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ARTICLE

Unilateral isometric muscle fatigue decreases force production and activation of contralateral knee extensors but not elbow flexors

Israel Halperin, David Copithorne, and David G. Behm

Abstract: Nonlocal muscle fatigue occurs when fatiguing 1 muscle alters performance of another rested muscle. The purpose of the study was to investigate if fatiguing 2 separate muscles would affect the same rested muscle, and if fatiguing the same muscle would affect 2 separate muscles. Twenty-one trained males participated in 2 studies ($n = 11$; $n = 10$). Subjects performed 2 pre-test maximum voluntary contractions (MVCs) with the nondominant knee extensors. Thereafter they performed two 100-s MVCs with their dominant knee extensors, elbow flexors, or rested. Between and after the sets, a single MVC with the nondominant rested knee extensors was performed. Subsequently, 12 nondominant knee extensors repeated MVCs were completed. Force, quadriceps voluntary activation (VA), and electromyography (EMG) were measured. The same protocol was employed in study 2 except the nondominant elbow-flexors were tested. Study 1: Compared with control conditions, a significant decrease in nondominant knee extensors force, EMG, and VA was found under both fatiguing conditions ($P \leq 0.05$; effect size (ES) = 0.91–1.15; 2%–8%). Additionally, decrements in all variables were found from the first post-intervention MVC to the last ($P \leq 0.05$; ES = 0.82–2.40; 9%–20%). Study 2: No differences were found between conditions for all variables ($P \geq 0.33$; ES ≤ 0.2; ≤3.0%). However, all variables decreased from the first post-intervention MVC to the last ($P \leq 0.05$; ES = 0.4–3.0; 7.2%–19.7%). Whereas the rested knee extensors demonstrated nonlocal effects regardless of the muscle being fatigued, the elbow-flexors remained unaffected. This suggests that nonlocal effects are muscle specific, which may hold functional implications for training and performance.

Key words: crossover fatigue, electromyography, endurance, strength, activation.

Résumé : La fatigue musculaire non localisée se présente lorsqu'un muscle fatigué modifie la performance d'un autre muscle reposé. Cette étude se propose d'examiner l'effet de l'épuisement de deux muscles distincts sur un même muscle reposé et l'effet de l'épuisement du même muscle se répercute sur deux muscles distincts. Vingt-et-un hommes entraînés participent à deux études ($n = 11$; $n = 10$). Les sujets effectuent avant le test deux contractions maximales volontaires (« MVC ») des extenseurs du genou du côté non dominant. Ensuite, ils effectuent deux MVC d'une durée de 100 s des extenseurs du genou, des fléchisseurs du coude du côté dominant ou ils se reposent. Entre les deux séries et après, les sujets effectuent une seule MVC des extenseurs du genou non épuisés du côté non dominant. Par la suite, les sujets effectuent 12 MVC des extenseurs du genou du côté non dominant. On évalue la force, le degré d'activation volontaire (« VA ») et l'activité myoélectrique (EMG) du quadriceps. On applique le même protocole dans la deuxième étude pour l'évaluation des fléchisseurs du coude du côté non dominant. Étude 1 : Comparativement à la condition de contrôle, on observe dans les deux conditions épuisantes une diminution significative de la force, de l'EMG et de la VA des extenseurs du genou du côté non dominant ($P \leq 0,05$; ampleur de l'effet (AE) = 0,91–1,15; 2–8 %). De plus, on observe une diminution de toutes les variables à partir de la première jusqu'à la dernière MVC suivant l'intervention ($P \leq 0,05$; AE = 0,82–2,40; 9–20 %). Étude 2 : On n'observe aucune différence des valeurs des variables d'une condition à l'autre ($P \geq 0,33$; AE ≤ 0,2; ≤3,0 %). Toutefois, toutes les variables présentent une diminution à partir de la première jusqu'à la dernière MVC suivant l'intervention ($P \leq 0,05$; AE = 0,4–3,0; 7,2–19,7 %). Les extenseurs reposés du genou ne présentent pas un effet localisé indépendamment du muscle épuisé et les fléchisseurs du coude ne sont pas touchés. Dès lors, les effets non localisés pourraient être spécifiques au muscle, ce qui suggère des implications fonctionnelles en matière d'entraînement et de performance. [Traduit par la Rédaction]

Mots-clés : fatigue croisée, électromyographie, endurance, force, activation.

