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Research article

Lack of Evidence for Crossover Fatigue with Plantar Flexor Muscles

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Abstract

The occurrence and mechanisms underlying non-local or crossover muscle fatigue is an ongoing issue. This study aimed to investigate crossover fatigue of the plantar flexor muscles. Sixteen recreationally active males (n = 6) and females (n = 10) visited the laboratory for four sessions and performed a single 5-s pre-test maximal voluntary isometric contraction (MVIC) with each plantar flexors muscle. Thereafter, the fatigue intervention involved two 100-s MVICs (60-s recovery) with their dominant plantar flexors or rested for 260-s (control). Subsequently, in two separate sessions, Hoffman reflexes (H-reflex) were evoked in the non-dominant, non-exercised, leg before and following the dominant leg fatigue or control intervention (Fatigue-Reflex and Control-Reflex conditions). MVIC forces and volitional (V)-waves were monitored in the non-dominant leg in the other two sessions (Fatigue-MVIC and Control-MVIC) before and after the intervention (fatigue or control) as well as during 12 repeated MVICs and immediately thereafter. Despite the force reduction in the dominant leg (42.4%, $p = 0.002$), no crossover force deficit with single ($F_{(1,9)} = 0.02$, $p = 0.88$, $p\eta^2 = 0.003$) or repeated ($F_{(1,9)} = 0.006$, $p = 0.93$, $p\eta^2 = 0.001$) MVIC testing were observed. The H-reflex did not change after the fatigue ($F_{(1,7)} = 0.51$; $p = 0.49$; $p\eta^2 = 0.06$) or repeated MVICs ($F_{(1,8)} = 0.27$; $p = 0.61$; $p\eta^2 = 0.03$). There were also no crossover effects of fatigue on the V-wave with single ($F_{(1,8)} = 3.71$, $p = 0.09$, $p\eta^2 = 0.31$) or repeated MVICs ($F_{(1,6)} = 1.45$, $p = 0.27$, $p\eta^2 = 0.19$). Crossover fatigue was not evident with the plantar flexors nor any significant changes in H-reflex and V-waves in the soleus muscle. This finding suggests that crossover fatigue may not necessarily occur in slow-twitch predominant muscle groups.

Key words: Non-local muscle fatigue, soleus, fatigue, Hoffman reflex, V-wave.

Introduction

Neuromuscular fatigue is defined as a decline in performance induced by exercise with the potential to disrupt homeostasis (Twomey et al., 2017) or a progressive reduction in the ability of a muscle to produce power or force, which can be attributed to neural and/or muscular origins (Halperin et al., 2015). Strong evidence for neural factors following local fatigue in one limb, is provided by crossover (fatigue in the homologous muscle) (Aboodarda et al., 2015a; 2016; Halperin et al., 2014c; Kavanagh et al., 2016; Kawamoto et al., 2014) or non-local muscle fatigue (NLMF) (contralateral or ipsilateral heterologous muscles) (Aboodarda et al., 2015b; 2017; Halperin et al., 2014a; 2014c; Sambaher et al., 2016).

While NLMF or cross-over fatigue has been shown in many studies (Aboodarda et al., 2015a; 2015b; 2016; 2017; Ben Othman et al., 2017; Brandenberger et al., 2021; Doix et al., 2013; Grabiner and Owings, 1999; Halperin et al., 2014a; 2014c; Kavanagh et al., 2016; Kawamoto et al., 2014; Kennedy et al., 2013; Li et al., 2019; Sidhu et al., 2014; Takahashi et al., 2011; Todd et al., 2003) other studies have not illustrated NLMF or cross-over effects (Arora et al., 2015; Elmer et al., 2013; Grabiner and Owings, 1999; Prieske et al., 2017). A meta-analysis by Behm et al. (2021) failed to show significant evidence for NLMF when examining the force or power output of single or discrete maximal contractions but did reveal moderate impairments with endurance measures (e.g., time to task failure, force output with repeated or prolonged duration MVICs).

In addition to this conflict in the literature, whereas many of the studies have fatigued and tested fast twitch predominant muscles such as the quadriceps and elbow flexors (Behm et al. 2021), there is a lack of crossover fatigue studies related to the muscles, which possess a higher percentage of slow twitch fibers such as the soleus muscle (Campbell et al., 1979; Costill et al., 1976; Monster et al., 1978). Slow twitch predominant muscles may have different responses to cross-over or NLMF fatigue. As fatigue can increase muscle inactivation (e.g., as measured by electromyography, interpolated twitch technique) (Behm, 2004), then a decrease in the muscle's ability to fully activate might not be as pronounced with the lower threshold, more fatigue resistant, slow twitch predominant soleus motor units (Henneman and Mendell, 1980; Henneman et al., 1965). Hence, it is prudent to investigate NLMF in muscles with differing fiber compositions and functions such as the primarily postural, predominantly slow twitch soleus muscle.

The effect of exercise-induced fatigue on the neuromuscular system has been attributed to both central and peripheral (muscle) mechanisms (Behm, 2004). But the studies which exhibited force and voluntary activation decrements in the rested non-local muscle groups have demonstrated an absence of peripheral fatigue, which strongly support the hypothesis that central mechanisms contribute to the NLMF phenomenon (Sambaher et al., 2016). However, the literature investigating corticospinal excitability is inconsistent. Aboodarda et al. (2016) showed that unilateral elbow flexion fatigue enhanced supraspinal responsiveness of non-exercised biceps brachii. Another study found that quadriceps fatigue facilitated but then reduced motor evoked potentials (MEP) and short interval intracor-

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tical inhibition with no change in the intracortical facilitation of the interosseous and biceps brachii (Takahashi et al., 2011). While Matsuura and Ogata (2015) reported increased corticospinal excitability from the M-1 hand area following fatiguing unilateral plantar flexions, the contralateral flexor digitorum interosseous (FDI) muscle experienced decrements in the ability to maximally activate. Similarly, Šambaher et al. (2016) showed an increase in $M_{max,}$ CMEP, and MEP, but reductions in EMG and MVIC in unilateral elbow flexion after bilateral knee extensors fatigue. Fatiguing the left knee extensors with two sets of 100-s MVICs increased the cervicomedullary motor evoked potential (CMEP) (at 5, 50 & 100% MVIC) and MEP (at 100% MVC) in the right elbow flexor muscles but decreased MEPs at the lower intensities (Aboodarda et al., 2017). Sidhu et al. (2014) reported unilateral elbow flexors' voluntary activation (VA), MVIC force and MEP reduction following lower body cycling fatigue. These NLMF inconsistencies make further studies necessary to elucidate possible mechanisms of NLMF effects.

