SEX-RELATED DIFFERENCES OF FATIGABILITY DURING ISOTONIC CONCENTRIC CONTRACTIONS OF THE PLANTAR FLEXORS IN HUMANS

by

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A THESIS

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Dr. Brian H. Dalton

Fatigue can be affected by several sex-related factors and the purpose of this study was to investigate those differences associated with maximal-effort isotonic contractions of the plantar flexors. The criterion measure of fatigue here was reductions in instantaneous peak power. It was hypothesized that males would fatigue more than females and this was supported as peak power was reduced in males by 34% and by only 22% for females at the end of the fatigue task. Novel aspects of this study include the sex-based investigation of fatiguing isotonic plantar flexor contractions and the inclusion of rate of torque development and rate of velocity development as factors that may be contributing to the decreases in production of power during fatigue tasks. Overall, this study shows that males are more fatigable during dynamic contractions of the plantar flexors.

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I would like to thank Dr. Dalton for helping me to fully examine the sex-related differences of fatigue. I am sincerely grateful for all of the discussion, troubleshooting, teaching, and editing that, in its final form, is displayed through this thesis. It was a privilege to have such an excellent professor to guide me through the strenuous, but rewarding process. I would also like to thank Dr. Christie for her assistance as a second opinion in all matters statistical and physiological. Finally, I would like to thank Professor Rosenberg for his willingness to serve as my CHC representative, and my family and friends for supporting me throughout this past year.

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List of Acronyms

ATP: adenosine triphosphate
Ca^{2+}: calcium
Ca^{2+}ATPase: calcium adenosine triphosphatase
HRT: half relaxation time
MVC: maximal voluntary isometric contraction
Nm: Newton meters
Pt: peak twitch torque
Rad: radians
RTD: rate of torque development
RVD: rate of velocity development
s: seconds
TPT: time to peak twitch
Tp: pre-twitch before MVC
Ts: superimposed twitch during MVC
Tr: relaxed twitch after MVC
VA: voluntary activation
W: watts

General Overview

Fatigue is defined as an activity-induced loss of the muscle's ability to develop maximal force or power, and is reversible upon rest (Williams and Ratel, 2009). It is the inability to keep performing at a consistently high level, not due to injury, but due to physiological deficiencies. It can alter task function by decreasing the ability to contract and control our muscles to their full capacity.

It is important to study sex-related differences of fatigue because there are relatively low proportions of comparative studies that address this topic. This is known as a "sex bias" because there are more single-sex studies performed on males than on females (Taylor 2009). It is important to differentiate between males and females in physiological studies because treatment or rehabilitation plans can vary depending on the discovered physiological differences. In 2011, Beery and Zucker reported that only <13% of physiological studies on human subjects reported results for both sexes, and sex-based analysis was only completed in 30% of those studies. The research areas of immunology, neurophysiology, and pharmacology are the most susceptible to this sex-bias where as behavior, endocrinology, and reproduction show the least amount of bias (Beery 2011). In 1993, the National Institute of Health (NIH) issued a mandate that encourages NIH-funded research teams to include females, minorities, and children in their study or to justify their exclusion of the underrepresented groups (Policy 2008). In a sample of various Research Ethics Board administrators of NIH-funded institutions across the country, however, only 25% of them consider this mandate to have succeeded in creating greater inclusion (Taylor 2009). This sex bias in research is indeed a great motivation for my interest in investigating the sex-related differences of

muscle fatigue on neuromuscular function in young males and females. Adding this research to the previous literature on the topic will help further the conversation surrounding how sex-related differences affect our performance of everyday activities (Hunter 2014).

Different tasks stress different neuromuscular sites (sites involved in a muscular contraction), and this is known as the task-dependent nature of fatigue (Enoka and Duchateau 2008). This phenomenon can explain why sex-related differences vary among a variety of tests. Assorted studies include variables such as the type (isometric, isotonic, or isokinetic), frequency (contractions per minute), speed (contraction velocity), and intensity (% maximal voluntary contraction) of contractions. One type of contraction is isometric which involves contraction of a muscle group against a resistance without limb movement. An example of this would be pushing against a stationary wall. Another type of contraction is isotonic which involves shortening (concentric) or lengthening (eccentric) of the muscle against a fixed resistance. An example of an isotonic shortening contraction is when the elbow flexors contract to lift an object held in the hand. Isotonic contractions seem to be the most applicable to activities of daily living such as walking, teeth brushing, driving, and cooking, which all require dynamic muscle contractions to accomplish the given task's goal. Over the last 20 years, however, research on fatigue has typically focused on sex-related differences during isometric contractions (Hunter 2014). The present study, and the topic of my thesis, focuses on isotonic contractions in an effort to mimic real-world tasks as closely as possible and to fill a gap in the literature.

