

## **Original Article**

# No sex differences in evoked contractile properties after fatiguing isometric and isotonic exercise for the plantar flexors

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#### **Abstract**

**Objectives**: Females tend to fatigue less than males after isometric exercise, but less is clear for isotonic exercise. Further, there have been relatively few sex comparisons for fatigability of the plantar flexors (PFs). We sought to investigate potential sex differences in contractile properties after a sustained maximal voluntary isometric contraction (MVIC) and isotonic contractions. **Methods**: Twenty-seven physically active males (n=14; 22±2 yrs) and females (n=13; 21±2 yrs) randomly performed a 2 min MVIC and 120 concentric isotonic (30% MVIC) contractions for the PFs on separate visits. Before and after each fatiguing task, muscle activation was obtained from brief MVICs, which was followed (~2 sec) by tibial nerve stimulation at rest. Contractile properties including peak twitch, absolute and normalized time to peak twitch, and half relaxation time were calculated. **Results**: No sex differences existed for fatigue-induced changes in muscle activation (p=0.09-0.41; d=0.33-0.69) or contractile properties (p=0.19-0.96; d=0.06-0.94). **Conclusions**: Peripheral fatigue, as indicated by contractile parameters, did not differ between sexes after isometric or isotonic exercise. The PFs similar fiber type proportions between sexes or greater fiber type heterogeneity may explain why sex differences in fatigability, though common in other muscle groups (e.g., knee extensors), were not expressed in this muscle group.

Keywords: Fatigue, Gender Differences, Nerve Stimulation, Peripheral Fatigue, Plantar Flexors

#### Introduction

Performance fatigue is commonly defined as an exerciseinduced decrease in the maximal strength, generated by skeletal muscle<sup>1</sup>. Performance fatigue occurs as a result of peripheral factors negatively affecting the contractile apparatus<sup>2</sup>, or by processes impairing the ability of the central nervous system (CNS) to optimally activate skeletal muscle<sup>3</sup>. Fatigue-induced decrements in maximal strength are influenced by biological sex, however, this appears to be dependent upon the contraction type<sup>4</sup> and muscle group<sup>5</sup>. Increasing knowledge on the influence these factors have on sex differences in performance fatigability should afford optimized exercise prescription, particularly for the less represented female population.

Females tend to be more fatigue resistant following isometric contractions<sup>5-10</sup>, particularly for lower intensity contractions<sup>9</sup>, but sex differences after dynamic contractions are less clear<sup>11</sup>. Potentially owing to the diversity in dynamic fatigue protocols, previous research on sex differences after dynamic contractions are equivocal<sup>12-16</sup>, with some studies reporting differences following isokinetic contractions<sup>12,13</sup>, and others reporting similar strength decrements after isotonic contractions<sup>14-16</sup>. Fatigue likely varies depending on the type (i.e., isokinetic versus isotonic) and velocity<sup>16,17</sup> of dynamic contractions. Isotonic contractions are not only important to study because the underpinning mechanisms for sex differences in fatigue may be unique<sup>18</sup>, but this contraction type also more closely resembles daily and

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Table 1. Group Characteristics.

Variable	Males	Females	% Difference			
Age (yrs)	22.3±2.3	21.0±2.5	5.83%			
Height (cm)	172.6±5.0	160.2±6.5*	7.18%			
Body Mass (kg)	77.4±8.2	58.8±7.8*	24.03%			
BMI (kg·m <sup>-2</sup> )	26.0±2.4	22.9±2.3*	11.92%			
Body Fat (%)	18.7±6.1	31.6±5.7*	40.82%			
CSA (cm²) 22.8±4.3		17.0±5.2*	25.44%			
Body mass index, BMI; Cross-sectional area, CSA; *significant (p≤0.05) difference between sexes						

athletic movements involving changes in velocity under submaximal loading<sup>19</sup>.