Introduction

Neuromuscular fatigue has been defined as a progressive reduction in the ability of the muscles to produce power or force (Gandevia 2001). One unique way to study exercise-related fatigue is to examine if fatigue is specific to the working muscles or affects rested, unrelated muscle groups. This is commonly performed by testing the rested contralateral homologous muscles (Amann et al. 2013; Doix et al. 2013; Martin and Ratttey 2007), or unrelated heterogonous muscle groups (Halperin et al. 2014; Kennedy et al. 2013), after a fatiguing task to other muscle groups. Results of such studies have been conflicting. On one hand it was shown that a sustained maximal voluntary contraction (MVC) of the knee extensors decreased force and voluntary activation (VA) of the contralateral knee extensors (Doix et al. 2013, Martin and Ratttey 2007). Similarly, a constant-load single-leg knee extension exercise to exhaustion of 1 leg subsequently decreased time to

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exhaustion of the opposite leg (Amann et al. 2013). Halperin et al. (2014) demonstrated that a dynamic bilateral knee extension fatiguing protocol led to decrements in force production with the elbow flexors, but only in the last few repetitions of a repeated MVC protocol. Similarly, Kennedy et al. (2013) found that a maximal and a submaximal isometric fatiguing task of the forearms hindered force production and VA of the plantar flexors. Nonlocal muscle fatigue effects were also found to shorten lower body cycling tasks when performed after an arm-cranking exercise (Bangsbo et al. 1996; Johnson et al. 2014; Nordsborg et al. 2003).

In contrast, Regueme et al. (2007) showed that a unilateral fatiguing protocol consisting of repeated jumps with the plantar flexors did not affect jump performance or force production with the contralateral plantar flexors. Grabiner and Owings (1999) reported no decrements in force production with the contralateral knee extensors after completing both a concentric and eccentric unilateral dynamic fatiguing protocol. Todd et al. (2003) showed that a sustained elbow flexor MVC was not affected by a previous sustained MVC with the contralateral elbow flexors. Finally, it was repeatedly found that extended aerobic activity such as cycling and marathon runs did not affect grip force, despite significant decrements in force and power production, as well as central activation with the lower limbs (Elmer et al. 2013; Millet et al. 2003; Place et al. 2004; Ross et al. 2010). Hence these conflicting results emphasize the need for further investigations.

Furthermore, Halperin et al. (2014) suggested that the controversy in the crossover fatigue literature might be partially attributed to the variable measured in the nonlocal muscle. Whereas many studies measure the effect of crossover fatigue on a single contraction, the Halperin et al. (2014) study measured both a single MVC and a repeated strength endurance protocol consisting of 12 MVCs performed with short rest periods (10 s) after fatiguing the knee extensors. Significant force decrements were reported only in the last 5 MVCs during the strength endurance task, but not with the single MVC.

Accordingly, the aims of the present study were 3-fold. The first goal was to investigate if nonlocal crossover effects would be found with 2 *different* nonfatigued muscle groups after fatiguing the *same* muscle (1. fatigue unilateral dominant quadriceps and heterogonous elbow flexors and test the rested quadriceps; 2. fatigue unilateral dominant quadriceps and heterogonous elbow flexors and test the rested elbow flexors). The second goal was to examine if nonlocal crossover effects measured in the *same* target muscles would differ after fatiguing *different* muscle groups (1. fatigue unilateral dominant quadriceps and test the contralateral quadriceps or heterogonous elbow flexors; 2. fatigue unilateral dominant elbow flexors and test the contralateral elbow flexors and heterogonous quadriceps). The decision to test the knee extensors and the elbow flexors stems from the differences between them in terms of function (extension vs. flexion, weight bearing vs. nonweight bearing; Kern et al. 2001), fiber type composition (Johnson et al. 2014; Miller et al. 1993), and spinal reflex connectivity (e.g., central pattern generator for locomotion; Duysens and Van de Crommert 1998; MacKay-Lyons 2002). Accordingly, there may be muscle-specific effects upon nonlocal crossover fatigue responses. The third goal was to examine if the nonlocal crossover effects would differ when measured in 2 ways: a single MVC performed after the fatiguing protocol and during a similar strength-endurance protocol (Halperin et al. 2014). It was hypothesized that fatiguing of the contralateral homologous limb, as well as the heterogonous diagonal limb, would decrease force production, fatigue resistance, electromyography (EMG), and VA in the rested knee extensors and elbow flexors.

Materials and methods

Participants

Twenty-one healthy resistance-trained males (age, 25 ± 4 years; height, 178 ± 6 cm; mass, 79 ± 8 kg) participated in the 2 studies (study 1: $n = 11$; study 2: $n = 10$). All of the participants performed resistance training at least 3 times a week for over 1 year. Subjects were requested to avoid training a day before testing days. Ethical approval for the study was granted by the institutional Health Research Ethics Board (HREB 2013.299). Before participation, subjects were verbally informed of the procedures and risks associated with the study. They were then asked to read and sign the consent form if they found it agreeable.

Experimental design

Study 1

Subjects attended the laboratory on 3 occasions separated by 3–6 days, and performed 1 of 3 conditions in a randomized fashion. During the first testing session subjects were initially familiarized with the equipment and testing procedures. Participants then performed a general warm-up of lower body cycling for 5 min at a cadence 70 rpm at 1 kp. This was followed by an assessment of the resting maximal evoked muscle twitch force from the nondominant knee extensors (see Stimulation section). Depending on the testing day, this was followed by a specific warm-up of either the knee extensors of the nondominant leg (control session), the dominant and nondominant knee extensors (leg–leg session), or the dominant elbow flexors and nondominant knee extensors (arm–leg session). The specific warm up consisted of ten 5-s isometric contractions followed by 5 s of rest (control) or alternated with a 5-s contraction with either the dominant leg (leg–leg) or arm (arm–leg). Participants were asked to apply force equal to approximately 50% of their perceived maximum.

