The effect of dominant first dorsal interosseous fatigue on the force production of a contralateral homologous and heterologous muscle

<table>
<thead>
<tr>
<th>Journal:</th>
<th>Applied Physiology, Nutrition, and Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID</td>
<td>apnm-2018-0583.R2</td>
</tr>
<tr>
<td>Manuscript Type:</td>
<td>Article</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>11-Nov-2018</td>
</tr>
<tr>
<td>Complete List of Authors:</td>
<td>Li, Yimeng; Memorial University of Newfoundland - School of Human Kinetics and Recreation, School of Human Kinetics and Recreation Power, Kevin; Memorial University of Newfoundland - School of Human Kinetics and Recreation, School of Human Kinetics and Recreation Marchetti, Paulo; California State University Northridge College of Health and Human Development, Department of Kinesiology Behm, David; Memorial University of Newfoundland,</td>
</tr>
<tr>
<td>Keyword:</td>
<td>fatigue, fatigue &lt; exercise, exercise physiology &lt; exercise, muscle fatigue &lt; muscle, sports science &lt; biomechanics, resistance exercise &lt; exercise</td>
</tr>
<tr>
<td>Is the invited manuscript for consideration in a Special Issue?</td>
<td>Not applicable (regular submission)</td>
</tr>
</tbody>
</table>
The effect of dominant first dorsal interosseous fatigue on the force production of a contralateral homologous and heterologous muscle

Authors: Yimeng Li¹, Kevin E. Power¹, Paulo H. Marchetti², and David G Behm¹

Institution: ¹ School of Human Kinetics and Recreation, Memorial University of Newfoundland, St. John’s, Newfoundland, Canada, A1M 3L8
             ² College of Health and Human Development, Department of Kinesiology, California State University, Northridge; Northridge, California, USA, 91330

Corresponding Author: David G Behm
                     School of Human Kinetics and Recreation, Memorial University of Newfoundland, St. John’s, Newfoundland, Canada, A1M 3L8
dbehm@mun.ca
Tel: 709-864-3408
Fax: 709-864-3979
Abstract

Crossover and non-local muscle fatigue (NLMF) has generally focused on large muscle groups. It is unclear whether fatigue of a small muscle can result in NLMF of a larger muscle. The purpose of the present study was to examine the effect of small muscle (first dorsal interosseous; FDI) fatigue on the force and activation of contralateral homologous and larger heterologous muscles (biceps brachii, BB). Fifteen right-handed, male subjects performed three pre-test index finger abduction or elbow flexion maximum voluntary isometric contractions (MVICs) on the non-dominant side. Subsequently, they performed two 100s index finger abduction MVICs on the dominant side (experimental [fatigue] group) or rested for 5 minutes (control group).

Afterwards, a single MVIC and a 12 repetition MVIC fatiguing protocol were completed with index finger abduction or elbow flexion on the non-dominant side. Force and electromyography (EMG) were measured from both sides. The force and EMG (median frequency:MDF) of non-exercised index finger abductors (IFA)/FDI and elbow flexors (EF)/BB significantly decreased after the fatiguing protocol. Compared with the control condition, the non-exercised IFA (12.5% and 5.7%) had significantly greater force and MDF fatigue indexes than the EF (5.2% and 1.7%).
There were no significant force differences with the single MVIC test between conditions. The small muscle fatiguing protocol produced NLMF effects on both contralateral homologous and larger heterologous muscles, with the force decrements greater with the homologous muscle.