Studies demonstrating greater fatigability in males have consistently reported this for the elbow flexors<sup>5,16,20</sup> and knee extensors<sup>7,20,21</sup>. Other important locomotive muscle groups, such as the plantar flexors (PFs), have received relatively little attention<sup>13,14,22</sup>. Nonetheless, it appears that fatigue-induced decrements in isometric PF strength may not differ between sexes<sup>14,22</sup>. We recently reported no significant difference between sexes (moderate effect size) for relative decreases in isometric strength of the PFs after a sustained, maximal isometric contraction<sup>23</sup>. The peripheral and central mechanisms of fatigue are dependent upon the fatiguing task<sup>24,25</sup>, and these adjustments have relevant implications for sex differences<sup>15</sup>. Further, peripheral and central fatigue-induced responses are expected to vary between muscles with heterogeneous phenotypes, such as the compositional differences between the PFs and knee extensors<sup>26-30</sup>. Examination of contractile properties would yield further information on the peripheral manifestation of fatigue; however, this is lacking in studies on the PFs. An improved understanding on the effect of sex on fatigability can be achieved by examining more diverse muscle groups, including those that may not be prone to sex differences. We sought to examine contractile properties to identify their role in our previously reported fatigue responses for males and females<sup>23</sup>. Thus, the purpose of this study was to investigate potential sex differences in contractile properties after a sustained maximal voluntary isometric contraction (MVIC) and isotonic contractions. We hypothesized that decrements in peripheral fatigue, as indicated by the response in contractile parameters, will be greater in males than females only after the sustained isometric contraction. Finally, the larger muscle size of males is believed to be a primary reason for their increased fatigability<sup>31,32</sup>, yet many studies do not incorporate a measure of muscle size. A secondary purpose of this study was to examine the relationship between ultrasoundderived muscle size and fatigue-induced changes.

## **Materials and Methods**

#### **Participants**

Twenty-seven healthy (18-30 yrs) males (n=14) and females (n=13), who reported having performed 1-3 days/ week of lower-body resistance training and endurance exercise over the past six months volunteered for this study. Characteristics for both groups are displayed in Table 1. Individuals were excluded if they reported being a studentathlete or club sports athlete, running more than 60 min per week, supplementing with beta-alanine or creatine, or having any disease or illness. In addition, individuals were excluded if they had a body mass index over 30 kg·m<sup>-2</sup>, were not cleared for physical activity via the Physical Activity Readiness Questionnaire, or suffered a leg injury within the past year. Pregnant females were excluded, and only those who reported taking the same oral contraceptive for at least six months were included<sup>33</sup>. Testing visits were performed during the first two weeks of the oral contraceptive consumption phase for females. A 24-hr dietary recall was provided prior to each testing visit in order to calculate carbohydrate and total calorie intake using the MyFitnessPal application (Version 20.7.0.29453). Participants were instructed to arrive after a 4-hr fast prior to only the first visit. Finally, participants were instructed to avoid alcohol as well as endurance and resistance exercise for 24 and 48 hrs, respectively, prior to all visits. Prior to data collection, this study was approved by the Institutional Review Board under the Ethical Principles and Guidelines for the Protection of Human Subjects of Research report (IRB# 19-478). All participants provided oral and written consent prior to beginning the study.

#### Experimental Design

This cross-over design study required participants to attend three laboratory testing visits, separated by 2-7 days. The first visit consisted of the consent process, body composition testing, and familiarization with PF testing and fatigue protocols. The isometric or isotonic fatigue protocol was performed on the second and third visit, and this order was randomized prior to the first visit. The fatigue response

for isometric strength in this cohort have been previously reported<sup>23</sup>, thus, here we report on the response of contractile parameters and relationship between muscle size and fatigue-induced changes in isometric strength.