Thereafter, testing commenced with the subjects performing 3 MVCs lasting 5 s with the nondominant knee extensors. Two minutes of rest were provided between each contraction. During the last 2 MVCs, the interpolated twitch technique (ITT) (Behm et al. 1996; Shield and Zhou 2004) was administered, which involved superimposed evoked twitches that were manually delivered when a plateau in force production was observed, and a second maximal evoked twitch delivered within 1 s after the MVC when the muscle was at rest. Consequently, participants performed 1 of the 3 conditions: (*i*) rested for 100 s, (*ii*) performed a 100-s continuous MVC with their dominant elbow flexors (arm–leg), or (*iii*) the dominant knee extensor (leg–leg). Participants were motivated during the protocol by 2 experimenters, and were reminded to keep their nondominant knee extensors as relaxed as possible during the protocol. EMG activity of the nondominant knee extensors was monitored throughout the protocol and at any sight of activation subjects were reminded to relax their leg. Ten seconds following the interventions, subjects performed a single ITT MVC with the nondominant knee extensors. After 1 min of rest, subjects repeated the 100 s of rest or MVC interventions for the second time followed 10 s later by another ITT MVC. One minute afterwards, subjects performed 12 MVCs with the nondominant knee extensors, using a work to rest ratio of 5/10 s. An ITT stimulus was delivered only at the first, sixth, and twelfth MVCs.

Study 2

The protocol for study 2 was identical to study 1 with the only difference being that the nondominant elbow flexors were tested instead of the nondominant knee extensors. That is, force and activation levels were measured before and after the 3 interventions, consisting of 100 s of rest (control), MVC with the dominant arm (arm–arm), or MVC with the dominant leg (leg–arm).

MVC force

In both studies force values were collected with the same load cells (Omega Engineering Inc., LCCA 500 pounds; sensitivity = 3 mV/V, OEI, Canada). Force from knee extensors (study 1) was collected by having subjects sit on a chair with their hips and knees flexed to 90°and their shin inserted into a padded strap attached to a load cell. Force from the elbow flexors (study 2) was collected with the elbow flexed at 90°and supported by an armrest. The wrist was inserted into a padded strap attached to the load cell. The strap placement location was consistent for both studies. The mean force for each MVC of the nondominant limb was determined either over a 0.3-s window before the interpolated twitch during the ITT MVC or 0.15 s before and following the peak force during the MVCs without interpolated twitches. To account for variability in force production between the 3 testing days, all mean force data for the nondominant limbs were normalized to the highest mean force recorded during the 3 pre-test trials. As such, force data are reported as percentage of maximum pre-test values. Force decrement during the 100-s MVCs intervention with the dominant limbs was analyzed by comparing force applied during the first and last 5 s of the task. Since only 2 values were compared, forces are therefore reported in Newtons (N).

EMG

EMG activity was collected from the mid-belly (midway between the anterior superior iliac spine to the superior edge of the patella) of the vastus lateralis and biceps femoris (midway between the gluteal fold and the popliteal space) of the nondominant leg (study 1), and from the mid-belly of biceps brachii and the lateral head of the triceps brachii (midway between the acromion process and the humeral epicondyles) nondominant arm (study 2). Self-adhesive, 3.2-cm diameter Ag/AgCl electrodes (Meditrace TM 130 ECG conductive adhesive electrodes) with an edge to edge inter-electrode spacing of 20 mm were used. A reference electrode was placed over the fibular head (study 1) and over the proximal lateral aspect of the ulna (study 2). Prior to electrode placement, the skin was shaved and cleansed with an isopropyl alcohol swab. Using the same 0.3-s window as applied to the force analysis, mean root mean square (RMS) EMG was collected and analyzed. Mean amplitude of the RMS EMG was determined from a series of 50-ms segments over the 0.3-s force and EMG window. These values were then normalized to the highest pre-test value and reported as a percentage.

Evoked muscle stimulation

The stimulating electrodes (10 cm × 4 cm) were placed in approximately the same position for each subject. Peak twitches were evoked with electrodes connected to a high-voltage stimulator (Digitimer Stimulator Model DS7AH, Hertfordshire, UK). Maximal twitches were elicited by sequentially increasing the voltage and amperage (maximum 150–200 V) of a 50-μs pulse duration, square-wave signal until the evoked force output reached a peak, plateaued, and then a subsequent decrease in force. The subsequent decrease in force would indicate antagonist activation and thus the stimulation was decreased to the initial current used to find the peak or plateau of force, indicating full muscle activation without an antagonist contribution. For the elbow flexors, electrical stimuli were delivered superficially to the intra-muscular nerve fibers of the biceps brachii via an anode over the bicipital tendon and a cathode located proximal to the elbow crease. For the knee extensors, anodes and cathodes were placed superficially over the inguinal triangle and distal portion of the quadriceps, respectively. Single electrical stimuli were manually delivered during the MVC and 1 s afterwards. For the ITT, the researcher monitored the force output on the computer screen and manually delivered the stimulus at the point of peak force. The stimulation intensities ranged from 100 to 400 mA for the elbow flexors and 550–999 mA for the knee extensors. An interpolated force ratio was calculated comparing the force amplitudes of the superimposed stimulation with the postcontraction stimulation to estimate the extent of activation during a voluntary contraction (Behm et al. 1996). The maximal VA of both muscle groups was calculated using the following equation: VA = [1 − (superimposed twitch/potentiated twitch)] × 100 (Behm et al. 1996). Post-intervention values were normalized to the highest pre-test. Figures 1 and 2 illustrate sample ITT force tracings.

