralateral homologous EF ($d = 0.43$-0.5) (Chen et al., 2016; Humphry et al., 2004) and first dorsal interosseous muscle ($d = 0.49$) (Li et al., 2019; Post et al., 2008). Similarly, there is evidence of NLMF when exercising the lower body and testing the EF ($d = 0.5$-0.85) (Aboodarda et al., 2017; Ben Othman et al., 2017; Šambaher et al., 2016) or handgrip muscles ($d = 0.22$-0.97) (Amann et al., 2013; Ben Othman et al., 2017; Decorte et al., 2012; Elmer et al., 2013). These studies have primarily examined contralateral muscles whereas the response of non-exercised, heterologous, ipsilateral muscles has not been adequately pursued.

According to the Halperin et al. review (2015), the predominance of lower body NLMF may be related to differences in the muscle volume, ability to fully activate a greater number of motor units (Piasecki et al., 2016), and reflex connectivity (i.e. more extensive locomotor pattern generator in legs: (Cappellini et al., 2006)). However,

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studies demonstrating the lower body NLMF predominance have almost always involved KE (quadriceps) testing with only two investigations of plantar flexors (PF) (Kennedy et al., 2013; Regueme et al., 2007). It would be important to question whether NLMF predominance is a general lower body phenomenon or specific to the KE. Differences in motor unit and muscle fibre composition and associated threshold activation between the KE, EF (higher type II) and soleus (higher type I) (Jennekens et al., 1971; Johnson et al., 1973) might impact NLMF effects.

Furthermore, evidence for NLMF is less prevalent when a single, discrete isometric maximal voluntary contraction (MVC) (strength test) is employed versus testing with repeated fatigue-inducing repetitions (Halperin et al. 2015). A recent meta-analysis of 52 articles reported trivial magnitude NLMF when testing with single MVCs but moderate effects when repeated MVCs (muscle endurance) were tested (Behm et al., 2021). Proposed mechanisms underlying the greater susceptibility of fatigue resistance to NLMF effects as opposed to single MVC strength evaluations (Bogdanis et al., 1994; Halperin et al., 2014b) may be related to the distribution of metabolites from the previously exercised muscle (biochemical factors) (Bangsbo et al., 1996; Bogdanis et al., 1994; Halperin et al., 2014b; Johnson et al., 2014). Type III and IV muscle afferents can inhibit the central nervous system attenuating central drive to the exercised muscle and potentially to non-exercised muscles (Amann, 2011; Amann et al., 2013; Sidhu et al., 2014).

With few studies investigating NLMF effects upon the PF or muscles ipsilateral to the unilaterally fatigued muscle, the goal of the present study was to further investigate muscle specificity and quantify NLMF effects by directly comparing the effects of a KE fatigue intervention on heterologous ipsilateral and contralateral EF and PF while utilizing a combination of single and repeated MVCs as testing protocols. Based on the reported spatial arrangement and neuronal interconnectivity (i.e., activation or inhibition of contralateral neurons would involve innervation across the corpus collosum, whereby ipsilateral neurons would be located on the same side) of ipsilateral versus contralateral motor neurons (Balter and Zehr, 2007; Burke, 1980), it was hypothesized that the PF and EF ipsilateral to the fatigued KE would have greater NLMF effects than muscle groups contralateral to the fatigued muscles. In addition, based on the prior literature reporting greater lower limb NLMF susceptibility (Halperin et al., 2014a), it was hypothesized that ipsilateral PF would demonstrate greater NLMF than ipsilateral EF.