**Key words:** fatigue; exercise physiology; muscle fatigue; sports science; resistance exercise
Introduction

Neuromuscular fatigue is not limited to the working muscle but also may present on non-exercised muscles both contralateral and/or ipsilateral to the actively fatigued muscle. This phenomenon is known as crossover fatigue or non-local muscle fatigue (NLMF) (Martin and Ratty, 2007; Halperin et al. 2015). There is substantial evidence demonstrating crossover effects on contralateral upper (Aboodarda et al. 2016; Sidhu et al. 2014) and lower (Doix et al. 2013; Kennedy et al. 2013a; Halperin et al. 2014a; Hamilton and Behm, 2017) non-exercised limbs following a unilateral fatiguing protocol. However, the literature provides varied results. For example, Arora et al. (2015) did not find any changes in the maximal voluntary isometric contraction (MVIC) force of non-exercised knee extensors after a unilateral knee extensor isometric fatiguing protocol (16s repetitions of 30% MVIC with 4s rest until force decreased to 50% MVIC). Alcaraz et al. (2008) also reported that there was no NLMF effect on non-exercised upper body muscles followed a dynamic upper and lower body fatiguing protocol (5 sets of bench press + leg extensions + ankle extensions, 35-second inter-set rest; 6 repetition maximum [6RM] loads).
Presently, most NLMF studies focus on large muscle groups (e.g. elbow flexors (EF) or knee extensors (quadriceps)), with few studies involving small muscles (e.g. finger muscles). For instance, only three papers have examined NLMF effects on the unilateral first dorsal interosseous (FDI) after the fatigue of the contralateral homologous muscle, and the results were inconsistent (Zijdewind et al. 1998; Post et al. 2008; Kavanagh et al. 2016). This inconsistency may be attributed to the differences between protocols. A review by Boyas and Guevel (2011) indicated that lower intensity, sustained fatiguing contractions are particularly influenced by central factors, whereas peripheral factors play a more substantial role with higher intensity fatiguing contractions. However, Zijdewind et al. (1998) reported that a prolonged, unilateral submaximal isometric contraction fatigue protocol (30s cycles of 30% MVIC with 4s rest until failure) for the FDI did not elicit NLMF effects on the contralateral FDI, whereas Post et al. (2008) demonstrated significant NLMF effects on FDI from both sustained maximal (MVIC for 2 min) and submaximal (30% MVIC for 26s with 4 s rest until failure) isometric protocols. Kavanagh et al. (2016) also showed NLMF effects on the FDI by using an MVIC intermittent contraction protocol (4s MVIC with 2s rest until force decreased to 50% MVIC) to fatigue the
contralateral FDI. Despite the different fatigue protocols, the most important similarity of the three papers is that the tested, non-exercised muscles were the contralateral homologous muscle. However, the NLMF effect from fatigue of the FDI to a non-exercised heterologous muscle has not been investigated. Furthermore, since most of the NLMF studies have investigated larger muscle groups, the NLMF effect of a smaller muscle group upon a larger heterologous muscle group is also unknown.

Activation of group III/IV muscle afferents from the prolonged maintenance of muscle contractions provides inhibitory feedback to the central nervous system (CNS) (Bigland-Ritchie et al. 1986; Gandevia et al. 1996). This negative influence potentially could have a widespread effect to non-exercised muscles (Amann et al. 2011; Kennedy et al. 2013b; Sidhu et al. 2017). Indeed, Kennedy et al. (2013b) demonstrated that post-fatigued firing of group III/IV muscle afferents of the adductor pollicis, decreased the isometric force production of ipsilateral non-exercised EF. Furthermore, studies showed that a smaller muscle mass evokes stronger, local signals to group III/IV muscle afferents compared to weaker and more diffuse signals from a much larger muscle mass (Rossman et al. 2012, 2014). Therefore, it is reasonable to speculate
that a small muscle fatiguing protocol would produce NLMF effects not only to a non-exercised homologous muscle, but also to larger heterologous muscles.

The primary aim of the present study was to investigate the effect of small muscle (FDI) fatigue (2 × 100s MVIC) on the force production of the contralateral homologous and a larger heterologous muscle (biceps brachii: BB). It was hypothesized that the fatiguing contraction of the unilateral FDI could result in force and activation deficits with both contralateral non-exercised FDI and BB.

Methodology

Participants

A power analysis (G*Power 3.1.9.2) was used to calculate the sample size of this study using a statistical power of 0.80, and alpha level of p < 0.05. This was based on samples of four studies (Zijdewind et al. 1998; Post et al. 2008; Kennedy et al. 2013b; Kavanagh et al. 2016) that had participants engaged in NLMF with fatiguing hand muscles. The predicted mean sample size was calculated to be 8 participants. However, 15 participants from the university population were recruited to compensate for the possibility of any drop outs and ensure sufficient power of the
study. All subjects were right hand, dominant men, none of who had a history of musculoskeletal or neurological diseases. Subjects were verbally informed of the procedures and were then asked to read and sign the consent form if they were in agreement. Subjects were asked to refrain from ingesting caffeine and participating in vigorous physical activity at least 1 day before attending each experimental session. The study was conducted in accordance with the declaration of Helsinki and approved by the Interdisciplinary Committee on Ethics in Human Research of Memorial University of Newfoundland (20181017-HK).