There are several ways to quantify fatigue. In the current literature, the most common way is to perform a maximal voluntary isometric contraction (MVC) before and after a fatigue task in order to assess maximal strength and capacity of the neuromuscular system. In the present study, fatigue is quantified by assessing the decrease in muscle power at the end of task termination compared with the beginning of the task. Power is an important variable to collect because it is more applicable to a dynamic contraction than torque alone because it is the product of torque (or force) and velocity (speed), both of which are variables that were collected for each contraction in this study. As conveyed in table 1, power has not been thoroughly investigated as an objective measurement of fatigue even though it has the potential to better elucidate sex-related differences of fatigue.

Table 1. Literature review summary

Author	**Year**	**Muscle group**	**Number of contractions**	**Task type**	**Criterion of fatigue**	**Comparative Fatigability**
Maughan et al.	1986	Knee extensors	Contractions to task failure	Isometric at 20% MVC	# of contractions to task failure	Males more fatigable
				Isometric at 50% MVC		Similar
				Isometric at 80% MVC		Similar
		Elbow flexors	Contractions to task failure	Isotonic at 50%; controlled-velocity	# of contractions to task failure	Males more fatigable
				Isotonic at 60%; controlled-velocity		Males more fatigable

				Isotonic at 70%; controlled-velocity		Males more fatigable
				Isotonic at 80%; controlled-velocity		Similar
				Isotonic at 90%; controlled-velocity		Similar
Clark et al.	2003	Back extensors	Contractions to task failure	Isotonic at 50% MVC; controlled-velocity	# of contractions to task failure	Similar
				Isometric at 50% MVC		Males more fatigable
Pincivero et al.	2003	Knee extensors	30 contractions	Isokinetic at 3.14 rad/s	Decreases in power and torque,	Males more fatigable
		Knee flexors	30 contractions	Isokinetic at 3.14 rad/s		Males more fatigable
Pincivero et al.	2004	Knee extensors	Contractions to task failure	Isotonic at 50% 1RM; controlled-velocity	# of contractions to task failure	Similar
Labarbera et al.	2013	Knee extensors	Contractions to task failure	Isotonic at 20% MVC; max-velocity	# of contractions to task failure	Males more fatigable
Senefeld et al.	2013	Elbow flexors	90 contractions	Max-velocity isotonic at 20% MVC	Decreases in power and MVC	Power and MVC similar
		Knee extensors	90 contractions	Max-velocity isotonic at 20% MVC		Power: similar; MVC: males more fatigable
Stock et al.	2013	Knee extensors	50 contractions	Isokinetic at 3.14 rads/s	Decreases in torque	Similar

A comprehensive list of shortening conraction studies that investigated sex-related differences in order of year published.

Introduction

Neuromuscular fatigue is defined as activity-induced loss of the muscle's ability to develop maximal force or power, and is reversible upon rest (Williams and Ratel 2009). There have been a multitude of studies that have focused on fatigue but so far, there is no clear consensus on whether males are more or less fatigable than females. The differences may be due to several factors including anthropometric characteristics, fiber type proportions, metabolic pathway preferences and/or central (neurological) mechanisms.

Typically, stronger individuals, irrespective of sex, exhibit larger muscle mass and therefore have increased mechanical compression in the active muscle compartment during a muscle contraction. During low-to-moderate intensity, sustained contractions, this increased pressure leads to the occlusion of blood flow to the active muscles and likely increases fatigability due to lack of oxygen and build up of metabolic byproducts (Hunter & Enoka 2001). Since males are typically stronger than females (Laubach 1976), males generally display greater fatigue during sustained isometric contractions than females (Hunter 2014). Furthermore, females tend to experience more vasodilation during sympathetic activation, which can be initiated by exercise (Parker et al. 2007). These mechanisms could inherently allow females to experience greater muscle perfusion, and reduce muscle fatigue during isometric contractions.