Methods

Participants

Based on prior repeated measures (within) using NLMF MVC force data (Halperin et al., 2014a, Bogdanis et al., 1994), an "a priori" statistical power analysis (G*Power, Dusseldorf Germany) with an effect size of 0.5 (test family: F-tests), indicated that a minimum of 12 participants would be needed to achieve an alpha of 0.05 with a statistical power of 80%. Initially, 8 males and 7 females were recruited as participants, however 2 males and 1 female did not complete all data collection trials. Hence, six male (27.3 ± 2.5 years, 1.86 ± 0.02 m, 91.0 ± 4.1 kg) and six female (23.0 ± 1.6 years, 1.68 ± 0.07 cm, 60.0 ± 4.3 kg) participants completed this study. Participants were either recreationally active (2 male, 4 female) 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) participating in a provincial, national, or varsity competitive sports program for the past 5 years. Each participant was verbally informed of the procedures and risks associated with the study and then they signed the consent form. Participants were requested to avoid consumption of alcohol and caffeine for 4 hours prior to testing as well as training a day before the testing days (Canadian Society for Exercise Physiology Activity, Fitness and Lifestyle Approach 2003). None of the athletes used supplements during the experimental period. 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 order: 1) fatigue the dominant KE and test the ipsilateral PF (PF IPSI), 2) fatigue the dominant KE and test the contralateral PF (PF CONTRA), 3) dominant KE were rested and test the ipsilateral PF (PF Control), 4) fatigue the dominant KE and test the ipsilateral EF (EF IPSI), 5) fatigue the dominant KE and test the contralateral EF (EF CONTRA) and 6) dominant KE were rested and test the ipsilateral EF (EF Control).

Participants were familiarized with the 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 5s KE MVCs with the dominant leg KE, identified as the leg used to kick a ball (van Melick et al. 2017), with 1min of rest between each MVC trial. Depending on the randomly selected condition for the particular day, each participant then performed a specific warm-up for their 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. This was followed two minutes later by either two EF or PF MVCs based on the limb tested on the particular day. Thereafter, participants performed either the fatiguing intervention (2x100s KE MVC) or control (rest) protocol. In order to limit the number of sessions required for participants, the control sessions were only conducted on the ipsilateral side with the expectation that the response of a tested muscle group to knee extension rest would be similar regardless if ipsilateral or contralateral conditions were tested (Figure 1). Testing sessions were separated by a minimum of 48 hours and conducted at approximately the same time of day for each participant to avoid diurnal variations.