**Experimental setup**

Subjects were seated in a chair, elbow slightly flexed (120°-130° angle) (Kavanagh et al. 2016) with their pronated forearm supported on the table. All fingers were fully extended with the palm facing down, placed on a custom-designed device for measuring index finger abduction force. The elbow, distal forearm, digits 3-5 and the thumb were secured with Velcro straps to prevent any movements during the contractions. The index finger metacarpophalangeal joint was positioned at 0° abduction and 0° flexion, and the interphalangeal joints were maintained in extension. The proximal interphalangeal joint was pressed against a calibrated strain gauge.
(Transducer Techniques Inc., MLP-300-CO; sensitivity = 2mV/V, CA, USA) during the experiment, which was connected to the custom-designed device. (Fig.1a) Both sides of the custom designed device were identical such that the device could be rotated 180 degrees in order to test both limbs.

**Maximal voluntary isometric contractions (MVIC)**

The index finger abduction forces were recorded from the dominant side during the fatiguing intervention and from the non-dominant (non-fatigued) side during the pre- and post-tests. The forces were sampled by the Daytronic conditioner (Daytronic, Model 3270, OH, USA). The conditioner was connected to the Biopac MP150 (Biopac System Inc., DA 100: analog-digital converter MP150WSW; Holliston, MA) data collection system for force analysis. Before starting the contractions, subjects were instructed to maintain contact with the strain gauge.

The elbow flexion forces from the non-dominant side (non-fatigued, tested limb) were collected during the pre- and post-test. Forces from the tested (non-dominant) EF were collected by having subjects sit on a chair with hips and knees flexed to 90° with the elbow flexed at 90°
and supported by an arm-rest, the forearm was in a supinated position while the wrist was
inserted into a padded strap attached to a high tension wire attached to a load cell (Omega
Engineering Inc., LCCA 500 pounds; sensitivity = 3 mV/V, Quebec, Canada), which was used to
measure elbow flexion force (Fig. 1b). The forces were sampled at 500 Hz by the Biopac data
collection system (Biopac Systems Inc. DA 100, Holliston, MA).

Surface electromyography (EMG)

Surface electromyography (EMG) was recorded from the non-dominant (non-fatigued) FDI
or BB during the pre- and post-tests. Following the skin preparation, bipolar Ag/AgCl electrodes
(Ag/AgCl; Kendall MediTrace H69P foam electrodes, Holliston, Massachusetts, USA) were
placed over the muscle belly of the superficial head of FDI, and over the distal tendon at the
second metacarpophalangeal joint. The reference electrode was placed over the ulnar styloid
process (Post et al. 2008; Kavanagh et al. 2016). For the BB, bipolar Ag/AgCl electrodes
(Kendall130 MediTrace foam electrodes, H69P, Holliston, Massachusetts, USA) were placed
over the midpoint of the muscle belly. The inter-electrode spacing was 10 mm. All the EMG
signals were collected by the Biopac data acquisition system (AcqKnowledge III, Biopac System
Inc. Holliston MA. USA) at a sample rate of 2000 Hz (impedance = 2 MΩ, common mode
rejection ratio >110 dB min (50/60 Hz), noise >5 μV). A bandpass filter (10–500 Hz) was
applied prior to digital conversion.

*Experimental protocol*

Subjects were required to attend the lab for four sessions and performed one of the
following four conditions: 1) unilateral fatigue of the dominant FDI and test the contralateral FDI
(Fatigue-FDI); 2) unilateral fatigue of the dominant FDI and test the contralateral BB (Fatigue-
BB); 3) no fatigue intervention and test the contralateral (non-dominant) FDI (Control-FDI); 4)
no fatigue intervention and test the contralateral (non-dominant) BB (Control-BB). The
conditions were randomized and approximately 48 hours of rest was allowed between testing
days. This duration of recovery has been utilized in a number of isometric fatigue experiments
from this laboratory (Aboodarda et al. 2015; 2016; 2017; Halperin et al. 2014a;b; Hamilton et al.
2017; Sambaher et al. 2016). Subjects were familiarized with the testing procedures during the
first testing day.

Subjects initially performed a warm-up for all the conditions that included 10 isometric
contractions at an intensity level equating to approximately 50% of their perceived maximum on either index finger abductors (IFA) or EF. The work-to-rest ratio was 2s/2s.

(1) Pre-test

A minute after the warm-up, participants were required to perform 3 MVICs on the non-dominant test IFA or EF with each contraction lasting 5s and 1 minute of rest given between contractions.

(2) Fatiguing intervention

Following the warm-ups and pre-tests, subjects performed the fatiguing intervention which included two; 100s MVICs of the IFA on the dominant side with 30s of rest provided between repetitions. Participants were provided with verbal encouragement during the fatigue protocol.