The Hoffman (H-) reflex is a measure of the afferent excitability of the alpha spinal motoneuron (Enoka et al., 1980) and the excitability of the neural reflex arc (Young et al., 2018). In addition, changes in the voluntary activation of the α-motoneurons may be quantified with the volitional (V-) wave, which reflects the level of efferent and descending neural drive (Duclay et al., 2008). Muscle afferents can produce inhibitory effects inducing decrements in central drive to both the working muscle and potentially to the non-exercised muscles as well (Amann, 2011; 2012; Amann et al., 2013; Halperin et al., 2015; Sidhu et al., 2014). However, in contrast to the aforementioned studies examining corticospinal excitability or inhibition with NLMF, there are no studies investigating V-wave and H-reflex changes in crossover and NLMF.

Therefore, the present study aimed to investigate changes in contralateral, plantar flexors torque and soleus H-reflex, and V-wave following fatigue of the dominant plantar flexors. Based on prior reports (Behm et al. 2021; Halperin et al., 2014a; 2014c; 2015; Kawamoto et al., 2014), we hypothesized that a repeated MVIC testing protocol of the contralateral, non-dominant plantar flexors would exhibit decreased torque production following a fatigue intervention of the dominant plantar flexors. Moreover, based on possible fatigue-induced afferent inhibition (Amann, 2011; 2012; Amann et al., 2013; Halperin et al., 2015; Sidhu et al., 2014), we hypothesized that the fatigue protocol of the dominant plantar flexors would decrease H-reflex and the V-wave responses of the non-dominant, non-exercised, soleus.

Methods

Participants

Using a pairwise comparison, a priori sample size was calculated with G*Power using a similar study (Ben Othman et al., 2017). With an $\alpha = 0.05$ and the statistical power $(1-\beta) = 0.8$ and an effect size based NLMF force reductions (ES = 0.44), a total sample size of 14 participants were required. Therefore, 16 young healthy, recreationally active individuals (males = 6, 24.3 ± 1.5 yrs., 75.6 ± 4.2 kg, 176.8 ± 3.5 cm & females=10, 23.5 ± 1.1 yrs., 160.5 ± 2.4 cm, and 57.9 ± 1.5 kg) were recruited. Prior to the data collection, subjects were asked to identify the preferred leg for kicking a ball to determine the dominant leg. Exclusion criteria included musculoskeletal or neurological disorders. To mitigate confounding variables, participants were instructed to avoid strenuous physical activity and alcohol, caffeine or nicotine consumption 24-hours prior to participation. Testing sessions were performed at similar times during the day to avoid diurnal variations with at least 24-hours between sessions. Prior to testing and after a brief explanation of the procedures, each participant completed the Physical Activity Readiness Questionnaire-Plus (Canadian Society for Exercise, 2003) and read and signed a letter of informed consent. This study was approved by the Interdisciplinary Committee on Ethics in Human Research of Memorial University (ICEHR No. 20200936-HK) in accordance with the Declaration of Helsinki.

Experimental Design

A randomized cross-over, within subject, quasi-experimental design with pre- and post-intervention measurements was employed in this study. Using an online random allocation software (https://www.randomizer.org/), the participants attended the laboratory for four sessions: (1) dominant leg's 260-s rest then testing the non-dominant leg's single and repeated (12) MVICs torques and V-waves (Control-MVIC); (2) dominant leg's 2×100-s fatiguing MVICs then testing the non-dominant leg's single and repeated (12) MVICs torques and V-waves (Fatigue-MVIC); (3) dominant leg's 260-s rest then testing the non-dominant leg's H-reflexes (no single or repeated MVICS of non-dominant leg: Control-Reflex); (4) dominant leg's 2×100-s fatiguing MVICs then testing the non-dominant leg's H-reflexes (no single or repeated MVICs of non-dominant leg: Fatigue-Reflex) (Figure 1). The intervention involved 2×100-s MVICs of the dominant plantar flexor muscles interspersed with 60-s rest (Fatigue-MVIC and Fatigue-Reflex) or 260-s of seated rest with the foot and lower leg in the boot apparatus (Control-MVIC and Control-Reflex). After the dominant leg's fatiguing protocol, testing involved either 12 x 5-s plantar flexors MVICs interspersed with 10-s rest between the contractions (Fatigue-MVIC or Control-MVIC: Figure 1: rows 1 and 2) or resting the non-dominant leg (Fatigue-Reflex or Control-Reflex: Figure1: rows 3 and 4). Prior publications have reported NLMF effects when testing with 12 x 5-s MVICs interspersed with 10-s rest (Halperin et al., 2014a; 2014c; Sambaher et al., 2016). The H-reflex and M-wave were obtained before the intervention (pre-test) and 30-s after 2x100-s fatigue intervention (Fatigue-Reflex) or rest (Control-Reflex) (post-test) in the non-dominant leg (Figure 1: rows 3 and 4). The V-waves and corresponding M-waves were measured in the non-dominant leg before, during, and after the 12 repetitions of the fatiguing test (Figure 1: rows 1 and 2).