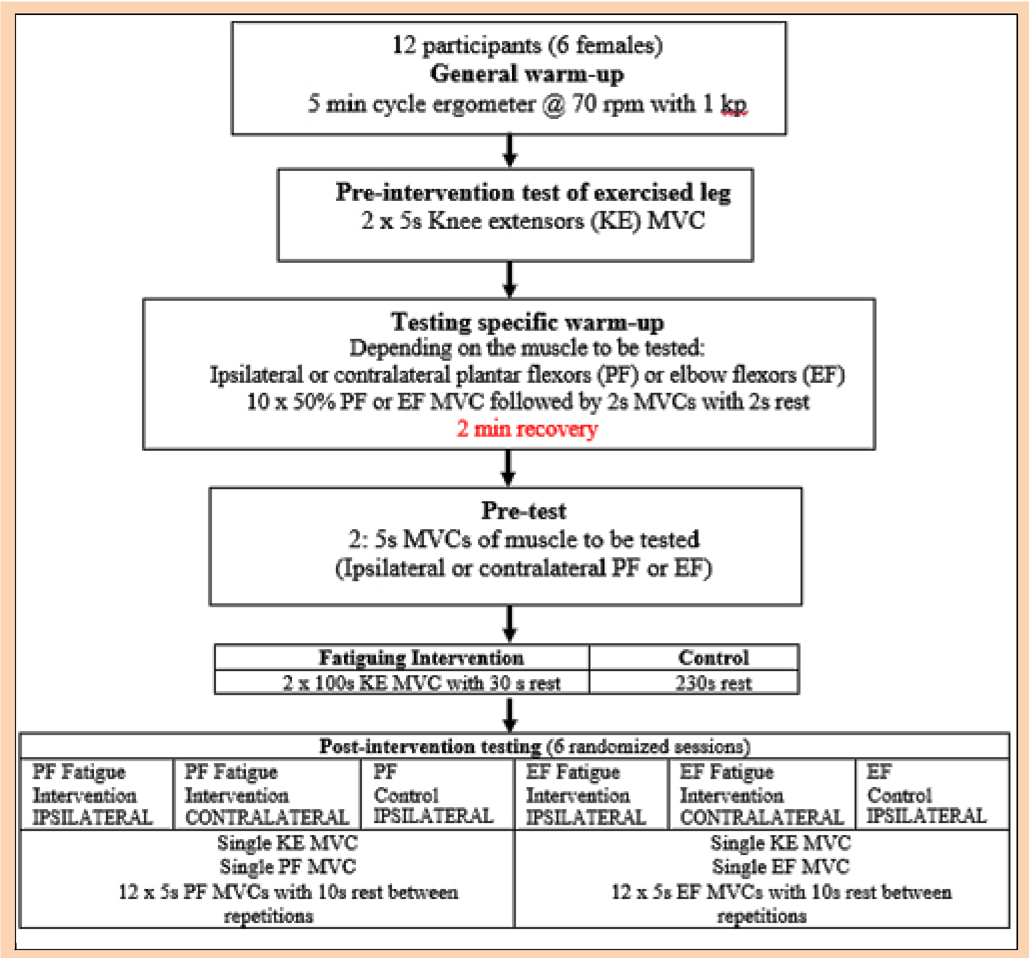

Figure 1. Experimental design: A within (repeated) subject design with 6 experimental sessions (EF and PF muscles (2) x (3) testing sessions that include ipsilateral, and contralateral muscles following the fatiguing intervention and testing of ipsilateral muscles after control (rest)).

Intervention

For the unilateral fatiguing protocol, participants completed two, 100s sustained MVCs with the dominant KE with 30s of rest after the first 100s (Halperin et al. 2014a; 2014b). The same device (chair) was used for the intervention and all testing. For the control protocol, participants were seated in the same chair for 230s (the time it took to complete the fatiguing protocol). Participants were constantly motivated during the fatiguing protocol by two experimenters and reminded to keep their upper body (arms crossed over chest) and PF as relaxed as possible during the protocol. EF (biceps brachii) and PF (gastrocnemius and soleus) EMG activity were monitored throughout the protocol and with any evidence of activation, participants were reminded to relax their arms and PF muscles. Participants could view the force output on the computer monitor for testing and the intervention.

Testing

Immediately after each protocol was completed, participants performed a unilateral KE MVC with the fatigued (dominant) limb. An ipsilateral or contralateral EF or PF MVC (i.e. 5s) was performed within 30s of the intervention, which would have provided some degree of recovery. One minute after the post-test EF or PF MVC, participants performed a repeated MVC (fatigue test) protocol of the same muscle group consisting of 12 MVCs at a work-to-rest ratio of 5:10s (Halperin et al. 2014b; 2014c; 2014d).

Dependent Variables

Maximal Voluntary Contractions (MVC)

To measure KE MVC force, participants were seated on a chair (constructed by Technical Services Division of Memorial University of Newfoundland) with their knees flexed at 90° and their arms crossed (Aboodarda et al. 2015; 2016; Halperin et al. 2014a; 2014b; 2014c; 2014d; Hamilton and Behm 2017, Šambaher et al. 2016). 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 intervention. To measure EF MVC 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. The supinated testing arm was inserted into a padded strap, connected to a similar load cell by a carabiner. To measure PF torque, the participants were seated with their hips, knees, and ankles flexed at 90° and their lower leg was secured in an isometric boot apparatus (Marsh et al. 1981)(constructed by Technical Services Division of Memorial University of Newfoundland) equipped with strain gauges (Omega Engineering Inc. LCCA 250, Don Mills, ON, Canada). In contrast to the EF and KE forces (N) exerted in line with the strain gauges, PF MVC forces from the forefoot were exerted at a distance perpendicular to the axis of rotation of the boot apparatus strain gauge and thus are reported as torque (Nm) values. All force or torque data were sampled pre- and post-intervention 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 was normalized to pre-test values for each participant and all data were reported as percentage of pre-test values.

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 20mm were placed on the six muscles (rectus femoris, biceps femoris, biceps brachii, triceps brachii, lateral gastrocnemius and soleus) in accordance with the SENIAM recommendations (Hermens et al. 1999). 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 collected with the force/torque data, digitally filtered by the software with a linear phase Blackman -61 dB band-pass filter between 10-500Hz, amplified (bi-polar differential amplifier, input impedance = 2MΩ, common mode rejection ratio > 110 dB min (50/60 Hz), gain × 1000, noise > 5 μV), and analog-to-digitally converted (12 bit). The moving root mean square (RMS) of the EMG signals were processed over each 50 samples and the mean amplitude was monitored over a 1s period encompassing the peak MVC force (500ms before and after the peak force). Post-test EMG RMS values were normalized to the highest pre-test MVC.