Torque was recorded during PF contractions of the dominant leg34 using a calibrated Biodex 4 isokinetic dynamometer (Biodex Medical Systems, Inc. Shirley, NY, USA). Torque and electromyography (EMG) were sampled at 2 kHz using an 8-channel Bagnoli Desktop System (Delsys, Inc., Boston, MA, USA). EMG of the medial gastrocnemius (MG) was recorded using parallel bar, bipolar surface electrodes (Delsys Bagnoli, Delsys, Inc., Natick, MA, USA). The electrode location (i.e., muscle belly of the MG) was marked immediately after the first testing visit to aid consistent placement across visits. A reference electrode was placed over the C7 vertebrae. Before electrode placement, the skin was shaved, abraded, and cleaned with alcohol, and subsequently, the electrodes were applied in accordance with the SENIAM project recommendations<sup>35</sup>. Participants were seated with hands across the chest, restraining straps over the trunk, pelvis, and thigh and the input axis of the dynamometer aligned with the axis of rotation of the ankle. The knee was extended to ~180°, and the hip was maintained at a comfortable angle<sup>36</sup>. The foot was secured to the footplate with two straps over the dorsal aspect and a custom ankle wrap technique using a non-elastic wrap to anchor the heel to the footplate. Ankle position was set at a neutral angle (neutral=90°) for isometric contractions and at the beginning of isotonic contractions, which involved a 25° range of motion (0°-25° plantar flexion). To prevent extensive contribution of the knee extensors during testing, EMG of the vastus lateralis was monitored.

## Body Composition and Ultrasonography

Height and body mass were measured using an electronic physician scale (Tanita WB 3000, Arlington Heights, IL, USA); and used to calculate body mass index (BMI). Total body fat % was obtained via bioelectrical impedance analysis (InBody770, InBody Co., Cerritos, CA, USA) following manufacturer recommendations. Briefly, to assess muscle cross-sectional area (CSA), panoramic images of the MG and lateral gastrocnemius were obtained using B-mode ultrasound (LOGIQ S7, General Electric Company, Milwaukee, WI, USA) using procedures similar to Olmos et al.37. Participants rested in the prone position for 10 min prior to the images being captured. Images were acquired with a multifrequency linear-array probe (ML6-15 L; 5–13 MHz; 50 mm field of view; General Electric Company, Milwaukee, WI, USA). Three images for each muscle were captured by the same investigator at 1/3 the distance from the tibial articular cleft between the femur and tibia condyle to the lateral malleolus on the dominant leg38. The polygon function in ImageJ software (version 1.46r, National Institutes of Health, Bethesda, Md.) was used to select as much of the muscle as possible without including the surrounding fascia to calculate CSA for each muscle. For statistical analysis, CSA was calculated as the sum of the gastrocnemii muscles. We have previously demonstrated "excellent" reliability for CSA using procedures similar to the current study<sup>37</sup>.

#### Transcutaneous Nerve Stimulation

Transcutaneous nerve stimulation began with electrical stimulation delivered in the popliteal fossa over the tibial nerve, while participants were seated in the Biodex dynamometer chair. A single 100 ms pulse, was delivered via a bar electrode (E.SBO2O, Digitimer, Ltd., Welwyn Garden City, UK) using a constant current stimulator (DS7AH, Digitimer, Ltd., Welwyn Garden City, UK) to find resting peak twitch. Using a low current (~50 mA), electrical stimulation was delivered in several locations over the popliteal fossa. The optimal location yielding the highest resting twitch was identified, marked, and used for all subsequent stimulations. Upon finding the optimal location, the current was progressively increased by 10-30 mA increments until no further increase in twitch amplitude could be found despite the increasing current. An additional 20% increase in current was used for subsequent stimulations (males=172.93±43.97 mA; females=177.62±40.71 mA) and this current was consistent between testing visits (p=0.58).