Statistical analysis

First, a normality (Kolmogorov–Smirnov) test was conducted for all dependent variables. If the assumption of Sphericity was violated, the Greenhouse–Geisser correction was employed. Second, intraclass correlation coefficients (ICC) were measured for the mean absolute force, EMG, and VA for the 2 pre-tests of each condition to assess consistency of this data in both studies. Third, paired *t* tests were used to compare the first and last 5 s of the 100-s MVCs with both the knee extensors and elbow flexors of the dominant limbs. For clarity the data across the 2 fatiguing sets was averaged into 1 set. Fourth, 2-way repeated measures ANOVA tests (3 conditions × 14 MVCs (time)) were conducted to determine differences between conditions in normalized mean force (study 1 = knee extensors; study 2 = elbow flexors) and EMG (study 1 = vastus lateralis and biceps femoris; study 2 = biceps brachii and triceps brachii). Finally, a 2-way repeated measures ANOVA test (3 conditions × 7 VA) was used to compare differences between conditions in voluntary muscle activation (study 1 = knee extensors; study 2 = elbow flexors). Least significant differences post hoc tests were used when main effects were found between conditions. Paired *t* tests with Holm–Bonferroni correction were employed when MVC main effects were found, comparing the averaged values of the first post-intervention MVC and the last MVC (no. 12) across conditions. Significance was set at $P \leq 0.05$. Cohen's *d* effect sizes (ES) (Cohen, 1988) were also calculated to compare the mean force and EMG, and activation between conditions. Data are reported as means ± SD.

Results

Study 1

The ICCs of the 2 pre-test values for each condition were highly correlated ($\alpha \geq 0.92$) for absolute force, vastus lateralis EMG, and VA measures. Biceps femoris EMG demonstrated relatively lower reliability for the pre-tests ($\alpha = 0.83$).

Force

Dominant limbs

The fatiguing protocol with the dominant elbow flexor led to a significant decrements in force (~60%) over the two 100-s MVCs sets ($P < 0.001$; ES = 4.1). Similarly, the fatiguing protocol with the dominant knee extensors led to a significant decline in force (70%) across to 2 sets ($P < 0.001$; ES = 3.8).

Nondominant knee extensors

A significant main effect was found for conditions ($P = 0.001$) and MVCs ($P < 0.001$) but no interactions were found ($P = 0.824$). Post hoc test revealed greater forces in the control session compared with arm–leg session ($P = 0.011$; ES = 0.82; Δ 6% [range = 4%–9%]), and leg–leg day ($P = 0.002$; ES = 1.1; Δ 8% [6%–10.5%]) (Fig. 3). Similarly, averaged forces significantly dropped from the first post-test MVC to the MVC (no. 12) across conditions ($P < 0.001$; ES = 2.4; Δ 21% [20%–23%]).

EMG

A significant main effect was found for conditions ($P = 0.048$) and MVCs ($P < 0.001$) but no interactions were found ($P = 0.896$) for vastus lateralis EMG activity. Post hoc tests found higher activity in the control session compared with arm–leg day ($P = 0.033$;

Fig. 1. Figure 1 illustrates overlaid interpolated twitch technique force tracings of the rested knee extensors with fatigue of contralateral knee extensors (A), elbow flexors (B), and rest (C). The top tracing illustrates the highest pre-test force, the middle tracing represents the first post-fatigue, and the bottom tracing represents the second post-fatigue forces.

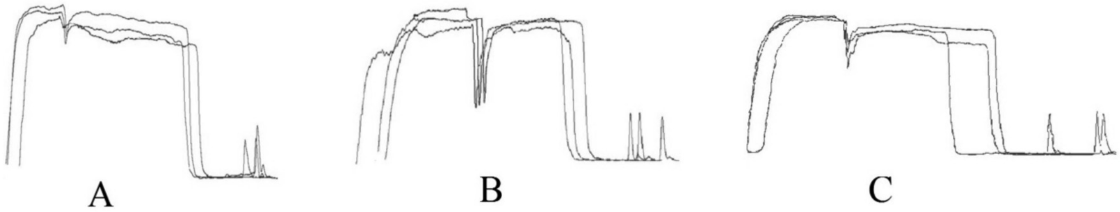


Fig. 2. Figure 2 illustrates overlaid interpolated twitch technique force tracings of the rested elbow flexors with fatigue of the contralateral elbow flexors (A), knee extensors (B), and rest (C). The top tracing illustrates the highest pre-test force, the middle tracing represents the first post-fatigue, and the bottom tracing represents the second post-fatigue forces.