Verbal encouragement involved the same verbiage (Go! Harder! Harder!) every 20 seconds to ensure consistent external motivation. The non-dominant, test arm was rested on the participant’s thigh with fingers relaxed and extended. The researchers monitored this arm and reminded the participant to keep the non-dominant, test limb in a relaxed state. Participants were initially informed of the duration of the fatigue protocol but were not informed of the end point of the
fatigue test in an attempt to minimize a pacing effect (Hamilton and Behm 2017). For the control condition, they were asked to be seated and rest for 5 mins, which was the estimated duration to complete the fatiguing protocol.

(3) Post-Intervention test

Immediately after the fatigue intervention of the dominant IFA, subjects performed a single and then a repeated MVIC protocol with either the contralateral, non-dominant IFA or EF (same movement as the pre-test). The rest interval between the single MVIC and the repeated MVIC protocol was 30 seconds. The repeated MVIC protocol consisted of 12 MVICs at a work to rest ratio of 5s/10s (Halperin et al. 2014a, 2014b). Standardized verbal encouragement was provided at the 3 second mark of each MVIC and included the same wording as during the MVIC fatigue protocol.

Data analysis

Force and EMG data were recorded and analyzed with a commercially designed software program (Acq-Knowledge III, Biopac Systems Inc., Holliston MA, USA). The mean force for each MVIC during pre- and post-test was determined over a 3s window defined as 1.5s before
and following the peak force of each contraction. All mean force data were reported as the percentage of highest pre-test values. The mean amplitude of the root mean square (RMS) EMG was calculated by the software from 50 ms bins within the same 3s window as applied to the force analysis. The absolute mean amplitude measures were then normalized to the highest pre-test value and reported as a percentage. A fast Fourier transform (FFT) was also applied to EMG signal for the pre- and the post-test. The FFT median frequency (MDF) was computed and normalized to the highest pre-test value and reported as a percentage. The EMG MDF is a common and sensitive indicator of fatigue (Bartuzi and Roman-Liu 2014, Dimitrova and Dimitrov 2003). The fatigue index (FI) was calculated for force RMS EMG, and FFT MDF during the post-test using following formula: FI (%) = (maximal – minimal) * 100/maximal (Adam, 2002).

Statistical analysis

First, normality (Kolmogorov–Smirnov) and homogeneity of variances (Levene) tests were conducted for all dependent variables. If the assumption of sphericity was violated, the Greenhouse-Geisser correction was employed. Secondly, two sets of two-way repeated measures
ANOVA tests were conducted. A paired t-test was used to compare the force and EMG values with the first and last 5 seconds of each set of the dominant IFA fatiguing intervention. The analysis of the contralateral, non-dominant, mean force, the FFT MDF and the EMG RMS involved the 2 conditions (fatigue vs. control) × 12 repeated MVICs for IFA/FDI and EF/BB.

The analysis of contralateral, non-dominant, a) single MVIC, b) the force differences between the single MVIC and the first MVIC of the 12-MVIC protocol, and c) the fatigue indexes (force, FFT MDF) involved a 2 conditions × 2 muscles analysis. Paired t-tests with Holm–Bonferroni corrections were used to decompose significant interactions, and Bonferroni post hoc tests were used if main effects were found. An alpha level of 0.05 was used to determine statistical significance. Cohen’s effect size (d) was calculated, and results evaluated on the following criteria: < 0.35 trivial; 0.35-0.80 small; 0.80-1.50 moderate; and >1.50 large, for recreationally trained subjects (Cohen, 1988). Data was reported as mean ± standard deviation (SD).

Results

Fatigue intervention of the dominant IFA

The fatiguing intervention resulted in significant (p<0.0001) 69.2% (t=27.6; d=11.3) and
67.3% (t=50.6; d=9.8) force decreases with the first and second set respectively. Initial forces in the first five seconds of the first set were 31.9 ± 2.1 kg, which decreased to 9.8 ± 1.8 kg. The second set forces dropped from 30.5 ± 2.9 to 9.9 ± 1.3 kg. EMG significantly (p<0.0001) decreased 44.9% (t=5.8; d=1.3) and 61.4% (t=12.4; d=2.8) in the first (0.46 ± 0.16 to 0.26 ± 0.14mV) and second (0.56 ± 0.14 to 0.22 ± 0.1mV) sets of the fatiguing intervention respectively.

**Mean force during the post-tests.**

A significant main effect was found for conditions (F (1,14) = 3.40, p = .036; d = 0.49) and repetitions (F (11,154) = 5.72, p < .001; d = 0.54) but no interactions were found (F (1,14) = 0.03, p = .370; d = 0.14) for the IFA (Fig. 2a). The averaged forces of non-exercised IFA in the control session were 10.6 ± 4.3% greater compared with the fatigue session. Also, the averaged forces significantly dropped 27.2 ± 2.3% from the single MVIC to the last post-test MVIC (#12) across both conditions.