Another possible cause for sex-related differences of fatigue involves the characteristics of the active muscle, which include the muscle fiber type. Muscles consist of type I and II fibers. Although many muscle fibers fall along a continuum between these two classifications, the extremes can be categorized by cross-sectional

area, conduction velocity, metabolic capacity, and force-production capacity (Herbison et al. 1982). Compared with type II, type I muscle fibers have a smaller cross-sectional area, a relatively slow contraction speed, high oxidative capacity, lower glycolytic capacity and lower levels of ATPase. Type I fibers are the predominant fiber in use during low-intensity endurance exercise events and thus, are unable to produce high levels of muscle force or velocity. Type II fibers, however, have a fast conduction velocity, a large cross-sectional area, and can generate greater power due to quick shortening velocities and greater force production than type I fibers. Type II fibers are more fatigable due to a lower mitochondrial density and higher usage of ATP than type I (Herbison 1982).

Females seem to have a higher proportion of type I fibers compared with males (Esbjornsson-Liljedahl et al. 2002) and therefore are likely more fatigue-resistant but are also not able to produce as much power as males. In a study investigating sex-related differences following several high-intensity sprints, females showed a smaller reduction in ATP stores, and lower levels of blood lactate and metabolic byproducts than males (Esbjornsson-Liljedahl 2002). Although unconfirmed, this could be attributed to the characteristics of type I muscle fibers that include: less ATP usage, higher oxidative capacity, and increased capillary density than type II.

Another muscle characteristic related to fiber types is calcium adenosine triphosphatase (Ca^{2+}ATPase) activity, which can aid in Ca^{2+} resequestration into the sarcoplasmic reticulum. Type II fibers have been shown to have Ca^{2+}ATPase activity that is three times faster than that of type I fibers and Ca^{2+} uptake that is two times faster (Li et al. 2002). This likely translates to quicker shortening and relaxation phases

(Gollnick et al. 1991) of whole muscle contractions, but it also can lead to more fatigue because adenosine triphosphate (ATP) is used at a faster rate. To confirm that lower Ca^{2+}ATPase in females than males is not due to different levels of activity, it was reported that Ca^{2+}ATPase activity was not altered following 12 weeks of high-intensity resistance strength training (Thom et al. 2001) or 10 days of immobilization (Hunter et al. 1999).

Assorted contraction types are affected in various ways by these sex-related differences. Compared with other types of contractions, research groups have focused on isometric contractions in order to study sex differences. In general, they have found that females are less fatigable than males during sustained and intermittent isometric contractions (Hunter 2014). During sustained isometric contractions, the perfusion of blood flow to the muscle seems to be the main factor in determining the level of fatigue. As mentioned above, the level of occlusion is based upon the absolute strength of the contracting muscle and the resultant, intramuscular pressures. Males, as the generally stronger individuals, experience less blood perfusion due to occlusion during a sustained isometric contraction than females and therefore, are more fatigable (Hunter and Enoka 2001). For example, one study reported that when subjects of each sex were strength-matched for elbow flexor torque, there were no sex-related differences in fatigue during a sustained isometric task because occlusion of the blood vessels were likely the same (Hunter et al. 2004a).

Blood occlusion is not the only determining factor of fatigue, however. During *intermittent* isometric contractions in which the strength-related blood occlusion factor is eliminated, females are still able to perform for a longer duration than males (Hunter

et al. 2014). This shows that even when occlusion is not a factor, other sex-related physiological differences take an effect. For example, in a study involving intermittent contractions of the elbow flexors at 50% MVC, males fatigued three times faster than females (Hunter et al. 2004b). This can be attributed to a higher proportion of type I fibers in females than males, which are more resistant to fatigue as described above. However, it is inconclusive that these sex-related differences hold true for isotonic contractions where the energetics and neural control of the contractions are likely different than isometric tasks.