#### **Baseline Testing**

Prior to testing, participants performed two submaximal isometric PF contractions at 50% and 75% of perceived maximal effort. Participants then performed three, 3-5 sec MVICs, separated by one min of rest. Additional MVIC trials were performed if peak torque from the first three trials varied by more than 5%. Electrical stimulation was delivered during the plateau phase of the brief MVICs to elicit a superimposed twitch for the calculation of voluntary activation, but for technical reasons this calculation was not possible (see limitations section). An additional singlet was delivered ~2 sec after the MVICs and this was used to measure contractile properties (see Data Analysis). Participants received consistent, *strong* verbal encouragement and visual feedback throughout the testing and fatigue protocols.

#### Isometric and Isotonic fatigue protocols

The isometric fatigue protocol consisted of a 2-min sustained MVIC. The dynamic fatigue protocol required the performance of 120 concentric isotonic contractions of the PFs at 30% of MVIC peak torque with ~1.5-2 sec separating contractions<sup>39</sup>. Participants were instructed to stay completely relaxed as investigators reset the level arm to a 90° joint angle in between concentric contractions during the dynamic fatigue protocol. In addition, participants were instructed to push "as hard and as fast as possible" for isotonic contractions, whereas "as hard as possible" were the instructions for the sustained MVIC. Immediately (~6 sec)

Table 2. Baseline Data.

Variable	Males	Females	% Difference	ICC	SEM	CV
Peak twitch (Nm)	27.64±6.86	21.71±3.67*	21.45%	0.859	2.43	9.8%
TPT (ms)	0.10±0.02	0.10±0.01	0.20%	0.828	0.007	6.9%
TPT <sub>NORM</sub> (ms·Nm <sup>-1</sup> )	0.004±0.001	0.005±0.001*	18.75%	0.774	0.0005	11.9%
HRT (ms)	0.08±0.01	0.09±0.01	11.11%	0.669	0.007	8.1%
RMS (mV)	0.17±0.05	0.15±0.05	11.76%	0.444	0.046	29.4%

Time to peak twitch, TPT; Half relaxation time, HRT; Root mean square, RMS; Intraclass correlation coefficient, ICC; Standard error of the mean, SEM; Coefficient of variation, CV \*significant (p<0.05) difference between sexes.

Table 3. Percent Changes after the Isometric and Isotonic Fatigue Protocols.

	Isom	etric	Isotonic				
Variable	Males	Females	Males	Females			
Peak twitch (Nm)	-27.20±13.64%	-30.39±16.13%	-20.01±15.25%	-18.07±11.53%			
TPT (ms)	-5.89±14.09%	-4.21±9.82%	-2.13±10.05%	7.38±10.15%			
TPT <sub>NORM</sub> (ms·Nm <sup>-1</sup> )	33.46±29.22%	44.84±36.90%	27.09±28.78%	33.76±24.03%			
HRT (ms)	38.34±23.21%	46.34±25.57%	22.92±25.00%	24.45±25.06%			
Time to peak twitch, TPT; time to peak twitch normalized to peak twitch, TPT <sub>NORM</sub> ; Half relaxation time, HRT.							

following each fatigue protocol, rate of perceived exertion (RPE; Category Ratio Scale-10)<sup>40</sup> was recorded along with a final (i.e., post-test) MVIC followed by a resting twitch.

## Data Analysis

All data analysis was performed using custom written software (LabVIEW, National Instruments), EMG was processed using a 4th order Butterworth filter with a low- and high-frequency cutoff of 20 and 400 Hz, respectively, which was applied to the scaled, zero means EMG signal. The resting twitch with the highest amplitude (i.e., peak twitch) was used for subsequent baseline analysis. Time to peak twitch (TPT) was the time from the onset of torque development to peak twitch. The same investigator viewed the torque signal with a high resolution and determined the onset manually as the last peak/trough prior to upward deflection of the signal<sup>41</sup>. TPT was also divided by the peak twitch (TPT<sub>NORM</sub>) for normalization. Half relaxation time (HRT) was determined as the time elapsed from peak twitch until torque decreased to 50% of the peak twitch. EMG amplitude was calculated as the average root mean square (RMS) for the 500 ms epoch corresponding to peak torque (250 ms either side). RMS values at post-testing were normalized to the baseline value and used for subsequent analysis. Percent change [(posttesting value – baseline value)/baseline value] × 10015,20 was calculated for the evoked contractile parameters and used for subsequent analysis.