Fatigue Index (FI)

Fatigue index of the 12 MVC post-test was calculated by obtaining the mean peak force values of repetitions 11 and 12 of the repeated MVC protocol and dividing this value by the mean peak 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. Hence, with the fatigue index, it was possible to compare the NLMF effects upon a single non-fatiguing MVC versus the relative extent of NLMF with a repeated MVC protocol.

Statistical Analysis

Statistical analyses were completed using the SPSS software (Version 26.0, SPSS, Inc. Chicago, IL). Assumption of sphericity (Mauchly's) and normality (Shapiro-Wilk) were tested for all dependent variables. If a significant violation of sphericity was noted, the corrected values for non-sphericity with Greenhouse-Geisser were reported. There were no significant violations of normality. The following analyses were conducted.

1. To investigate the efficacy of the intervention fatiguing protocol, a 2-way repeated (within subjects' design) measures ANOVA (6 conditions [EF IPSI, EF CONTRA, EF Control, PF IPSI, PF CONTRA, PF Control] × 2 time points) was performed to compare KE pre- and post-test MVC values.
2. For absolute pre- to post-intervention data, EF and PF required separate analyses since data were provided as force (N) and torque (Nm), respectively. To ensure a comprehensive comparison that included the control condition when examining the effect of dominant KE fatigue on ipsilateral and contralateral EF and PF discrete (single) MVC responses, separate 2-way repeated (within subjects' design) measures ANOVAs (3 conditions [IPSI, CONTRA, Control] × 2 times) were used to examine pre- to post-intervention changes in absolute (i) EF force and EMG (ii) PF torque and EMG.
3. The control condition was only incorporated on the ipsilateral side (to reduce the number of sessions from eight to six: see explanation in methods). Since the prior analysis compared absolute muscle responses separately, a comparison of muscle responses required normalization of the MVCs. The discrete, single, EF and PF MVC responses (i.e. the single MVC performed prior to the 12 repetitive contraction fatigue test) were compared post-test with a 2-way repeated measures (within subjects' design) ANOVA (2 muscles × 2 conditions [IPSI vs. Control]). Another 2-way ANOVA (2 muscles × 2 conditions [IPSI vs. CONTRA]) examined ipsilateral to contralateral responses of both muscles. Since there was no Control condition for the contralateral side, the three normalized conditions could not be integrated into one repeated measures ANOVA.
4. To analyze the fatigue index of the 12 repeated MVCs of the two tested muscles, a 2-way repeated (within subjects' design) measures ANOVA (2 muscles × 3 conditions [IPSI, CONTRA, Control]) was employed.

Table 1 provides the statistical analyses organized by research question. In the event of significant main effects or interactions, planned pairwise comparisons were made (paired t-tests) to identify differences among mean value time points. The level of significance was set at $p \leq 0.05$ and all results are expressed as mean ± SD. Partial eta squared (η_p^2) values were calculated and converted to Cohen's d values for consistency between reporting magnitude changes for overall main effects, interactions and individual post-hoc calculations. Cohen's d (Cohen 1988) were interpreted where d < 0.2: trivial, 0.2 - <0.5: small, 0.5 - <0.8: moderate and d ≥ 0.8: large. Inter-session reliability responses of three sessions each for the single MVC forces and mean amplitude of the RMS EMG of the PF and EF were assessed with Cronbach's alpha intraclass correlation coefficient (ICC) for all muscles and tests as classified by Koo and Li (2016). Coefficients of variation (CV) and standard error of the mean (SEM) were also reported with the reliability scores.