Isotonic contractions could be more functionally relevant than isometric contractions and thus, may reveal useful and distinctive sex-related differences. Isotonic contractions are important to study because they are involved in the majority of activities of daily living. However, to date, only a few studies have focused on isotonic-like contractions (Maughan et al. 1986; Clark et al. 2003; Pincivero et al. 2004; Labarbera et al. 2013; Senefeld et al. 2013). That being said, different studies have altered the task intensity, muscle group used, and criterion of fatigue in order to investigate how fatigue affects the various facets of daily life and exercise and thus, it is difficult to determine a decisive conclusion on whether males are more or less fatigable than females.

In a seminal study, Maughan et al. (1986) investigated the sex-related differences of isotonic concentric contractions of the elbow flexors. They showed that at intensity levels of 50%, 60%, and 70% of the one repetition maximum (1RM) in which velocity was unconstrained on the concentric phase but contraction frequency was controlled at 10 contractions per minute, females were able to complete more

contractions before failure than males. At 80% and 90%, however, there were no significant sex-related differences. This study showed that the sex-related difference of isotonic contractions decreases as the load increases (Maughan et al. 1986).

Senefeld et al. (2013) investigated the sex-related differences in the elbow flexors and knee extensors during 4.5 minutes of isotonic unconstrained-velocity concentric contractions at 20% MVC. There were no sex-related differences for power or velocity during the fatigue task for either muscle group (Senefeld et al. 2013). The only significant sex-related difference from this study was that the knee extensor MVC, which decreased more for males than females following the fatigue task. Another study involving knee extensors, showed that compared to males, females performed more isotonic contractions until task failure (Labarbera et al. 2013). The subjects in this study performed three sets of unconstrained-velocity isotonic contractions at 20% MVC. The common variable in these two knee extensor studies is that they both used a moderate load of 20% MVC but Senefeld et al. (2013) measured fatigue as a decrease in power, velocity, and MVC over a set amount of time; whereas Labarbera et al. (2013) quantified fatigue as the number of contractions to task failure. Because they measured fatigue in contrasting ways, it is difficult to compare these studies.

The other knee extensor isotonic task showed no sex-related differences in fatigue as measured by contractions to failure but this study involved continuous knee extensions at 50% MVC at a controlled, slow velocity (slow concentric and eccentric phases; hold for 2 s at full extension) (Pincivero et al. 2004). In another study involving controlled-velocity, isotonic contractions at 50% MVC, no sex-related differences were found either (Clark et al. 2003). This study involved the back extensors, which shows

that multiple muscle groups experience no sex-related differences during controlled-velocity isotonic contractions at 50% MVC.

Overall, as summarized in table 1, females seem to be less fatigable than males in studies that involve dynamic contractions, quantified by a greater number of completed contractions to task failure (Maughan et al. 1986; Labarbera et al. 2013; Senefeld et al. 2013). Females are also less fatigable than males in studies that involve a set number of isokinetic contractions (Pincivero et al. 2003). Thus, it seems when the intensity of the task is maximal during concentric contractions, males are more fatigable than females, at least for the muscle groups tested. One detriment of the current literature is the inconsistency of quantifying fatigue. In this way, it will be important, moving forward, to choose measures that are similar or comparable to previous variables used in order to be able to synthesize the results across studies.

Another novel aspect of this study is the investigation of the planter flexors. To date, no study has investigated the sex-related differences of dynamic contractions of the plantar flexors. This group of muscles is interesting because the soleus has a relatively greater proportion of type I muscle fibers than all other limb muscles and the gastrocnemii are generally comprised of more type II muscle fibers than the soleus (Trappe et al. 2001). Since the type I fibers are more fatigue resistant and the type II fibers are able to produce high levels of power, the plantar flexors provide a balanced muscle group to investigate. In addition to the muscle composition, I chose the plantar flexor muscle group because they are heavily involved in and highly important to several actions used in everyday living and exercise (i.e., gait and standing balance).

Thus, the purpose of the present study was to determine the sex-related differences of fatigue during and following unconstrained-velocity isotonic concentric contractions of the plantar flexors at 30% MVC. For consistency, I quantified fatigue as a loss of muscle power. I hypothesized that following fatigue, males would display greater fatigue than females as measured by a greater decrease in peak power.