# **Statistical Analyses**

Normality of data was assessed via the Kolmogorov-Smirnov test. Two-way (condition × sex) analyses of variance (ANOVAs) were used to compare baseline data between sexes for both conditions. Comparisons of carbohydrate and total daily calorie intake between visits were conducted using dependent samples t-tests. Independent samples t-tests were used to compare group characteristics and the percent change for normally distributed dependent variables. The Mann-Whitney test was used to analyze percent change in non-normally distributed dependent variables (i.e., TPT and HRT). Equality of variances were tested using Levene's Test for Equality of Variances. Test-retest reliability analyses were performed on baseline data from each visit to assess the relative and absolute reliability using intraclass correlation coefficients (ICC $_{2,1}$ ) $^{42}$  and standard error of measurement (SEM), respectively. The SEM, expressed in the units of measurement, was calculated as the square root of the mean square error term. Coefficient of variation (CV) was calculated as the SEM relative to the grand mean. ICC values of 1-0.80, 0.79-0.60, and <0.60 were interpreted as "excellent", "good", and "poor" reliability, respectively 43,44. Statistical analyses were performed using PASW version 28.0 (SPSS Inc, Chicago, IL, USA), and an a level of p≤0.05 was used to determine statistical significance. Effect sizes were reported using partial eta squared  $(\eta_{_D}{}^2)$  for ANOVA

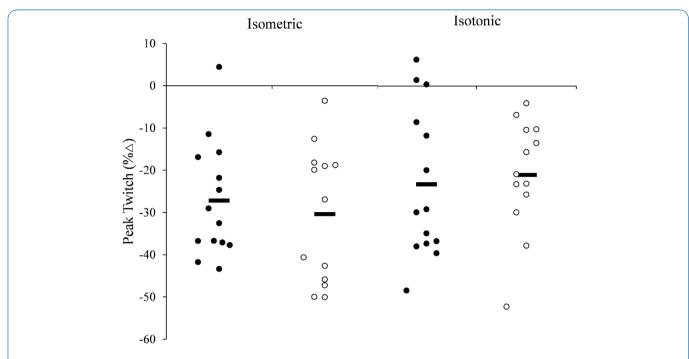


Figure 1. Individual responses for males (black filled circles) and females (open circles), and group means (bars) for percent changes in peak twitch after the isometric and isotonic fatiguing protocol.

analyses and indicated as small (<0.06), medium (0.07-0.14) and large (>0.14) effect sizes; whereas Cohen's d was used for pairwise comparisons with 0.30, 0.50, and 0.80 indicating the same effect size classifications<sup>45</sup>. Data is provided as mean  $\pm$  standard deviation (SD) in the text and tables, while figures display individual level data. Figure were designed using templates based on Weissgerber, Milic, Winham, and Garovic<sup>46</sup>.

#### Results

## Baseline Measurements

Self-reported carbohydrate intake (203.33 $\pm$ 119.86 kcal vs. 183.33 $\pm$ 80.98 kcal) and total calories (1,808.18 $\pm$ 1,108.23 kcal vs. 1,638.92 $\pm$ 619.58 kcal) were similar between visits (p=0.45, d=0.14 and p=0.337, d=0.18, respectively). Males were taller (p<0.01, d=2.15) and possessed a greater body mass (p<0.01, d=2.31) and BMI (p=0.02, d=1.31) (Table 1). Males had a lower body fat % (p<0.01, d=2.19) and larger gastrocnemii CSA (p<0.01, d=1.21) (Table 1).