A significant main effect was found for conditions (F (1,14) = 2.78, p = .044; d = 0.46) and repetitions (F (11,154) = 4.55, p = .004; d = 0.41) for the EF (Fig. 2b), but no interactions were
found \( F_{(1,14)} = 1.10, p = .420; d = 0.15 \). The averaged forces of non-exercised EF in the control session were 14.8 ± 10.5% greater than the fatigue session. Also, the averaged forces (main effect for repetitions : data collapsed over conditions) were significantly decreased 14.7 ± 3.1% from the single MVIC to the last post-test MVIC (#12).

**EMG MDF during the post-tests**

A significant main effect was found for repetitions \( F_{(11, 154)} = 3.19, p = .041; d = 0.41 \), but no significant differences between conditions \( F_{(1,14)} = 0.07, p = .281; d = 0.10 \) or interactions \( F_{(1,14)} = 0.14, p = .288; d = 0.15 \) were found for the FDI (Fig.3a). The mean MDF of non-exercised FDI EMG were significantly decreased from the single MVIC to the last repeated MVIC (#12) across two conditions by 8.3 ± 4.0%.

A significant main effect was found for conditions \( F_{(1,14)} = 2.98, p = .045; d = 0.42 \), but no significant main effect was found for repetitions \( F_{(11, 154)} = 1.05, p = .252; d = 0.22 \) or interactions for the BB \( F_{(1,14)} = 0.97, p = .178; d = 0.23 \) (Fig.3b). The mean MDF of non-exercised BB EMG were 4.3 ± 2.9% higher in the control session than in the fatigue session.

**Single MVIC Force**
No significant main effect was found for conditions ($F_{(1,14)} = 0.05, p = .945; d = 0.01$), muscles ($F_{(1,14)} = 1.06, p = .589; d = 0.04$) or interactions ($F_{(1,14)} = 0.02, p = .696; d = 0.02$).

**Force differences between the single MVIC and the 1st MVIC of the 12-MVIC protocol**

A significant main effect was found for conditions ($F_{(1,14)} = 3.88, p = .021; d = 0.49$) and muscles ($F_{(1,14)} = 2.78, p = .047; d = 0.43$) but no interactions were found ($F_{(1,14)} = 0.06, p = .773; d = 0.01$) (Fig. 4). After the fatiguing protocol, the force differences between the single MVIC and the first repetition of the repeated MVICs protocol increased by $10.2 \pm 7.2\%$, the EF $(12.7 \pm 18.9\%)$ had greater force decrease than the IFA $(6.2 \pm 8.8\%)$.

**Force Fatigue index**

A significant main effect was found for conditions ($F_{(1,14)} = 4.62, p = .021; d = 0.49$) and muscles ($F_{(1,14)} = 3.89, p = .029; d = 0.43$) but no interactions were found ($F_{(1,14)} = 1.79, p = .754; d = 0.03$). After the fatiguing protocol, the force fatigue index increased by $8.9 \pm 6.3\%$. The IFA fatigue index $(12.5 \pm 8.9\%)$ increased more than the EF $(5.2 \pm 3.7\%)$.

**FFT MDF fatigue index**

A significant main effect was found for conditions ($F_{(1,14)} = 3.31, p = .041; d = 0.38$) and
muscles \(F_{(1,14)} = 4.69, p = .039; d = 0.33\) but no interactions were found \(F_{(1,14)} = 0.57, p = .658; d = 0.03\). After the fatiguing protocol, the MDF fatigue index increased by 3.7 ± 2.4%.

The FDI MDF fatigue index \(5.7 \pm 1.9\%\) increased more than the BB \(1.7 \pm 3.5\%\).

**RMS EMG**

After the fatiguing protocol, no significant FDI or BB RMS EMG main effect were found for conditions \(F_{(1,14)} = 0.02, FDI: p = .724; d = 0.02; F_{(1,14)} = 1.05, BB: p = .672; d = 0.03\), repetitions \(F_{(11,154)} = 1.02, FDI: p = .462; d = 0.12; F_{(11,154)} = 2.01, BB: p = .581; d = 0.11\) or interactions \(F_{(1,14)} = 1.27, FDI: p = .748; d = 0.09; F_{(1,14)} = 1.97, BB: p = .230; d = 0.16\). There were also no significant RMS EMG fatigue index results.