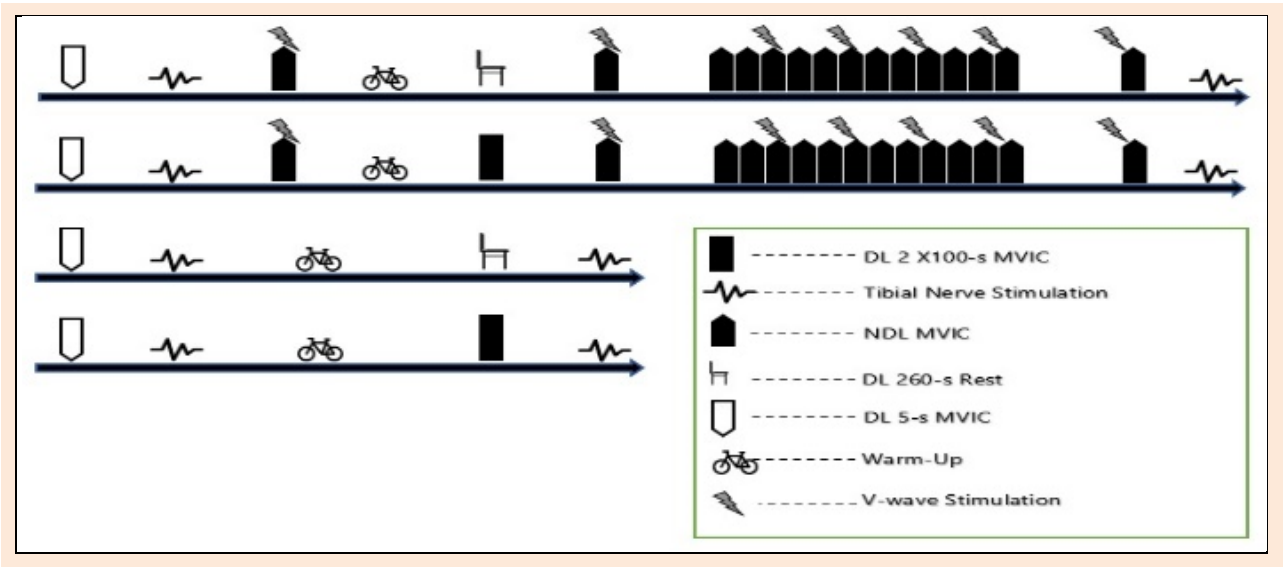

Figure 1. Experimental protocol. Abbreviations: DL 2 X 100-s MVIC: dominant leg 2 X 100-s maximal voluntary isometric contraction, NDL MVIC: non-dominant leg 5-s MVIC, DL 260-s Rest: dominant leg rest for 260-s, DL 5-s MVIC: dominant leg 5-s MVIC, Tibial Nerve Stimulation: the stimulation of the non-dominant leg to evoke the H-reflex and the M_{Max} at the beginning and at the end of each session. Conditions: First Row: Control-MVIC, Second Row: Fatigue-MVIC, Third Row: Control-Reflex, Fourth Row: Fatigue-Reflex.

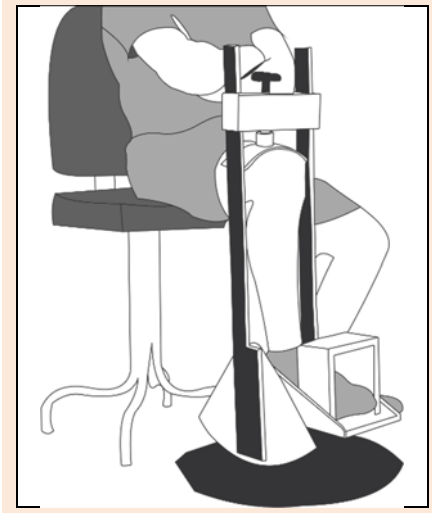

Figure 2. Boot apparatus for measuring the maximal voluntary isometric contraction with the plantar flexors.

Intervention

All interventions and tests were performed on a modified and reliable "Boot" Apparatus (Technical Services, Memorial University of Newfoundland: Figure 2) with the thigh horizontal to the floor while the knee and the ankle joints were flexed 90°. The straps prevented extraneous movement of the lower leg, while a thigh fixture securely restrained the foot so that any attempt to plantar flex the ankle joint resulted in an isometric contraction (Figure 2). The device was calibrated before each session by hanging known weights off the foot plate. Participants performed a general warm-up of lower body cycling for 5-min at a cadence of 70 RPM at one kilopond prior the intervention. At the beginning of each session, the participants were asked to do 2-3 plantar flexion warm-ups in their dominant leg equal to 50% of their maximum force for 5-s prior to fatiguing protocol. Based on prior published reports using the same intervention protocol to induce force and neuromuscular excitability decrements (e.g., EMG, motor evoked potentials) (Aboodarda et al., 2015b; 2017; Halperin et al., 2014c; Martin and Rattey, 2007), the fatiguing intervention involved a 2 × 100-s fatiguing protocol interspersed with 60-s rest with their arms crossed on their chests (Fatigue-MVIC and Fatigue-reflex sessions) or in the control sessions, they rested for 260-s (Control-MVIC or Control-Reflex). The peak-peak torque amplitudes in the first and last 5-s of each set at the 2 × 100-s dominant leg's intervention were calculated. The MVIC torque from the boot apparatus was achieved to determine the effect of fatigue on both the fatigued and contralateral non-fatigued leg. The participants were asked not to contract their non-dominant leg during the dominant leg's fatiguing intervention. The change from the unilateral dominant leg fatigue intervention to the non-dominant leg testing involved a 30-s transition from one leg to the other.