Methods

Participants. Nine female and eight male subjects were recruited from the University of Oregon student population, who were matched for physical activity levels. Activities included ultimate frisbee, rowing, cross-training, bicycling, running, and strength training. All subjects participated in several of these activities such that no subject was highly endurance or strength trained. Subjects were free from any neuromuscular or orthopedic disorders of the lower limb. Participants' anthropometrics and activity levels are reported in Table 2. Prior to participation, the subjects granted oral and written informed consent. All procedures were approved by the local University's institutional review board for research involving human subjects and conformed to the declaration of Helsinki.

Table 2. Participant information

	Age (years)	**Activity Level (hours/week)**	**Height (cm)**	**Weight (kg)**
Female	21.9 ± 2.7	8.9 ± 4.1	169.3 ± 5.1	63.7 ± 7.5
Male	22.9 ± 2.5	9.8 ± 4.3	177.5 ± 3.9*	73.6 ± 6.6*

The males were taller and heavier than the females (*$p<0.05$), but both sexes were matched for activity levels and age.

Experimental Set-Up.

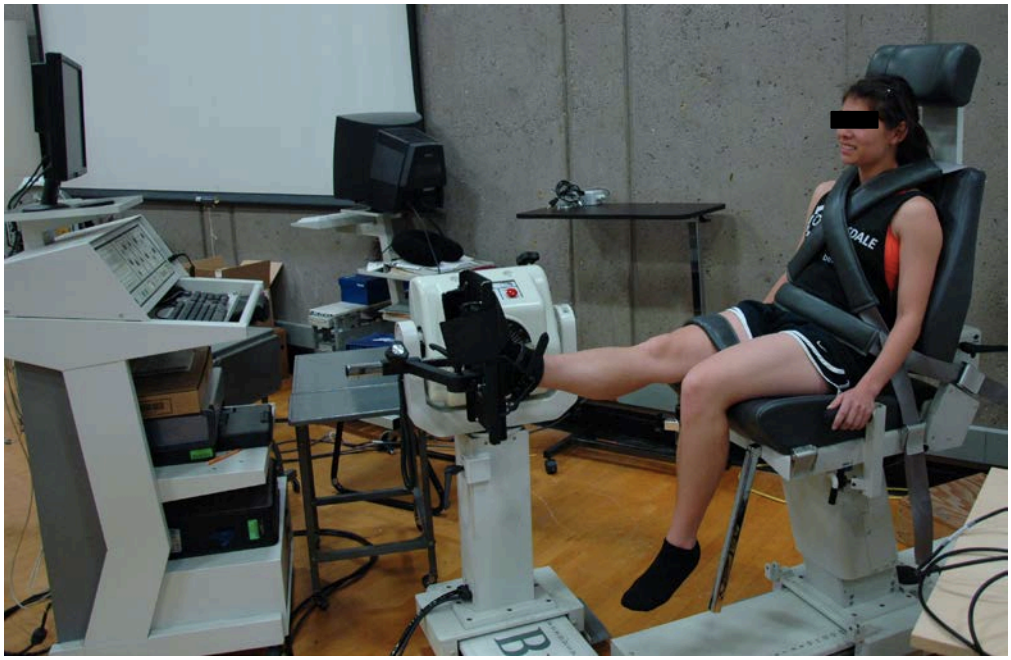

Figure 1. Participant in the Biodex System 3 multi-joint dynamometer.

Data were collected during one visit to the motion analysis laboratory at the University of Oregon. Subjects were positioned in an upright seated position in a Biodex System 3 multi-joint dynamometer (Biodex Medical Systems Inc., Shirley, NY,USA), which was used a to record plantar flexion torque, and ankle joint angular velocity and position. The knee was extended to 170° (full extension equivalent to 180°), the hip joint at 90°, and the ankle in a neutral position (90°) for the isometric and initial position for the isotonic shortening contractions of the fatigue task (Figure 1). The range of motion for the fatigue task contractions was set from neutral to 25° of plantar flexion. A custom-made binding and inelastic Velcro strap, positioned across the dorsum and toes, respectively, secured the foot to the footplate of the device. To restrict extraneous torso movements, inelastic straps were also fastened across each shoulder, waist, and right thigh. All contractions were performed with the right leg and the ankle

joint was aligned with the axis of rotation of the dynamometer. The plantar flexor torques, angular velocities, and positions were sampled at 1000 Hz using a 16-bit analog-to-digital data acquisition board (Power 1401-3, Cambridge Electronics Design, Cambridge, UK) and stored online using Spike 2 version 8 software (Cambridge Electronics Design, Cambridge, UK).