Table 2 shows baseline data, averaged across the two visits, and corresponding reliability statistics. Except for RMS, all measures demonstrated "good" or "excellent" reliability. No condition  $\times$  sex interactions were present for any measures (p>0.05) indicating performance was consistent between baseline visits. Peak twitch (p=0.01,  $\eta_p^2$ =0.234) was greater in males. TPT (p=0.98,  $\eta_p^2$ =0.000) was similar between

sexes, while TPT $_{\rm NORM}$  (p=0.03,  $\eta_p^{~2}$ =0.173) was lower in males. HRT (p=0.22,  $\eta_p^{~2}$ =0.060) and RMS (p=0.23,  $\eta_p^{~2}$ =0.057) were similar between sexes.

# Isometric Fatigue

Table 3 displays percent changes after isometric fatigue. Peak twitch (p=0.58, d=0.21; Figure 1), TPT (p=0.64, d=0.14; Figure 2), HRT (p=0.38, d=0.33), and TPT<sub>NORM</sub> (p=0.38, d=0.34) demonstrated similar changes between sexes. Initially, normalized RMS demonstrated a sex difference (p=0.05, d=0.78), but upon removal of an outlier in the female group, there was no sex difference (p=0.09, d=0.69; males: 0.94±0.25 %MVIC vs. females: 1.19±0.37 %MVIC; Figure 3). Figure 4 displays the non-significant, "weak" relationship between CSA and our previously reported<sup>23</sup> percent change in isometric peak torque data. RPE (p=0.81, d=0.10) was similar between males (8.64±1.39) and females (8.77±1.24).

## Isotonic Fatigue

Table 3 displays percent changes after the isotonic contractions. Peak twitch (p=0.72, d=0.14; Figure 1), TPT $_{NORM}$  (p=0.52, d=0.25), and HRT (p=0.96, d=0.06) demonstrated similar changes between males and females. A large effect size was demonstrated for TPT but no statistical difference between groups was found (p=0.13, d=0.94; Figure 2). Normalized RMS (p=0.41, d=0.33; Figure 3) demonstrated similar changes between males (1.02±0.24 %MVIC) and

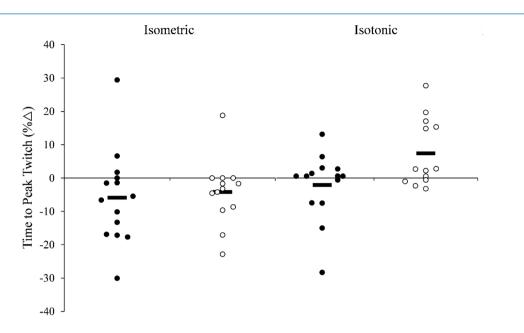


Figure 2. Individual responses for males (black filled circles) and females (open circles), and group means (bars) for percent changes in time to peak twitch after the isometric and isotonic fatiguing protocols.

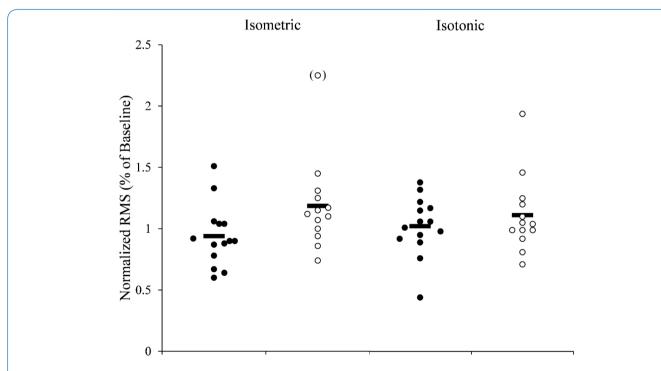


Figure 3. Individual responses for males (black filled circles) and females (open circles), and group means (bars) for normalized RMS after the isometric and isotonic fatiguing protocols. Outlier enclosed in parentheses.