Electromyography (EMG)

The skin surface was prepared by shaving the target area, followed by cleaning and abrading with an abrasive pad and alcohol swabs to remove dead epithelial cells, obtain low resistance between the electrodes (<5-kOhms) and an adequate signal-to-noise ratio. The point of 5-cm distal to the insertion of the gastrocnemii on the Achilles tendon was measured and marked carefully to attach a pair of surface electrodes (Kendall 130 foam electrodes, Conductive Adhesive Hydrogel, Covidien IIc,) on the soleus muscles in both legs with an inter-electrode distance of 2-cm. The reference electrode was attached to the lateral malleolus of the non-dominant leg. The noise of the EMG signals was monitored to ensure they were less than 0.05mV (Konrad, 2005). The integral amplitude of the EMG activity was collected 500ms before and after the maximum amplitude of the torque during the MVICs (1-second total). The peak-peak amplitude of the torque between the baseline and the maximum torque (not including the stimulation amplitude) was reported as the force of the non-dominant leg during MVICs. Root mean square (RMS) EMG of the non-dominant leg during the 1st and the last 30-s of the dominant leg

fatiguing protocol was monitored to determine the extent of relaxation/activation of the non-dominant leg during the dominant leg fatiguing protocol. As relaxation of the non-dominant leg was desired for reflex measures (Fatigue-reflex and Control-reflex), the participants were not asked to perform a pre-MVIC in the non-dominant leg at the beginning of these sessions. Therefore, the baseline peak RMS EMG of the non-dominant leg was normalized to the average RMS EMG of pre-test Fatigue-MVIC session. The EMG signals were filtered with 10-500 Hz band pass filter and amplified (×1000 bipolar differential amplifier, input impedance = 2MΩ, common mode rejection ratio > 110dB min (50/60 Hz), noise > 5 μV) and analog-to-digitally converted (12 bit). EMG were collected at a sampling rate of 2000 Hz (Biopac System, Inc., DA 100: analog-digital converter MP150WSW; Holliston, Massachusetts, USA) and dedicated software (AcqKnowledge 4.1, Biopac System Inc.).

Stimulation

The H-reflex, M-wave, and V-wave were evoked in the non-dominant soleus muscle by percutaneous stimulation. The posterior tibial nerve was stimulated with a single rectangular pulse (1-ms) delivered by a Digitimer stimulator (model DS7AH, Hertfordshire, UK). For both optimal site identification and testing, the stimulator cathode probe (MYO004 Stimulator Probe, SS; Neurospec Research Neuroscience, Switzerland) was placed in the popliteal fossa and the anode electrode (Kendall 130 foam electrodes, Conductive Adhesive Hydrogel, Covidien IIc) was placed over the patella. The stimulation site, giving the greatest amplitude of the evoked potentials, was first located by the probe and marked. We asked the subjects to close their eyes and refrain them moving their hands or head to maintain constant cortico-vestibular influences on the excitability of the motor pool and limit afferent feedback from other peripheral receptors. A H-reflex and M-wave recruitment curve was produced (Young et al., 2018). The recruitment curve involved testing under a resting condition with an initial evoked stimulation at 2mA, with four stimuli provided at each intensity interspersed with 10-s rest and the intensity were raised by 2mA to the point of no further increase in evoked peak twitch torque and concomitant peak-to-peak M-wave amplitude (M_{max}). Following identification of the peak H-reflex amplitude (H_{max}: Figure 3b), the amperage that elicited 50% of the Hmax (H_{50}) of the ascending limb in the recruitment curve was chosen for testing purposes since it is sensitive to both facilitation and inhibition (Meinck, 1980). An evoked M-wave is recommended to monitor the stimulation conditions and to ensure a consistent level of motoneuron pool and muscle membrane action potential activity (Chen et al., 1999; Zehr, 2002). A H_{50}/M_{max} normalization ratio was calculated and used for statistical analysis. The participants were tested for afferent excitability of the spinal motoneuron (H-reflex) under resting conditions in the non-dominant soleus before and after the fatigue intervention (2 repetitions × 100-s interspersed with 60-s rest) or control rest period (260-s) (Fatigue-Reflex and Control-Reflex).

The V-waves were recorded in the non-dominant leg in two conditions (Fatigue-MVIC and Control-MVIC) and during the non-dominant leg's 5-s MVICs. The V-waves were normalized to the M-wave elicited during the MVIC ($M_{superimposed}$) and the $V/M_{superimposed}$ ratio was calculated for further analysis. The V-waves were obtained during the MVICs using the stimulation intensity equaled to 150% of the M_{max} (Figure 3a). The V-waves were recorded as the EMG potentials occurred generally between 30-45 ms after the stimulation artifact, respectively. Single MVICs were performed prior to the warm-up, immediately after the intervention and after the fatigue test (Figure 1). The V-waves were obtained during the MVIC prior to the warm-up, after the intervention, at the 3rd, 6th, 9th, and 12th repetitions of the fatigue test and after the fatigue test. (Fatigue-MVIC and Control-MVIC) (Figure 1).

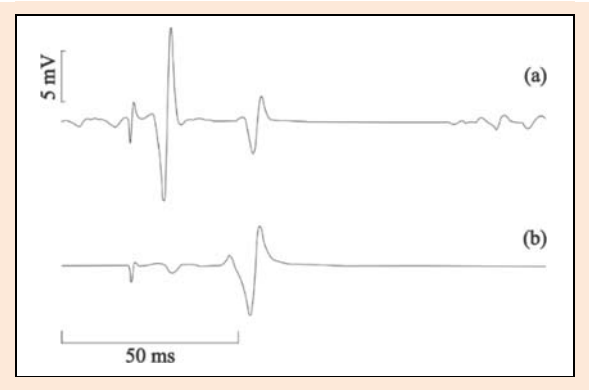

Figure 3. Typical H-reflex and V-wave from one representative participant evoked at the non-dominant leg's soleus muscle; (a) V-wave, (b) H-reflex. Initial spikes represent the stimulus artifact. The H-reflex was evoked on a relaxed muscle. The V-wave was evoked during the non-dominant leg's MVICs with a stimulation equal to 150% of Mmax.