Table 1. **Statistical analyses organized by the research question.**

Research Objective	Statistical Analysis
Did the unilateral KE intervention (2x100s MVCs) induce fatigue in the same KE? Compare KE force pre- and post-test MVC values.	2-way repeated (within subjects design) measures ANOVA (6 conditions [EF IPSI, EF CONTRA, EF Control, PF IPSI, PF CONTRA, PF Control] × 2 time points)
Did the unilateral KE intervention (2x100s MVCs) or control condition induce changes in the ipsilateral and contralateral PF single MVC torque and EMG (absolute data)?	2-way repeated (within subjects design) measures ANOVA (3 conditions [PF IPSI, PF CONTRA, PF Control] × 2 times)
Did the unilateral KE intervention (2x100s MVCs) or control condition induce changes in the ipsilateral and contralateral EF single MVC torque and EMG (absolute data)?	2-way repeated (within subjects design) measures ANOVA (3 conditions [EF IPSI, EF CONTRA, EF Control] × 2 times)
Did the unilateral KE intervention (2x100s MVCs) or control condition have different relative effect on the EF and PF single MVC force/torque and EMG (normalized data)?	2-way repeated measures (within subjects design) ANOVA (2 muscles × 2 conditions [IPSI vs. Control]). (2 muscles × 2 conditions [IPSI vs. CONTRA])
Did the unilateral KE intervention (2x100s MVCs) or control condition affect the EF and PF fatigue index differently?	2-way repeated (within subjects design) measures ANOVA (2 muscles × 3 conditions [IPSI, CONTRA, Control])

Table 2. **Absolute (N), mean relative (%) changes, significance (p) and Cohen's d effect sizes for pre- to post-test changes in knee extension MVC force. The first row lists the six conditions.**

Conditions	PF IPSI	PF Control	EF IPSI	EF Control	PF CONTRA	EF CONTRA
Pre-test	587.6 ± 132.4	575.8 ± 162.8	565.1 ± 140.3	585.6 ± 148.1	563.1 ± 146.2	572.9 ± 119.5
Post-test	405.1 ± 63.7	540.5 ± 163.8	406.1 ± 102.2	570.9 ± 130.5	424.7 ± 100.1	391.4± 64.7
% Change	-29.2*	-4.7	-27.3*	-1.6	-23.7*	-30.5*
p	0.009	1.00	0.006	1.00	0.007	0.005
d	1.86	0.21	1.31	0.10	1.13	1.9

Asterisk (*) indicates post-test was significantly altered from pre-intervention (pre-test). CONTRA: contralateral limb, EF: elbow flexors, IPSI: ipsilateral limb, PF: plantar flexors.

Table 3. **Absolute pre- and post-test single MVC elbow flexor (EF) force and plantar flexor (PF) torque outputs.**

	Ipsilateral Pre-Test	Ipsilateral Post-Test	Contralateral Pre-Test	Contralateral Post-Test	Control Pre-Test	Control Post-Test
EF (N)	316.8 ± 116.7	295.3 ± 115.7*	295.2 ± 104.9	307.1 ± 130.5	314.3 ± 124.6	323.8 ± 136.3
PF (Nm)	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 post-test values.

Results

Reliability

Reliability scores were classified as excellent for EF (ICC = 0.97; CV: 0.3, SEM: 2.7) and KE (ICC = 0.98, CV: 0.24, SEM: 3.4) MVC force and good for gastrocnemius EMG (ICC = 0.77, CV: 0.45, SEM: 0.03). Reliability ranged from poor (triceps brachii EMG (ICC = 0.40: CV: 0.56, SEM: 0.045)), to moderate correlations for biceps brachii EMG (ICC = 0.59, CV: 0.54, SEM: 0.14) as well as for PF MVC force (ICC = 0.73; CV: 0.17, SEM: 17.1), and soleus EMG (ICC = 0.73, CV: 0.49, SEM: 0.03).

Intervention: Knee Extensors (KE) MVC Force

A significant interaction effect ($F_{(2,24)} = 5.23$, $p = 0.001$), revealed that after the interventions, dominant KE MVC force demonstrated significant, large-sized decrements for all fatiguing conditions (PF IPSI, PF CONTRA, EF IPSI, EF CONTRA) and no changes occurred under the control conditions (Table 2).

Elbow Flexor (EF) Single Absolute MVC Force and EMG

A large magnitude, condition × time interaction ($F_{(2,24)} = 3.81$, $p = 0.04$, $d = 1.1$) revealed a 6.6% ($p = 0.04$, $d = 0.18$) pre- to post-test ipsilateral EF MVC force decrease with no significant changes in the contralateral or control conditions (Table 3). A main effect for conditions ($F_{(2,24)} = 3.35$, $p = 0.05$, $d = 1.05$) demonstrated that the post-fatigue ipsilateral EF MVC (93.3% ± 10.5) was 8.7% ($p = 0.03$, $d = 1.04$) lower than the control (102.3% ± 6.7) condition. The contralateral (101.9% ± 12.4) condition was not significantly different compared with the control or ipsilateral conditions. There were no significant biceps brachii EMG, or triceps brachii EMG pre- to post-test differences.