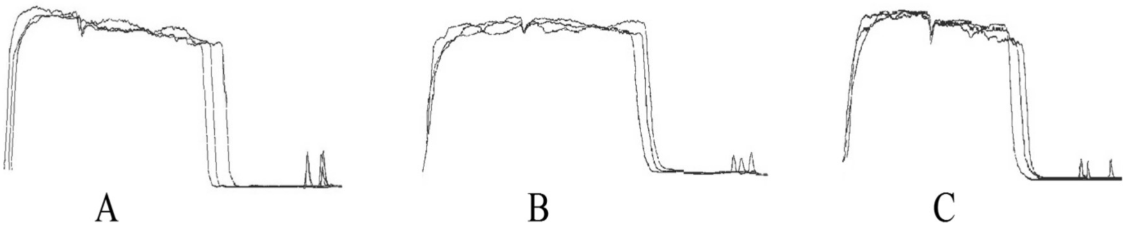


Fig. 3. Mean (SD) normalized knee extensors force profile over the 14 maximum voluntary contractions (MVCs) for the 3 conditions. Data are presented in percentage relative to the highest value of the pre-test. P1 and P2, post-interventions MVC1 and MVC2, respectively. *, Force was significantly higher ($P \leq 0.05$) in the control condition relative to both fatiguing conditions; $, significant ($P \leq 0.05$) drop in force across all conditions from P1 to MVC no. 12.

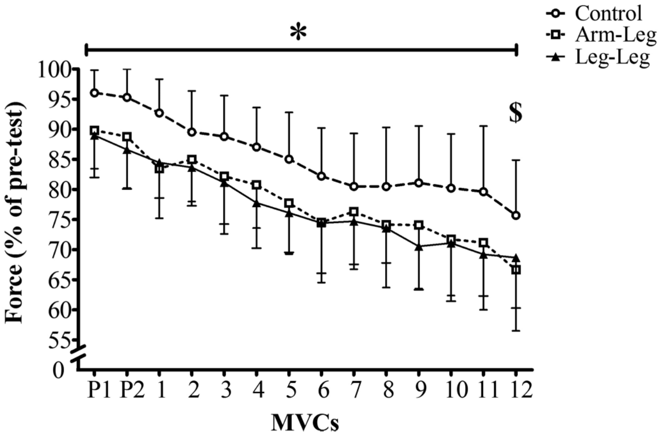
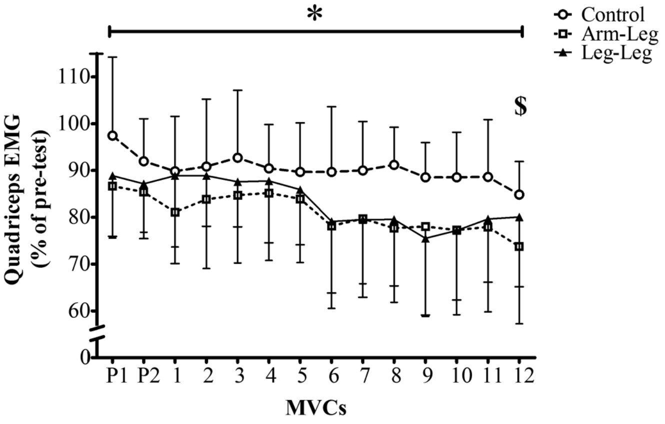


Fig. 4. Mean (SD) normalized electromyography (EMG) activity from vastus lateralis muscle over the 14 maximum voluntary contractions (MVCs) for the 3 conditions. Data are presented in percentage relative to the highest value of the pre-test. P1 and P2, post-interventions MVC1 and MVC2, respectively. *, EMG was significantly higher ($P \leq 0.05$) in the control condition relative to both fatiguing conditions; $, significant ($P \leq 0.05$) drop in EMG across all conditions from P1 to MVC no. 12.



ES = 0.7; Δ 9% [3%–11%]), and leg–leg day ($P = 0.043$; ES = 0.55; Δ 6.8% [0%–11%]) (Fig. 4). Averaged vastus lateralis EMG dropped across conditions from the first post-intervention MVC to the last MVC (no. 12) ($P = 0.002$; ES = 0.82; Δ 9% [8.8%–12%]). No significant effects were found between conditions for biceps femoris EMG in terms of conditions ($P = 0.570$), MVCs ($P = 0.090$), and interactions ($P = 0.679$).