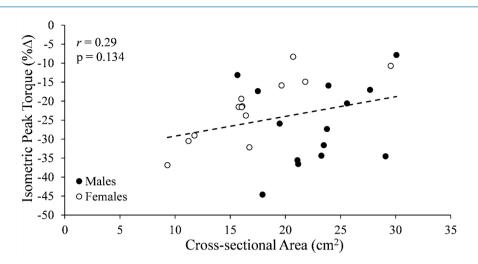


Figure 4. Scatterplot with line of best fit for cross-sectional area and our previously reported<sup>23</sup> percent change in isometric peak torque data.

females (1.11 $\pm$ 0.31 %MVIC). There was no relationship (r=-0.23; p=0.24) between CSA and our previously reported<sup>23</sup> percent change in isometric peak torque data. RPE (p=0.09, d=0.67) was similar between males (7.71 $\pm$ 1.64) and females (8.77 $\pm$ 1.48).

## **Discussion**

The purpose of this study was to investigate potential sex differences in contractile properties after a sustained MVIC and isotonic contractions. The topic of sex differences in performance fatigue has received substantial attention within the last decade<sup>47-49</sup>. However, a few themes in the present work allow our findings to extend current knowledge in this area. While the majority of studies have examined sex differences after isometric fatigue, the current study expands upon this by also examining fatigue after dynamic muscle contractions. Furthermore, an important aspect of this study was the investigation of the less frequently reported PFs. The examinator of unique muscle groups with heterogenous phenotypes provides a more comprehensive understanding of sex differences in fatigability. The current findings indicated that, regardless of contraction type, responses for contractile parameters were not different signifying a similar degree of peripheral fatigue between sexes after isometric and isotonic exercise.

The similar response for peripheral fatigue between sexes provide a physiological basis for our previous report on the same cohort indicating no sex differences in fatigue-induced decrements for isometric strength<sup>23</sup>. Peripheral fatigue measures included peak twitch and time-dependent markers of contractile function, including the relaxation phase, which in conjunction, reflect a reduced

number of active cross-bridges, slowing of cross-bridges, or decrements in calcium kinetics resulting from metabolite accumulation<sup>50</sup>. Contractile properties are a primary contributor to sex differences in fatigue after isometric exercise<sup>8,9,31</sup>, with some evidence existing for slow, dynamic exercise<sup>16</sup>. Our findings contrast with another recent report that investigated sex differences using high-velocity isotonic knee extensions as a fatiguing modality<sup>15</sup>. Senefeld et al. 15 reported greater decrements in males for peak twitch and HRT than females following dynamic contractions but not an isometric task, which suggest sex differences in excitation-coupling and/or intracellular Ca2+ reuptake. Further, there were no sex differences in corticospinal or cortical adjustments when assessed with peripheral nerve or motor cortex stimulation, which further emphasized that peripheral, but not central, mechanisms were responsible for sex differences. Studies indicating greater fatigability in males have consistently reported this for the elbow flexors<sup>5,16,20</sup> and knee extensors<sup>7,20,21</sup>. There are limited reports comparing contractile properties between sexes after fatiguing exercise for the PFs, but the current findings suggest a divergence relative to the elbow flexors and knee extensors. Muscle specific factors such as fiber type distribution and cross-sectional area are influential for sex differences in fatigability and likely explain the similar fatigue response between sexes.