**Discussion**

The primary findings were that unilateral fatigue of the dominant index finger led to significant decrements in the force production and EMG MDF of contralateral non-exercised homologous and a larger heterologous muscle group (EF/BB). The contralateral non-exercised IFA/FDI exhibited a greater force and EMG MDF fatigue index than the non-exercised EF/BB after the unilateral fatigue protocol.
Although NLMF has been examined, results are conflicting and the possible mechanisms are still debatable (Halperin et al. 2015). Most NLMF studies focus on large muscle groups such as knee extensors and EF (Halperin et al. 2014a, 2014b; Kawamoto et al. 2014; Aboodarda et al. 2015, 2016, 2017; Šambaher et al. 2016). Even though there are three studies that fatigued a small muscle, the tested muscles were homologous only (Zijdewind et al. 1998; Post et al. 2008; Kavanagh et al. 2016). Based on our knowledge, the present study is the first study that examined NLMF effects on both a homologous and a larger heterologous muscle from the fatiguing of a contralateral small volume muscle.

The force reduction of non-exercised IFA after fatiguing of contralateral IFA is in agreement with prior work (Post et al., 2008; Kavanagh et al., 2016). Although the fatiguing protocols in these two studies and the present study were not precisely similar, all three studies included a maximal contraction fatiguing protocol. On the contrary, a submaximal contraction (30% of MVIC) fatiguing protocol (Zijdewind et al. 1998) did not find any NLMF on non-exercised FDI after contralateral FDI fatigue. However, Post et al. (2008) presented significantly reduced non-exercised IFA force after both submaximal (30% MVIC) and maximal fatiguing
contractions of the contralateral IFA. Based on a limited scope of studies, maximal contraction protocols have produced more consistent NLMF in small muscles.

Although there are few studies investigating the NLMF effect on a larger muscle from fatigue of a small muscle group, the force reduction of non-exercised EF after fatiguing of unilateral IFA results were in partial agreement with some similar studies (Rossman et al. 2012, 2014; Kennedy et al. 2013b). Kennedy et al. (2013b) found that maintained firing of group III/IV muscle afferents after a fatiguing adductor pollicis contraction could significantly reduce the force of non-exercised ipsilateral EF. Contrary to the present study, instead of testing the NLMF effect on contralateral EF immediately after a hand muscle fatiguing protocol, Kennedy et al. (2013b) subsequently blocked hand circulation for two minutes to keep firing of group III/IV muscle afferents, to investigate the contribution of post-fatigued activated group III/IV muscle afferents on NLMF. Similar to the present study, EF force deteriorated after hand muscle fatigue (Kennedy et al. 2013b). Indeed, the inhibitory feedback from activated group III/IV muscle afferents to the CNS has been shown to provide a negative influence on exercise performance of the affected limb (Amann et al., 2011, 2012; Kennedy et al. 2013b; Sidhu et al. 2017) and
potentially to the non-exercised muscles as well (Amann 2011, Amann et al. 2013, 2015, Sidhu et al. 2014). Afferent information does not only influence the affected muscle, but may also influence ipsilateral and/or contralateral heteronymous muscles at either segmental (Zehr et al. 2016) and/or suraspinal levels (Mrachacz-Kersting et al. 2018). Thus there are multiple afferent pathways to disseminate information regarding local fatigue processes to non-local or distant muscles throughout the central nervous system.

Kennedy et al. (2013b) demonstrated that this inhibitory feedback plays an important role in NLMF, even when the effects are transferred from a small fatigued muscle to a larger non-exercised muscle. Consequently, in the present study, the force decrement of a larger non-exercised muscle from the unilateral fatigue of a small muscle (without ischemia) might also be attributed to muscle afferent (i.e. group III/IV muscle afferents) inhibition. Moreover, it has been proposed that the less muscle mass involved in the exercise, results in a greater relative contribution of peripheral fatigue (Rossman et al. 2014). This is attributed to a smaller muscle mass evoking stronger, local group III/IV muscle afferent signals compared to more diffuse signals provided by a larger muscle mass (Rossman et al. 2012, 2014).
Supraspinal or cortical influences could also impact NLMF. NLMF effects have elicited decreased supraspinal excitability and enhanced spinal motoneuron excitability when examining the effect of bilateral EF fatigue on contralateral knee extensor force (Aboodarda et al. 2015), as well as with unilateral knee extensor fatigue effects upon contralateral EF force (Sambaher et al. 2016). Conversely, increased supraspinal excitability has also been reported when examining unilateral EF fatigue effects upon contralateral EF (Aboodarda et al. 2016). Furthermore, it was found that corticospinal excitability of the EF following a knee extensors fatiguing protocol, was either increased when tested with a 100% MVIC or suppressed when testing with a 5% MVIC (Aboodarda et al. 2017). Although these studies highlight that upper limb (i.e. BB) corticospinal responses are not only dependent upon the contraction history of non-local or distant muscles (i.e. FDI), the varied findings make it presently difficult to ascertain the excitatory or inhibitory role of the cortical responses in this study. Further research is needed in this area.