VA

Because of technical difficulties, data from 3 subjects were not included (inability to reach a plateau in the initial twitch force); therefore, the presented results are from 8 subjects. Significant main effect for conditions ($P = 0.008$) and MVCs ($P < 0.001$) were found, but no interactions ($P = 0.751$). Post hoc tests demonstrated greater VA in the control session compared with the arm–leg ($P = 0.027$; ES = 0.9; Δ 3.7% [1.8%–5.5%]), and leg–leg sessions ($P = 0.018$; ES = 1.15; Δ 5% [3%–8.3%]). Additionally, averaged VA dropped across conditions from the first post-intervention MVC to the last MVC (no. 12) ($P = 0.003$; ES = 1.46; Δ 7.5% [5.5%–9.5%]) (Fig. 5).

Study 2

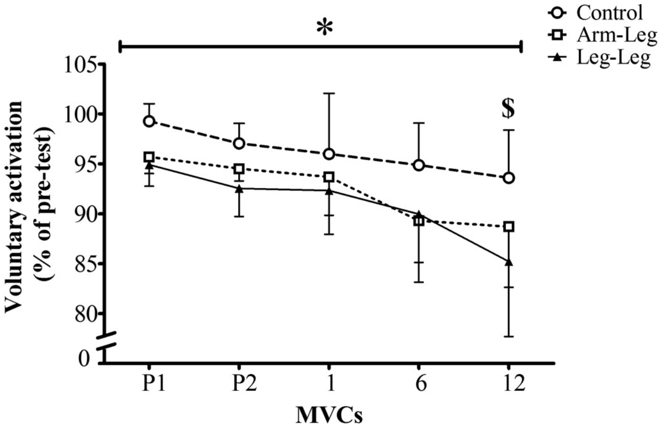
The ICCs of the 2 pre-test values for each condition were highly correlated ($\alpha \geq 0.93$) for absolute force measures, biceps, and triceps brachii EMG. Reliability for the pre-tests of VA was relatively lower ($\alpha = 0.86$).

Force

Dominant limbs

Both fatiguing conditions led to similar force decrements as found in study 1.

Fig. 5. Mean (SD) normalized knee extensors voluntary activation (VA) over the 5 post-interventions interpolated twitch technique maximum voluntary contractions (MVCs) for the 3 conditions. Data are presented in percentage relative to the highest value of the pre-test. P1 and P2, post-interventions MVC1 and MVC2, respectively. *, VA was significantly higher ($P \leq 0.05$) in the control condition compared with both fatiguing conditions; $, significant ($P \leq 0.05$) drop in VA across all conditions from P1 to MVC no. 12.



Nondominant elbow flexors

No significant interactions (P = 0.899) or conditions main effect (P = 0.391) were found; however, an MVC effect (P < 0.001) was found in which force gradually declined across all conditions (Fig. 6). Overall, average forces did not differ by more than 3% between conditions, with ES smaller than 0.2. However, averaged force significantly dropped across conditions from the first post-intervention MVC to the last MVC (no. 12) (P < 0.001; ES = 3.0; Δ 19.7% [18%–21.5%]).

EMG

No significant interactions (P = 0.900) or conditions effect (P = 0.889) were found for biceps brachii EMG; however, a main effect for MVCs (P < 0.013) was found in which EMG gradually declined across conditions (Fig. 7). Average EMG did not differ by more than 3% between conditions, with ES smaller than 0.2. In contrast, averaged EMG of biceps significantly dropped from the first post-intervention MVC to the last MVC (no. 12) (P = 0.049; ES = 0.4; Δ 7.6% [5.5%–8.4%]).

Similarly, no significant results were found for triceps brachii EMG in terms of interactions (P = 0.223) or conditions effect (P = 0.478), but an MVC effect was found (P = 0.044). Averaged EMG activity did not differ by more than 3% between conditions, with ES smaller than 0.2. Despite not reaching statistical significance (P = 0.082), averaged EMG of triceps dropped across conditions from the first post-intervention MVC to the last MVC (no. 12) (ES = 0.52; Δ 12.5% [5.5%–18%]).

VA

Because of technical difficulties, data from 2 subjects were not usable; therefore, the presented results are from 8 subjects. No interactions (P = 0.333) or significant main effect for conditions (P = 0.752) were found. However, a main effect for MVC (P = 0.050) was found (Fig. 8). Averaged VA did not differ by more than 2% between conditions with ES that were smaller than 0.2. In contrast, averaged VA significantly dropped across conditions from the first post-intervention MVC to the last MVC (no. 12) (P = 0.004; ES = 1.44; Δ 7.2% [6.4–8.4%]).

Discussion

The results of the present study were as follows: first, in accordance with the hypothesis, fatiguing of the contralateral (knee extensors) and the heterogonous diagonal (elbow flexors) limbs led to significant decrements in the nondominant knee extensors' force production, EMG activity, and VA (study 1). Second, in contrast to the hypothesis, the nondominant elbow flexors' force production, EMG activity, and VA were not affected by the fatiguing tasks performed with both the contralateral (elbow flexors) and heterogonous diagonal (knee extensors) limbs (study 2). Third, the degree of impairment of the single MVC performed immediately after the fatiguing tasks and the following 12 repeated MVCs protocols in both studies were similar. That is, the single and repeated MVCs were both impaired after the fatiguing protocols in study 1, and remained unaffected by the same fatiguing protocols in study 2.