Statistical analyses

Data were analyzed using SPSS-27 software. Assumption of normality (Shapiro-Wilk test) and sphericity (Mauchley test) were tested for all of the dependent variables. If the sphericity assumption was violated, the corrected value for non-sphericity with Greenhouse-Geisser epsilon was reported.

A two-way repeated measures ANOVA involving two conditions (Fatigue-reflex and Fatigue-MVIC) X four times (torques of the 1st and the last 5-s of the intervention protocol in two sets) was used to compare the dominant leg fatiguing protocol between the two sessions to observe whether there were any differences between the dominant leg fatigue and also to confirm that the fatiguing intervention was effective in fatiguing the dominant leg.

A two-way repeated measures ANOVA involving two conditions (Control-MVIC and Fatigue-MVIC) X three times (torques of pre-intervention, post-intervention, and post-fatigue testing) was used to analyze and compare any possible differences in the non-dominant leg's torque prior and after the intervention and after the fatigue testing. Another two-way repeated measures ANOVA involving two conditions (Control-MVIC and Fatigue-MVIC) X five times was used to analyze the non-dominant leg's torque changes during the fatiguing test.

The H_{50}/M_{max} ratio was analyzed with a two-way repeated measures ANOVA involving two conditions

(Control-Reflex, Fatigue-Reflex) X two times (pre-intervention vs. post-intervention) and another two-way repeated measures ANOVA involving two conditions (Control-MVIC and, Fatigue-MVIC) X two times (pre-intervention vs. post-fatiguing test) were used to determine pre-to-post changes with the M_{max} amplitude and H_{50}/M_{max} ratio in the four conditions (Fatigue-Reflex vs. Control-Reflex & Control-MVIC vs. Fatigue-MVIC).

The $V/M_{superimposed}$ ratio was analyzed with a two-way repeated measures ANOVA involving two conditions (Control-MVIC and Fatigue-MVIC) X three times (pre-intervention, post-intervention and post-fatigue testing) and another two-way repeated measures ANOVA involving two conditions (Control-MVIC and Fatigue-MVIC) X four times (repetitions 3, 6, 9, and 12 of fatigue testing,) were used to analyze the V-wave changes prior and post the intervention, post-fatigue testing and also during the fatigue testing repetitions.

Results

Fatigue intervention

There was no statistically significant difference between conditions (Fatigue-Reflex vs. Fatigue-MVIC) on the dominant leg, fatigue intervention, force reduction ($F_{(1,7)}$ = 0.007; p = *0.93;* $p\eta^2$ = 0.001). There was no significant condition*repetition interaction for force reduction in the dominant leg with the fatiguing intervention ($F_{(3,21)}$ = 0.11; p = 0.95; $p\eta^2$ = 0.016). A significant main effect for time was evident ($F_{(3,21)}$ = 37.7; p < 0.001; $p\eta^2$ = 0.84). The torque reduced 33.02% (89.5 ± 11.84 to 59.94 ± 8.83, Nm.s) from the first 5-s to the last 5-s of the first set (*p = 0.001*). The torque significantly recovered 44.51% (59.94 ± 10.89 to 86.62 ± 10.89, Nm.s) during the 60-s resting period (*p = 0.001*). There was a significant 40.52% (86.62 ± 10.89 to 51.52 ± 8.52, Nm.s) torque reduction in the second set (*p = 0.001*). Overall, there was a 42.43% torque reduction from the beginning to the end of the intervention (*p = 0.002*). The average RMS EMG of the non-exercising, non-dominant leg during the first 30-s and the last 30-s of the dominant leg's fatiguing intervention revealed that the non-dominant leg's activity at the beginning and end of the dominant leg's MVIC fatigue significantly (*p = 0.01*) increased from 3% to 12% of the non-dominant leg's MVIC RMS EMG.

Fatigue test single and repeated MVICs

There was no statistically significant effect of the condition (Control-MVIC vs. Fatigue-MVIC) ($F_{(1,9)}$ = 0.02, p = 0.88, $p\eta^2$ = 0.003) or interaction ($F_{(2,18)}$ = 0.02, p = 0.97, $p\eta^2$ = 0.003) on the torque changes when testing with a single MVIC. However, there was a significant effect of the time ($F_{(2,18)}$ = 5.58, p = 0.013, $p\eta^2$ = 0.38) on the torque reduction (12.3% post-fatigue test vs. pre-intervention) when testing single MVICs during Fatigue-MVIC and Control-MVIC sessions (Table 1, Figure 4).

There was no significant effect of the condition (Control-MVIC vs. Fatigue-MVIC) ($F_{(1,9)}$ = 0.006, *p = 0.93, $p\eta^2$ = 0.001*) or interaction ($F_{(4,36)}$ = 0.33, *p = 0.85, $p\eta^2$ = 0.036*) during the fatigue testing. However, there was a significant effect of the time ($F_{(4,36)}$ = 8.56, p < 0.001, $p\eta^2$ = 0.48) as the plantar flexors torque reduced 14.3% in repetition-12 compared to repetition-1 of the fatigue testing (*p < 0.001*). (Figure 4).