The PFs possess a more diverse fiber type composition due to the contrast in proportion of type I fibers between the soleus and gastrocnemii, whereas muscles comprising the knee extensors typically have a mixed (~50/50) fiber type composition<sup>26-30</sup>. Further, sex differences in fiber type composition, which is well evidenced for the vastus lateralis<sup>51,52</sup>, may be negligible for muscles of the PFs<sup>53</sup>, though

there is limited evidence on fiber type proportions for each lower-leg muscle in males and females. The higher relative proportion of type II fibers for the knee extensors in males is expected to cause greater peripheral impairment during fatiguing exercise<sup>54</sup>. During sustained isometric contractions, the greater muscle size in males increases intramuscular pressure<sup>31</sup>, thereby limiting blood flow and increasing metabolite accumulation<sup>4,32</sup>. Despite our verification of larger gastrocnemii in males, it was not a factor in the current study given the lack of differences between groups. Avin et al. 5 showed no difference between sexes for fatigability of the dorsiflexors but demonstrated greater fatigue resistance for the elbow flexors in females. Further, baseline isometric strength (used as a proxy of muscle size) poorly explained the variance in endurance time for the dorsiflexors ( $r^2$ =0.03), whereas much greater variance was explained for the elbow flexors ( $r^2$ =0.30). Figure 4 displays the non-significant, "weak" association between CSA and percent change in isometric peak torque (previously reported) in this cohort. Our findings are similar to those reported for the dorsiflexors with CSA explaining little variance ( $r^2$ =0.08) for percent change in isometric peak torque. Therefore, while sex differences in muscle size undoubtedly influence fatigability, this appears to be dependent upon the muscle group and the lower-leg muscles may have unique mediating factors (e.g., fiber type composition). Sex differences in fatigability are most prominent at lower intensities during sustained isometric exercise<sup>9,55</sup>, perhaps due to the increased time for metabolite accumulation, which is an important consideration for future research. It appears that sex differences in fatigability are limited or non-existent for PFs, and greater representation of this locomotive muscle in future research will enable more conclusive inferences. Despite no sex differences, the similar decrements between contractile parameters and isometric strength (Table 3) suggest that peripheral fatigue had a relatively large role in reducing isometric strength. The similar response for muscle activation between sexes should be interpreted cautiously given its "poor" reliability and since EMG affords little specificity into fatigue-related mechanisms<sup>56</sup>. Though CNS adjustments due to fatigue were likely<sup>3,57</sup>, any sex-specific changes cannot be confirmed since the present study did not measure voluntary activation or record motor unit behavior.

A limitation of the current work, despite our efforts, is the lack of outcomes describing responses of the CNS and potential sex differences for these changes. We attempted to measure voluntary activation, but did not have appropriate sensitivity given our strategy. More specifically, superimposed torque during MVICs was elicited using a single pulse, but the electrically induced torque was not discernable for several trials due to a poor signal-to-noise ratio. This limitation and other challenges associated with using singlets to determine voluntary activation have been discussed in more detail<sup>58,59</sup>. Doublet stimulation was not possible given our laboratory setup at the time of data collection. It could be speculated that fatigue-related impairments of the CNS did not differ between sexes due to the similar changes in performance fatigue

and contractile responses; however, this is not a certainty. Another limitation of the present study was the large withingroup variability in the fatigue response, which was likely a result of biological variation across subjects, given measures were shown to be reliable. It was not possible to control the relative fatigue due to the different modalities of fatiguing exercise and unique fatigue response during isometric and isotonic exercise<sup>60,61</sup>. Finally, while our inclusion of muscle CSA provided additional information regarding its role as a correlate of fatigue-induced decrements in performance, it is important to note that this measurement did not include the soleus which accounts for ~50% of total PF area<sup>62</sup>.

#### Conclusion

Males and females demonstrated a similar response for peripheral fatigue of the plantar flexors after fatiguing isometric and isotonic contractions. These findings, in conjunction with others<sup>14,22</sup>, indicate that the commonly reported sex difference in fatigability for muscles such as the knee extensors and elbow flexors does not extend to the plantar flexors. The reason for this discrepancy between muscles is unclear, but similarities in fiber type proportions between sexes or greater heterogeneity of fiber types for the muscles comprising the plantar flexors are plausible candidates. Greater diversity of muscle groups tested, particularly lower-body muscles, is needed to identify musclespecific factors relevant to sex differences in fatigability and determine the potential implications for performance.

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