The results of first study are in agreement with Doix et al. (2013) and Martin and Rattey (2007). All 3 studies showed decrements in force production with the rested knee extensors after the continuous 100 s MVC performed with the contralateral limb. Force decrements varied between ~13% (Martin and Rattey 2007), ~10% (Doix et al. 2013), and ~8% (present study: averaged across the 14 post-test MVCs). Similarly, VA of the rested knee extensors decreased by ~9% (Martin and Rattey 2007), ~9.1% (Doix et al.

Fig. 6. Mean (SD) normalized elbow flexors force profile over the 14 maximum voluntary contractions (MVCs) for the 3 conditions. Data are presented in percentage relative to the highest value of the pre-test. P1 and P2, post-interventions MVC1 and MVC2, respectively. $, significant ($P \leq 0.05$) drop in force across all conditions from P1 to MVC no. 12.

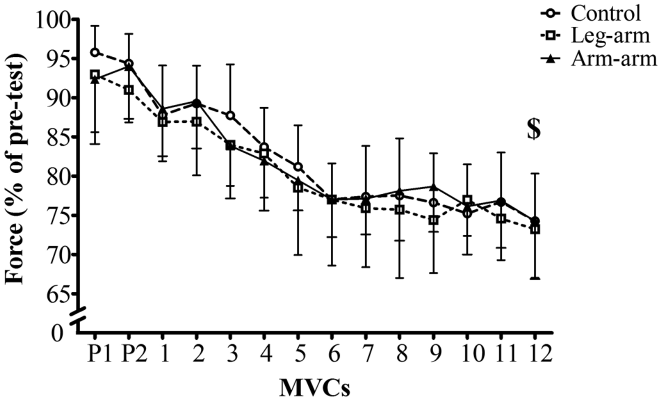
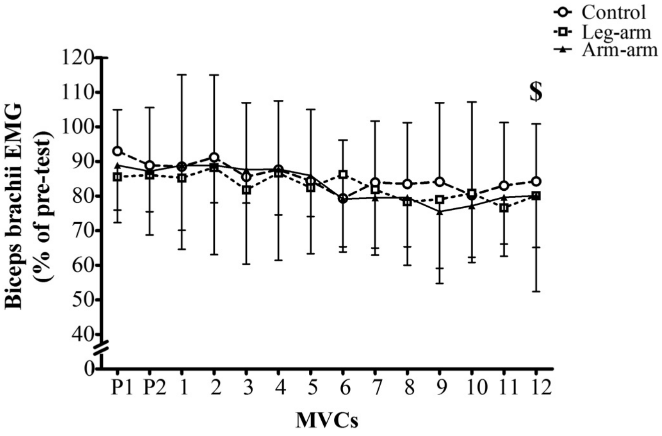


Fig. 7. Mean (SD) normalized electromyography (EMG) activity from biceps brachii muscle over the 14 maximum voluntary contractions (MVCs) for the 3 conditions. Data are presented in percentage relative to the highest value of the pre-test. P1 and P2, post-interventions MVC1 and MVC2, respectively. $, significant ($P \leq 0.05$) drop in EMG across all conditions from P1 to MVC no. 12.



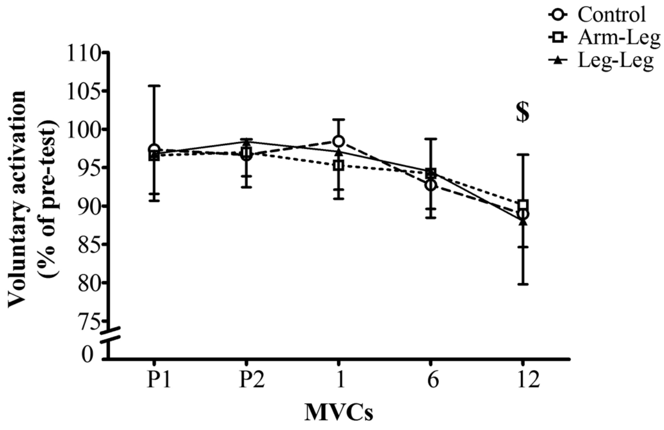


Fig. 8. Mean (SD) normalized elbow flexors voluntary activation (VA) over the 5 post-interventions interpolated twitch technique maximum voluntary contractions (MVCs) for the 3 conditions. Data are presented in percentage relative to the highest value of the pre-test. P1 and P2, post-interventions MVC1 and MVC2, respectively. $, significant ($P \leq 0.05$) drop in VA across all conditions from P1 to MVC no. 12.

2013), and ~5% (present study: averaged across the 5 post-test ITT MVCs) as a result of the contralateral fatiguing protocol. The relatively lower force and VA values in the present study could be explained by the fact that participants were experienced in resistance training in contrast to the recreationally active subjects in Martin and Rattey (2007) and Doix et al. (2013). Finally, compared with the control conditions, no significant differences were found between the single and repeated MVCs protocol in both studies. That is, the fatiguing protocols either impaired (study 1) or did not affect (study 2) force values performed with a single and the repeated MVCs protocol.