M_{max} and H-reflex

There were no significant effects of the condition ($F_{(1,7)}$ = 2.05; p = 0.19; $p\eta^2$ = 0.22), interaction (condition*time) ($F_{(1,7)}$ = 0.73; p = 0.41; $p\eta^2$ = 0.09), or time ($F_{(1,7)}$ = 1.47; p = 0.26; $p\eta^2$ = 0.17) on the pre-to-post M_{max} amplitude changes during Control-Reflex and Fatigue-Reflex sessions. The effects of the condition ($F_{(1,9)}$ = 0.19; p = 0.67; $p\eta^2$ = 0.02), interaction (condition*time) ($F_{(1,9)}$ = 4.65; p = 0.059; $p\eta^2$ = 0.34) or the time ($F_{(1,9)}$ = 2.9; p = 0.12; $p\eta^2$ = 0.24) on M_{max} were also not significant during Control-MVIC and Fatigue-MVIC sessions. There were no significant effects of the condition ($F_{(1,7)}$ = 0.51; p = 0.49; $p\eta^2$ = 0.06), interaction (condition*time) ($F_{(1,7)}$ = 3.23; p = 0.11; $p\eta^2$ = 0.31), or time ($F_{(1,7)}$ = 0.01; p = 0.9; $p\eta^2$ = 0.002) on the pre-to-post H_{50}/M_{max} ratio during Control-Reflex and Fatigue-Reflex sessions (Table 2). The effects of the condition ($F_{(1,8)}$ = 0.27; p = 0.61; $p\eta^2$ = 0.03), interaction (condition*time) ($F_{(1,8)}$ = 0.08; p = 0.78; $p\eta^2$ = 0.01) or time ($F_{(1,8)}$ = 0.41; p = 0.53; $p\eta^2$ = 0.04) on the H_{50}/M_{max} ratio were also not significant during Control-MVIC and Fatigue-MVIC sessions.

There was no significant effect of the condition (Control-MVIC and, Fatigue-MVIC) ($F_{(1,8)}$ = 3.71, *p = 0.09, $p\eta^2$ = 0.31*), time ($F_{(2,16)}$ = 1.79, *p = 0.19, $p\eta^2$ = 0.18*), or interaction (condition*time) ($F_{(2,16)}$ = 0.8, *p = 0.46, $p\eta^2$ = 0.09*) on the $V/M_{superimposed}$ at pre-intervention, post-intervention and post-fatigue testing. There was also no significant effect of the condition (Control-MVIC and, Fatigue-MVIC) ($F_{(1,6)}$ = 1.45, *p = 0.27, $p\eta^2$ = 0.19*), time ($F_{(3,18)}$ = 1.17, *p = 0.34, $p\eta^2$ = 0.16*) or, interaction (condition*time) ($F_{(3,18)}$ = 1.29, *p = 0.30, $p\eta^2$ = 0.17*) on the $V/M_{superimposed}$ at four different times of the fatigue testing (at the 3rd, 6th, 9th and 12th repetitions).

Table 1. MVIC fatigue index, peak torque (PT) and V-wave mean and standard deviation values.

	PRE-INT	POST-INT	REP-1	REP-3	REP-6	REP-9	REP-12	POST-FATIGUE
MVIC Fatigue Index (normalized: REP-12 / REP-1)								
Fatigue-MVIC	100 ± 0.0	95.11 ± 11.9	105.5 ± 24.7	95.2 ± 20.2	94.9 ± 20.2	90.8 ± 19.2	88.6 ± 21.4	88.42 ± 20.9
Control-MVIC	100 ± 0.0	94.79 ± 11.5	103.9 ± 10.4	93.9 ± 9.4	93.2 ± 8.9	90.7 ± 12.7	90.9 ± 11.6	87.0 ± 11.1
MVIC Peak Torque								
Fatigue-MVIC	90.5 ± 10.7	85.3 ± 9.6	93 ± 10.07	84.9 ± 10.2	85.5 ± 11.3	81.8 ± 10.6	79.6 ± 10.7	79.1 ± 9.9
Control-MVIC	98.04 ± 7.8	92.8 ± 8.5	101.6 ± 8.2	91.9 ± 7.7	91.2 ± 7.4	89.7 ± 8.6	86.2 ± 8.6	89.8 ± 8.6
$V/M_{superimposed}$								
Fatigue-MVIC	0.62 ± 0.5	0.57 ± 0.5	No V- measurement	0.28 ± 0.2	1.3 ± 2.7	0.85 ± 1.5	0.7 ± 1.1	0.68 ± 1.2
Control-MVIC	0.8 ± 1.7	0.2 ± 0.1	No V- measurement	0.16 ± 0.07	0.16 ± 0.05	0.13 ± 0.07	0.15 ± 0.1	0.04 ± 0.2

PRE-INT: pre-intervention, POST-INT: post-intervention, REP-1,3,6,9,12: repetitions of the post-test, 12 repeated contractions, $V/M_{superimposed}$: V wave normalized to the superimposed muscle action potential.