Plantar Flexor (PF) Single Absolute MVC Force and EMG

There were no significant pre- to post-test differences between PF MVC force, soleus EMG, or gastrocnemius EMG activity. The main effect for time was small, albeit non-significant ($F_{(1,12)} = 3.8$, $p = 0.09$, $d = 0.35$) with overall PF MVC decrease of 4.8% for all conditions combined (includes controls).

EF vs. PF Single Normalized MVC Force and EMG

When comparing ipsilateral and control EF and PF conditions, a main effect for conditions ($F_{(1,12)} = 4.99$, $p = 0.045$, $d = 1.30$) revealed that the ipsilateral MVC peak force was 8.8% lower than control conditions. There were no significant main effects for muscles (EF vs. PF) or muscle × condition (IPSI vs Control) interactions. A comparison of ipsilateral and contralateral EF and PF conditions did not reveal any significant main effects for muscles, conditions ($p = 0.10$, $d = 0.55$, IPSI 92.1 ± 7.2% vs. CONTRA 97.8 ± 13.5% of pre-test) or interactions. There were no significant differences in EMG activity (Table 4).

Table 4. **Fatigue Index.**

Conditions	EF Fatigue Index	PF FatigueIndex
Ipsilateral	0.86 ± 0.11*	0.94 ± 0.13
Contralateral	0.82 ± 0.09*	1.03 ± 0.21
Control	0.85 ± 0.07	0.92 ± 0.09

Asterisks (*) indicate significant differences between the elbow flexors (EF) and plantar flexors (PF) for each identified condition (i.e. EF ipsilateral vs. PF ipsilateral and EF contralateral vs. PF contralateral).

EF and PF Fatigue Index

A significant muscle × condition interaction ($F_{(2,24)} = 4.08$, $p = 0.03$, $d = 1.10$) demonstrated greater fatigue indexes for the EF ipsilateral over PF ipsilateral (9.5%, $p = 0.04$, $d = 0.75$) and EF contralateral was greater than PF contralateral (20.3%, $p < 0.01$ $d = 1.5$) (Table 5). A significant main effect for muscle type ($F_{(1,12)} = 11.21$, $p < 0.01$, $d = 1.9$) was evident with higher fatigue index (12.6%, $d = 0.78$) for the EF (0.845 ± 0.13) versus the PF (0.967 ± 0.18), irrespective of the side (Figure 2).

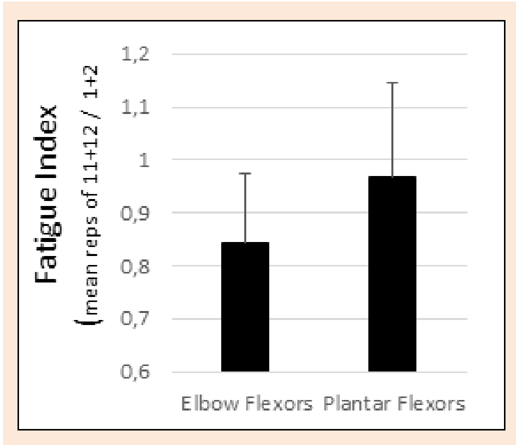

Figure 2. **Elbow flexors (EF) and plantar flexors (PF) testing fatigue protocol, post-unilateral dominant quadriceps fatigue: A fatigue index main effect for muscle type ($F_{(1,12)} = 11.21$, $p < 0.01$, $d = 1.9$) with all conditions combined was revealed.**

Table 5. **Pre-test and post-test MVC electromyographic (EMG: mV) activity over the six conditions. There were no significant main effcts or interactions.**