The results also demonstrated that non-exercised IFA/FDI had a higher fatigue index for both force and EMG MDF compare to non-exercised EF/BB after the contralateral fatiguing of the IFA. This implies that the NLMF elicited from the IFA on non-exercised heterologous larger
muscles was not as substantial as with a homologous muscle. This may be attributed to alterations of corticospinal excitability. Since hand and finger muscles have larger corticospinal projections than many other muscles (Takahashi et al. 2009), the alteration of corticospinal excitability that contributes to the fatigue of contralateral hand and finger muscles might be greater than other muscles (Takahashi et al. 2009; Matsuura et al. 2015).

It has been suggested that there is movement coordination between homologous muscles when a person moves limbs simultaneously, in other words, a tendency to synchronize movement between homologous muscles (Swinnen, 2002). Furthermore, this phenomenon is most common in fingers, for instance, bimanual index finger oscillation paradigm has been a classical model to study coactivation of homologous muscles (Kelso, 1984; Haken et al. 1985). One possible explanation is that contralateral homologous muscles share a common neural pathway (Carson, 2005), thus there might be mediating bilateral interactions between limbs (Ridderikhoff et al. 2005; Post et al. 2008). Indeed, Post et al. (2008) found that during the unilateral FDI fatiguing protocol, the coactivation of contralateral non-exercised FDI increased, and NLMF also presented after the fatiguing protocol. However, a limitation of this study is that
co-activation levels were not monitored.

Fatiguing studies are not only physically demanding, but can also be psychologically challenging (Budini et al. 2014, Dorris et al. 2012; Marcra, 2008, Pageaux et al. 2014). In the present study, participants performed a maximal intensity fatiguing protocol on a muscle group (index finger abductor) that is not frequently subjected to such a protocol. A smaller muscle mass can elicit greater perceived exertion compared to a larger muscle mass at the same contraction intensity (Faigenbaum et al. 2004; Sweet et al. 2004; Mayo et al. 2014). An uncommon or unfamiliar action could produce response inhibition (Pageaux et al. 2014) greater perception of effort (Marcra et al. 2009, Van Cutsem et al. 2017, Wright 2008), decreased motivation (Marcra et al. 2009), adding to the mental challenge and fatigue (Pageaux et al. 2014, 2016).

Although not directly measured, psycho-physiological effects may have provided some contributions to the small muscle fatigue protocol-induced NLMF effects on a non-exercised larger muscle.

Our results also showed that, after the fatiguing protocol, no significant force decrements were observed with a single MVIC of non-exercised EF and IFA, whereas significant force
decreases for both muscles were presented in the first MVIC of the repeated MVICs protocol.

This is in agreement with Halperin et al. (2014b), who demonstrated that the EF only had force decrement in the last five MVICs during the repeated MVICs protocol after knee extensor fatigue. Thus it has been suggested that the NLMF effect is more evident during repeated MVICs protocol rather than a single MVIC (Halperin et al. 2015) and has also been shown with EF (Triscott et al. 2008) and knee extensors (Amann et al. 2013).

Interestingly, our study found a significant and substantial force decrease from the single MVIC to the first repetition of the MVICs repeated protocol (Figure 4). In anticipation of the subsequent series of contraction, the participants may subconsciously decreased their initial MVIC force output to cope with the subsequent fatiguing task possibly to avoid a future catastrophic event (St Clair-Gibson et al. 2006; Tucker, 2009). The setting of initial work rate is based on previous experience and the knowledge of exercise duration (St Clair-Gibson et al. 2006). In the present study, all the participants were informed that they had to perform a repeated (12 repetitions) MVICs fatigue protocol immediately after they finished the single MVIC test. In this case, as a pacing strategy, exercise performance could be subconsciously attenuated from the
beginning of exercise (St Clair-Gibson et al. 2006; Tucker, 2009). Further, during the test, most of the participants were not accurately aware of how many MVICs remained and they were not informed when the final repetition was to be performed. Hence, the participants lacked knowledge of the task endpoint. Knowing the endpoint is crucial for the brain to generate an appropriate strategy during the exercise (St Clair-Gibson et al. 2006). It has been suggested that the most considerable effect of the knowledge of the endpoint occurs during the initial and the final stage of the task (Billaut et al. 2011; Hamilton and Behm, 2017).