Interestingly, the nonlocal detriments found in the knee extensors after fatiguing the dominant elbow flexors were similar to those found after fatiguing the contralateral knee extensors. These findings may suggest that the knee extensors are more susceptible to nonlocal muscle fatigue effects *regardless* of the muscle group being fatigued. It is therefore suggested that future studies will further examine this possibility by fatiguing other muscle groups, such as the plantar flexors and the forearms, and measure the effects on the rested knee extensors.

The results of the second study are in partial agreement with other experiments. Similar to the current study, Todd et al. (2003) found that a sustained elbow flexor MVC (60 s) did not affect the following identical MVC performed with the contralateral elbow flexors. Whereas in the present study there were no force decrements in the strength endurance elbow flexion protocol, Halperin et al. (2014) did find force decrements only in the last 5 MVCs during the same protocol. The disparate results may be explained by the different fatiguing protocols: in the present study 2 sets of unilateral extended isometric MVCs were employed. In contrast, Halperin et al. (2014) employed 5 sets of dynamic bilateral knee extensions.

It was beyond the scope of this study to determine the precise mechanisms underlying why the knee extensors, but not the elbow flexors, were affected by the preceding fatiguing protocols. However, there are a number of potential possibilities. With fatigue, the extent of muscle inactivation can increase (Behm 2004). If a particular muscle has a higher threshold for full activation then a decrease in the central nervous system's ability to fully activate a muscle may be more apparent in 1 muscle than another. Compared with the elbow flexors, the knee extensors possess a greater number of motor units (McComas 1991) and a higher percentage of high-threshold fast-twitch fibres (Johnson et al. 2014; Miller et al. 1993) and are more difficult to fully activate than the elbow flexors (Behm et al. 2002).

The ability to fully activate a muscle is based on a contingent of supraspinal and spinal excitatory and inhibitory influences (Behm 2004). Motor cortical neurons firing rates have been shown to decline during sustained contractions (Behm 2004; Enoka and Stuart 1992), indicating a fatigue-induced decrement in supraspinal functioning (Pappas et al. 2001). The fatiguing protocols could also have altered the metabolic environment in the working muscles leading to activation of group III and IV muscle afferents (Amann 2011, 2012; Martin et al. 2008). By this feedback loop, the muscle afferents provide an inhibitory effect to the global central nervous system leading to decrements in the central drive to the working muscles, and possibly to rested muscles as well (Amann 2011, 2012; Martin et al. 2008). Gandevia (2001) in his comprehensive review provides extensive evidence of supraspinal inhibition and concludes that muscle feedback concerning biochemical and force-generating status can impair cortical sites. Long loop reflexes from muscle spindle afferents (Chan 1983; Marsden et al. 1983) as well as skin and subcutaneous afferents (Corden et al. 2000) can influence cortical activation of the affected and remote muscles (Kagamihara et al. 2003). Since the discharge frequency from Ia afferents of intrafusal stretch receptors can contribute up to 30% of the motoneuron excitation with sustained isometric contractions (Gandevia 2001), fatigue-induced reductions in afferent excitability could adversely affect muscle force and activation. Indeed, VA of the rested knee extensors was ~5% lower after both fatiguing conditions (Fig. 4).

Since the lower limbs serve as locomotion generators in humans (Duysens and Van de Crommert 1998; MacKay-Lyons 2002), a possibility exists in which the lower limbs have different neural and reflex connectivity than the upper limbs. Guertin (2013) asserts that sensory feedback is important in modulating and adapting central pattern generator motor output. Thus there could be fatigue-induced alterations in the extent of lower body spinal connectivity. It can therefore be speculated that such differences may affect the susceptibility of the knee extensors to nonlocal muscle fatigue effects in contrast with the elbow flexors. Future studies need to address the mechanisms underlying the aforementioned speculations.

One limitation of the present study was the inability to pinpoint the location of the recorded central fatigue (e.g., spinal, cortical excitability), as procedures such as transcranial and cervicomedullary stimulation were not available. Second, the relatively small sample size increases the risk of both type I (study 1) and type II (study 2) statistical errors. However, the utilization of a crossover design in which the participants acted as their own control in a randomized manner increases the statistical power despite the smaller sample size. Finally, the size of the stimulating electrodes and their placement could have led to some minor activation of the antagonist hamstrings, which may have contributed to an underestimation of the quadriceps activation because of antagonist action reducing the size of the superimposed twitch.

Conclusions

To the best of our knowledge this is the first study to demonstrate that the knee extensors are susceptible to nonlocal effects of muscle fatigue, regardless of the muscles being fatigued (contralateral knee extensors and the heterogonous diagonal elbow flexors), and that the elbow flexors were immune to such effects. Strengthening this conclusion is the fact that both studies utilized the same fatiguing protocols and subjects and thereby controlling for these important variables. The findings may offer some functional implications in which muscle fatigue of unrelated muscle groups may negatively affect the performance of the knee extensors in the following activity, but not the elbow flexors.

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