	PF IPSI	PF CONTRA	PF Control
Soleus pre-test	0.30 ± 0.10	0.27 ± 0.16	0.23 ± 0.11
Soleus post-test	0.25 ± 0.11	0.27 ± 0.15	0.25 ± 0.18
Gastrocnemius pre-test	0.26 ± 0.15	0.26 ± 0.12	0.22 ± 0.15
Gastrocnemius Post-test	0.21 ± 0.17	0.27 ± 0.17	0.23 ± 0.16
Biceps Brachii pre-test	0.78 ± 0.38	0.78 ± 0.41	0.74 ± 0.35
Biceps brachii post-test	0.74 ± 0.41	0.74 ± 0.42	0.78 ± 0.45
Triceps brachii pre-test	0.08 ± 0.03	0.08 ± 0.03	0.079 ± 0.02
Triceps brachii post-test	0.07 ± 0.03	0.08 ± 0.03	0.076 ± 0.02

Discussion

Important findings in the present study included the significant fatigue-induced maximal force impairment (during single MVC) that was only observed for ipsilateral EF and not the PF. Additionally, the ipsilateral EF experienced significantly greater fatigue index than the PF ipsilateral and the contralateral EF exceeded the contralateral PF during the repeated MVCs. However, there were no corresponding significant changes in EMG activity. There were no significant differences between contralateral EF and PF post-intervention single MVC force/torque or EMG. The ipsilateral EF experienced significantly greater fatigue than the ipsilateral and contralateral PF during the repeated MVCs.

The findings of the present study are in accordance with several other investigations that found a reduction of upper body muscle force output following lower body fatigue (Aboodarda et al., 2017; Ben Othman et al., 2017; Rasmussen et al., 2010; Šambaher et al., 2016; Sidhu et al., 2014). Indeed, the 6.6% decrease in ipsilateral EF MVC immediately following KE fatigue is consistent with the 10.7% (Ben Othman et al., 2017), 5% (Halperin et al., 2014b), and 6.1% (Šambaher et al., 2016) values reported previously. However, both the Ben Othman et al. (2017) and Šambaher et al. (2016) studies employed dynamic bilateral KE to induce fatigue whereas Halperin et al. (2014b) employed the same protocol as the present study. Additionally, both Halperin et al. (2014b) and Šambaher et al. (2016) found endurance deficits with a repeated MVC protocol, similar to the results of this study. Analyses of both the fatigue index and the overall pattern of repeated MVC deficits in the present study emphasized the greater NLMF effects with ipsilateral EF.

However, contradictory to the present study's findings, Halperin, et al. (2014a) 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 regardless of whether the dominant KEs or EFs were fatigued, whereas no differences were found for the non-dominant EFs. Other studies have also not detected contralateral EF force or activation deficits following unilateral fatigue (Aboodarda et al., 2016; Humphry et al., 2004; Li et al., 2019). Potential explanation could be the differences in experimental protocols (e.g. fatiguing and testing the ipsilateral vs. contralateral limbs) or training status of participants (recreationally active vs. competitive athletes). It is possible that trained individuals may not accumulate as much circulating metabolites (Halperin et al., 2014b;

Halperin et al., 2015), or experience a similar degree of neural inhibition (Behm, 2004), mental fatigue (Marcora et al., 2009) or perceived fatiguability (Enoka and Duchateau 2016). However, in the present study with both recreationally active and trained participants, there was evidence of NLMF of the ipsilateral EF. Interestingly, the present study found significant NLMF in ipsilateral EF and not contralateral EF and this asymmetry could explain the difference between studies. The Behm et al. (2021) NLMF meta-analysis which reported evidence of only trivial magnitude NLMF, examined primarily contralateral responses, generally corresponding with the lack of contralateral NLMF in the present study. These present results suggest that NLMF is not only muscle specific, but also side specific (ipsilateral vs. contralateral effects).

The main underpinning mechanism for the greater NLMF in ipsilateral versus contralateral EF is not clear. Cortically, contralateral motor signals from one hemisphere to another would necessitate a transit across the corpus callosum (Meyer et al., 1995) and then to the target muscle groups. It is indeed unclear how the geometry of the motor cortex mapping between neighboring motor cortical areas (e.g. EF and KE) and transfer of motor signals across transcallosal connection to the contralateral motor cortex could affect the NLMF effects between ipsilateral and contralateral limbs. However, it is worth noting that prior studies have demonstrated that unilateral exercise (EFs and KEs) could enhance corticomotor excitability in the hemisphere controlling descending motor output to the contralateral limbs (Aboodarda et al., 2015; 2016; 2017; Carson et al., 2004; Hess et al., 1986; Hortobagyi et al., 2003; Šambaher et al., 2016). Since the ipsilateral and contralateral PF did not experience significant NLMF, possible changes in trans-hemispheric excitation or inhibition of the PF may not have played a role due to factors outlined in the next paragraph. Therefore, although speculative, it could be postulated that increased excitatory motor output to the contralateral hemisphere could explain the distinct ipsilateral and contralateral NLMF responses observed in the EFs after the KE fatiguing protocol.