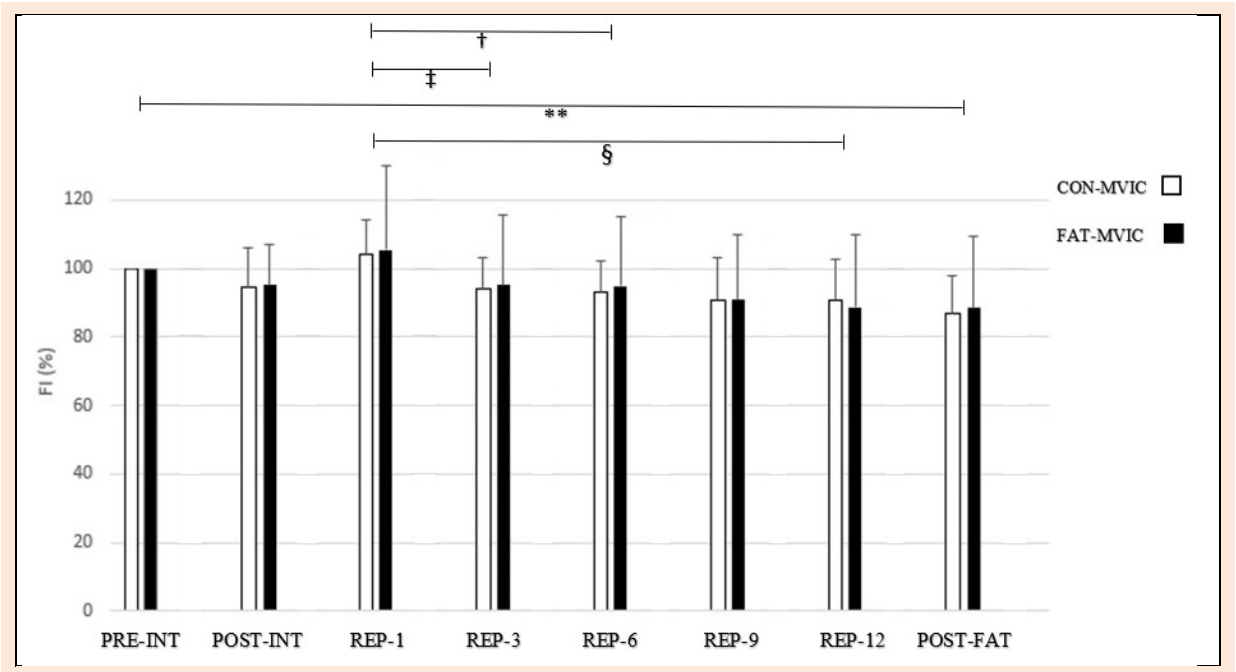

Figure 4. Mean normalized plantar flexors torque (Fatigue index, FI) changes in the non-dominant leg during two conditions [(Control-MVIC, 260-s rest in the dominant leg and, 12 repetitions of fatiguing test in the non-dominant leg) and (Fatigue-MVIC, 2 X 100-s fatigue intervention and, 12 repetitions of fatiguing test in the non-dominant leg)] at pre-intervention, post-intervention 15-s prior fatigue testing, repetitions one-twelve of the testing and 15-s post fatigue testing. **, difference between pre-intervention and post-fatigue test ($p < 0.05$), ‡, difference between repetition (REP)1 and REP3 ($p = 0.006$), †, difference between REP1 and REP6 ($p = 0.041$) and §, difference between REP1 vs. REP12 ($p = 0.026$). CON-MVIC: Control MVIC condition, Fat-MVIC: Fatigue MVIC condition.

Discussion

The major findings of this study showed that a) fatiguing the dominant plantar flexors (2x100-s) did not significantly affect the torques of the single or repeated MVICs with the non-dominant leg; b) muscle's direct response to the stimulation (M_{max}) did not change significantly in the non-dominant soleus; c) non-dominant soleus's H-reflex did not change with fatigue of the dominant plantar flexors; d) no significant changes were found in the non-dominant soleus V-wave.

The dominant limb fatigue intervention (2x100-s with 60-s recovery) was chosen based on prior published reports that induced contralateral force and neuromuscular excitability decrements (e.g., EMG, motor evoked potentials) (Aboodarda et al., 2015b; Halperin et al., 2014c; Martin and Rattey, 2007). However, these non-local effects seem to be inconsistent as a lack of crossover or NLMF effects with single discrete MVIC was recently reported in the Behm et al. (2021) meta-analysis and our results were in accordance with this finding. It seems that the contralateral single MVICs may not be as sensitive to crossover fatigue (Arora et al., 2015) as the adequate rest enables the participants to provide sufficient neural drive to prevent a significant decline in muscle performance (Aboodarda et al., 2019a).

Our MVIC testing fatiguing protocol was similar to Halperin et al. (2014a), Martin and Rattey (2007), and Aboodarda et al. (2015b) who found significant reductions in both force and EMG after fatiguing unilateral knee extensors. Despite using the same fatiguing protocol, the torque reductions in the fatigued muscles were greater in the Halperin et al. study (2014a) compared to the present results (70% vs. 42.4% torque reduction). The difference in fatigue may be related to the different muscle groups. Knee extension, which is used in many NLMF studies, would utilize the quadriceps with higher proportion fast-twitch fibers vs. plantar flexion in a seated, flexed knee position, which disadvantages the gastrocnemius and induces a greater reliance upon the soleus with a greater predominance of slow-twitch fibers (Campbell et al., 1979; Costill et al., 1976; Monster et al., 1978). According to Henneman's size principle (Henneman et al., 1965), type I (slow twitch) motor units with their smaller somas have lower recruitment thresholds. Since muscle inactivation can increase with fatigue (Behm, 2004), then a decrease in the central nervous system's ability to fully activate the muscle might not be as great an issue with the lower threshold slow twitch predominant soleus motor units.

Lack of crossover or NLMF effects with repetitive fatiguing MVICs in our study contradicts the Behm et al. (2021) meta-analysis report of moderate magnitude crossover effects. Force decrements have been reported when testing the contralateral quadriceps and elbow flexors with 12 MVICs (5-s:10-s, contraction-recovery) after five sets of dynamic knee extensions (Halperin et al. 2014a; Šambaher et al. 2016). Amann et al. (2013) tested the contralateral knee extensors with a constant load to failure following unilateral knee extensors fatigue with 85% of peak power to exhaustion and reported 50% shorter time-to-exhaustion compared to control conditions. In another study, Halperin et al. (2014c) fatigued the dominant knee extensors and elbow flexors with 2x100-s MVIC and reported a reduction in the repeated MVIC force in the non-dominant

knee extensors. Despite the aforementioned studies regarding NLMF effects, fatigue crossover effects of the lower limbs are complex (Kennedy et al., 2015). Although central fatigue has been suggested to mediate NLMF effects (Sambaher et al., 2016) and group III/IV muscle afferents were suggested to cause spinal and supraspinal fatigue to remote muscles (Sambaher et al., 2016), the maintenance of group III/IV firing with blood occlusion in knee extensors could not result in force or voluntary activation reduction contralaterally (Kennedy et al., 2015). This question could not be confirmed in our study.

Lower limb NLMF effects seems to be sex dependent with crossover effects found more consistently in males than in females (Halperin et al., 2015; Kennedy et al., 2015; Martin and Rattey, 2007). Women tend to exhibit greater fatigue resistance (Hunter, 2009; Russ and Kent-Braun, 2003). Since this study used a greater proportion of female participants, the impact of the fatigue intervention on the contralateral repeated MVIC testing may be attenuated with women versus men. With only six men vs. ten women, there was a lack of statistical power to detect possible significant sex differences.