There were no significant changes in EMG RMS neither between conditions nor repetitions for both tested muscles. This is in accordance with Halperin et al. (2014a, 2014b) who also did not find significant NLMF-induced changes in EMG RMS of non-exercised muscles. It has been suggested that EMG RMS is less sensitive to changes in muscle force compared to MDF so it is a less reliable indicator of muscle fatigue (Dimitrova et al. 2003; Bartuzi et al. 2014). The EMG MDF is a measure of the power spectra of the EMG signal (contributing components can include neural conduction velocity and firing frequency), which shifts to a lower frequency with fatigue and is considered a more sensitive measure of neuromuscular fatigue than
the amplitude of the EMG RMS signal (Bartuzi et al. 2014, Kwatny et al. 1970, Dimitrova and Dimitrov 2003). Similarly, in the present study, while there were no significant changes in EMG RMS, there were significant decrease of MDF which relatively paralleled the muscle fatigue.

The lack of EMG of ipsilateral, proximal muscles such as the biceps brachii during the MVCs and fatiguing task could be considered a limitation since heterologous effects (BB) to the contralateral limb were of particular interest.

To the best of our knowledge, this is the first study to demonstrate that a small muscle fatiguing protocol is able to elicit NLMF effects both on homologous and larger heterologous muscles. Future studies may take a deeper insight into the relationship between muscle mass and the extent of NLMF effect by conducting a similar protocol in lower limbs. Also, further investigations may include the objective measures of motivation or perceived exertion during and/or after fatiguing protocol to test the contribution of psychological effect to NLMF effect.

**Conflict of Interest:** The authors declare no conflicts of interest with the contents of this manuscript.


References:


Bartuzi, P., & Roman-Liu, D. 2014. Assessment of muscle load and fatigue with the usage of


Rossman, M. J., Garten, R. S., Venturelli, M., Amann, M., & Richardson, R. S. 2014. The role of


Neuromechanical interactions between the limbs during human locomotion: an evolutionary perspective with translation to rehabilitation. Exp. Brain Res. 234: 3059-3081.
**FIGURE 1:** Experimental set-up for dominant and non-dominant index finger abduction (IFA).

Both sides were identical such that the device could be rotated 180 degrees in order to test both limbs.

**FIGURE 1b:** Experimental set-up for contralateral, non-dominant elbow flexor maximum voluntary isometric contraction (MVIC).

**FIGURE 2:** Mean force of index finger abductors (IFA) and elbow flexors (EF) over the post-tests for two conditions. Data is presented in percentage relative to the highest value of the pre-test. 2a: Index finger abduction (IFA). 2b: Elbow flexion (EF). Numbers 1-12 indicate post-test maximal voluntary isometric contractions (MVIC) 1-12; * indicates significant differences for repetitions and ! indicates significant differences between conditions (p < 0.05).

**FIGURE 3:** EMG Fast Fourier Transform Median Frequency (FFT MDF) of first dorsal interosseous (FDI) and biceps brachii (BB) over the post-tests for two conditions. Data are presented in percentage relative to the highest value of the pre-test. 3a: FDI FFT MDF. 3b: BB FFT MDF. Number 1-12 indicate post-test maximum voluntary isometric contractions (MVIC) 1-12; * indicates significant differences for repetitions, ! indicates significant differences.
between conditions ($p < 0.05$).

**FIGURE 4:** Force differences between the single maximal voluntary isometric contraction (MVIC) and the first repetition of the repeated MVICs protocol. Data is presented in percentage relative to the highest value of the pre-test. ! indicates significant differences between conditions and # indicates significant differences between muscles ($p < 0.05$).
Figure 2

a) Elbow Flexor Force (% pre-test)

b) IFA Force (% pre-test)
Figure 3
a) FDI Median Frequency (% pre-test)

<table>
<thead>
<tr>
<th>MVC</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

b) BB Median Frequency (% pre-test)

<table>
<thead>
<tr>
<th>MVC</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 4

![Bar chart showing Force Differences (% pre-test) between Control and Fatigue conditions.

- **Control**
  - Black bar represents IFA, with a force difference of approximately 4% pre-test.
  - Gray bar represents EF, with a force difference of approximately 3% pre-test.

- **Fatigue**
  - Black bar represents IFA, with a force difference of approximately 18% pre-test.
  - Gray bar represents EF, with a force difference of approximately 20% pre-test.

The chart indicates a significant increase in force differences between Control and Fatigue conditions for both IFA and EF, with EF showing the greatest increase.