There are a number of possible mechanisms for EF displaying greater NLMF effects than PF. The most likely factor contributing to the noted differences in fatigability during the post-test repeated MVCs between ipsilateral EF and PF is the variation of fibre composition in the observed muscles. The soleus muscle is composed of more fatigue-resistant type I fibers (Edgerton et al., 1975; Johnson et al., 2014). In contrast, the biceps brachii contains a higher density of type II fibres (Jennekens et al., 1971; Johnson et al., 1973). The rectus femoris, part of the fatigued KE 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 contribute to its susceptibility to NLMF. In addition, the PF would be influenced by different patterns of reflex actions such as the central pattern generator for locomotion (Kern et al. 2001) and thus their respective spinal reflex connectivity will differ (Duysens and Van de Crommert, 1998; MacKay-Lyons, 2002). Hence, the greater PF fatigue endurance may obscure any possible ipsilateral versus contralateral NLMF differences in this muscle group. The possibility of these postulated mechanisms needs to be further investigated.

The EMG signal is not a sensitive measure of spinal or cortical inhibition as it includes all neural activity from the cortex to muscle compound action potential activity (Sadoyama and Miyano, 1981; Viitasalo and Komi, 1975). Furthermore the curvilinearity of the EMG-force relationship shows a plateau of EMG activity at higher force intensities resulting in no apparent change in neuromuscular activity with either increases or decreases in force output at near maximal efforts (Perry and Bekey, 1981; Solomonow et al., 1990). Hence, any small differences in central motor output may not have been detected by the surface EMG electrodes.

The Halperin et al. review (2015) postulated that in addition to neural inhibition, NLMF may be influenced by biochemical, biomechanical, or psychological factors. Exercise-induced circulating metabolites travel globally as shown by increased blood lactate concentration at the contralateral non-exercised muscle (Aboodarda et al., 2020; Halperin et al., 2014b) and thus biochemical factors would not contribute to solely greater ipsilateral impairments. Biomechanical factors are related to a unilateral exercise protocol that would necessitate trunk muscle activation to maintain stability (Behm and Anderson, 2006; Behm et al., 2005), but there is no rationale that this deficit would be more predominant with ipsilateral versus contralateral muscles. Finally, mental fatigue may arise from the prolonged focus and attention needed to maintain fatiguing contractions causing participants to perceive the subsequent exercise as more strenuous, and thus to cease the activity sooner (Marcora et al., 2009; Pageaux et al., 2013; 2014). Similarly, this mental fatigue should have a global effect and it is unlikely for this factor to inhibit one side to a greater extent than the other.

A methodological limitation of this study is related to the post-intervention MVC of the non-local muscles. While EF were tested within 5-10s post-intervention, PF testing was performed within 30s following the intervention, PF MVCs were typically delayed accommodating transferring the subject to the PF testing device. This short delay may have been sufficient to partially recover from fatigue-induced deficits to PF peak force. PF fatigue has been shown to recover approximately 85% following as little as 1min rest (Iguchi and Shields, 2012). Therefore, it is possible that NLMF in the PF was underestimated in the present study. Further, recruiting both sexes and individuals of varying trained states increased the variability of results possibly affecting the ability to observe statistical significance.

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 fatigue index performance deficits. The results of this study suggest that NLMF effects are muscle specific and could be influenced by 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 (i.e., KE) hindering subsequent upper body performance could be an important consideration for rehabilitation, recreation, and athletic 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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Key points

- Non-local muscle fatigue effects were found in the el bow flexors ipsilateral to the fatigued knee extensors but not in the contralateral elbow flexors.
- Non-local muscle fatigue effects were not apparent in ipsilateral or contralateral plantar flexors to the fatig ued knee extensors.
- Ipsilateral elbow flexors displayed single MVC as we ll as fatigue index performance deficits.
- The results of this study suggest that non-local muscl e fatigue effects are muscle specific.

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