To the best of our knowledge, this was the first study to investigate crossover H-reflex responses (indication of excitability and presynaptic inhibition of Ia afferents, and the capacity of the motoneurons to respond to synaptic input) (Aagaard et al., 2002; Duclay et al., 2008; Meinck, 1980) following unilateral voluntary isometric fatigue. Prior studies have shown the H-reflex amplitudes depression when evoked on the right flexor carpi radialis following short (5-s) unilateral contractions with different intensities in the wrist flexors/extensors and the ankle dorsiflexors (Hortobagyi et al., 2003) or following rhythmic (2Hz) contralateral homologous muscle contractions (Carson et al., 2004). Voluntary muscle contractions may change the contralateral motor pathway acutely and the crossed effects can be mediated by the afferents' pre-synaptic pathways (Hortobagyi et al., 2003). As the activation of the afferents in a working muscle can alter function in the ipsilateral motor cortex (Chen et al., 1999), we suggest that further studies investigate MEP and H-reflex simultaneously with crossover fatigue in various muscles.

The V-wave reflects both reflex excitability and pre-synaptic inhibition of Ia afferents (spinal processes) (Del Balso and Cafarelli, 2007). In addition, the V-wave response is also indicative of the level of neural drive in descending corticospinal pathways (supraspinal mechanisms) (Girard et al., 2011). To the best of our knowledge, no previous studies investigated the possibility of crossover V-wave changes following unilateral voluntary isometric fatigue. However, previous investigations attribute NLMF to the central drive at both spinal and supraspinal levels with the investigation of EMG, spinal, and supraspinal excitability in non-fatigued limbs (Aboodarda et al., 2015b; 2016; 2017; Sambaher et al., 2016). Aboodarda et al. (2015b) reported EMG decrements combined with transient higher spinal motoneuron excitability and no changes in peripheral excitability (M_{max} amplitude) in knee extensors following five sets of unilateral fatiguing of the elbow flexors suggesting a supraspinal mediated decrease in voluntary central drive. Halperin et al. (2014c) fatigued the dominant elbow flexors and knee extensors and reported EMG, voluntary activation, and force reductions in the non-dominant knee extensors. Šambaher et al. (2016) did not report EMG and MEP changes in dominant elbow flexor following bilateral knee extensor fatigue. However, they found lower elbow flexors MEP/CMEP ratio and higher CMEP values. In contrast, increases in cortical motor drive have also been shown to outweigh the disfacilitation of cortical cell excitability (Martin et al., 2006) and the net result of this process has been shown in the maintenance of MEP amplitude (Sambaher et al., 2016). With the lack of changes in peripheral (M-wave amplitude) and spinal (H-reflex) properties and using the process of elimination, we may infer that the supraspinal excitability was also unchanged with crossover soleus muscle. However, this cannot be confirmed as we did not measure the direct responses from the supraspinal levels. Therefore, further investigations are suggested with the soleus muscle to clarify possible spinal and supraspinal excitability modifications.

Limitations

Due to COVID restrictions, it was difficult to recruit equal numbers of female and male participants. Although the "a priori" statistical power analysis indicated 14 subjects was sufficient to attain adequate statistical power, an increased number of participants, especially males may have increased power and permitted a more in-depth examination of sex differences. Changing from the testing of dominant to non-dominant plantar flexors on the boot apparatus took approximately 30 seconds. H-reflex modulation has been suggested to exhibit a brief time course (Oza et al., 2017). According to Loscher et al. (1996) α-motoneuron pool excitability can return to the pre-fatigue state within about 30-s. Thus, it is possible that H-reflex and V-wave alterations may have recovered. However, if reflex activity returns to baseline within seconds, then the application or impact of these findings to practical activities would suggest any possible deficits are too transitory to affect daily activities. Furthermore, the H-reflex reflects changes in the afferent excitability of the alpha spinal motoneuron and since H-reflexes are more discernable from the soleus (Young et al., 2018), these reflex results may not totally reflect all plantar flexor muscles. Finally, the mean RMS EMG of the non-exercising, non-dominant leg during the first 30-s and the last 30-s of the dominant leg's fatiguing intervention increased from 3% to 12% of the non-dominant leg's MVIC RMS EMG. While the participants were exhorted to relax the non-exercised leg during the dominant limb fatigue intervention, there was trivial (3%) to minimal (12%) activation. However, this extent of contralateral contraction was insufficient to induce any changes in force, M-wave, H-reflex or V-wave. Finally, although this 2x100-s MVIC intervention did induce contralateral fatigue in prior studies using muscles such as the quadriceps and biceps brachii (Aboodarda et al., 2015b; 2017; Halperin et al., 2014c; Martin and Rattey, 2007), the more slow twitch predominant, fatigue resistant soleus may have played a role in the lack of crossover effects and hence, a greater volume (more sets or longer durations) of contractions may be needed to elicit non-local or crossover fatigue effects in this muscle group.

Conclusion

The present study indicates that there was no significant crossover fatigue with the plantar flexors as no crossover deficits were observable in the force, H-reflex, or V-wave. Although fatiguing of the dominant plantar flexors was apparent, it did not affect the crossover reflex excitability within the time frame of this testing protocol.

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Key points

- There were no significant crossover impairments in muscle endurance suggesting that when unilaterally training the plantar flexors, crossover decrements may not be an issue.
- Unilaterally fatiguing the plantar flexors induces only a trivial chance of experiencing single or discrete contraction force or strength decrements in the contralateral limb.

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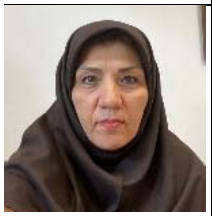

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