Single electrically evoked plantar flexion twitches were elicited via 100-μs square wave pulses at a maximal stimulator voltage of 400 V (DS7AH, Digitimer Ltd., Welwyn Garden City, UK). A bar electrode was held manually in the distal portion of popliteal fossa between the origins of the heads of the gastrocnemii to activate the tibial nerve, which innervates the plantar flexor muscles.

Experimental Procedures. Once a subject was positioned in the dynamometer, a maximal plantar flexion twitch was determined. Starting at a low amplitude (~50 mA), the current was increased progressively and gradually until a plateau was achieved in peak twitch torque (Pt). Then, the current was increased a further 10-15% to ensure supramaximal activation (stimulator dial setting range: 200-350 mA) of the motor unit pool throughout the protocol. To ensure non-activation of the antagonist muscles, the dorsiflexors were monitored visually and through palpation.

Next, the subject performed three to four 7-s isometric MVCs. An extra MVC was completed if the first three MVC values varied in peak torque by more than 5%. The third and fourth MVC attempts were accompanied by a single twitch ~2 s preceding the MVC, another delivered during the plateau of the MVC (Ts; a superimposed twitch), and a single twitch delivered ~2 s following the MVC when the

muscles were fully relaxed (Tr). Subjects were provided visual feedback on a computer monitor and encouraged verbally during all maximal voluntary efforts.

Following the MVC attempts, the subjects were familiarized with the isotonic shortening contractions. Subjects performed dynamic plantar flexion contractions through a 25° range of motion with a set resistance equivalent to 30% MVC. Once each contraction was completed through the entire range of motion, the subject relaxed and the dynamometer moved the foot passively back to the starting position for subsequent contractions. During the familiarization, subjects attempted several isotonic shortening contractions until a consistent peak velocity was achieved (no distinct changes in peak velocity over five consecutive contractions). Each familiarization contraction was separated by 5-10 s of rest. Once a consistent peak velocity was observed, subjects performed five consecutive isotonic contractions to practice the fatigue task. In total, familiarization included 10-15 isotonic shortening contractions. To ensure the dynamic contractions were performed maximally, each subject was instructed to plantar flex as quickly and forcefully as possible for all contractions. The subjects were also provided visual feedback of velocity and torque on a computer monitor. These familiarization contractions were followed by 3 min of rest. Next, the subject performed the fatigue task, which comprised of 200 maximal-effort, isotonic plantar flexions against a resistance equivalent to 30% MVC. Again, the subject was instructed to contract as fast and as hard as possible during each contraction upon the “go” prompt of the investigator for a consistent frequency of 1 contraction per ~1.5 seconds. Approximately 10 seconds following the fatigue task completion, the subject performed a final MVC with the corresponding twitches.

Data and Statistical Analyses. Spike2 version 7 software (Cambridge Electronics Design, Cambridge, UK) was used to analyze all data. Prior to analysis, the torque and velocity channels were filtered at 40 Hz with a low-pass fourth-order digital filter. The baseline MVC with the highest peak torque was chosen to represent all the parameters of the MVC. Reported values included MVC peak torque (Nm), MVC peak RTD (rate of torque development; Nm/s), and voluntary activation (VA; %). RTD was calculated for the MVC as the peak tangential slope, using a moving mean method (10 ms) of the torque-time curve (Δtorque (Nm)/Δtime(s)) over the initial portion of contraction onset (Power et al. 2013). Voluntary activation was calculated as VA = ((1-(Ts/Tr))×100)%.

The twitch parameters were all collected from the twitch with the highest peak torque. Analyzed values included peak twitch torque (Pt), TPT (time to peak torque ms/Nm) and HRT (half relaxation time; ms/Nm) normalized to the Pt, and potentiation (calculated as Tr/Tp×100, where Tr is the relaxed twitch post-MVC and Tp is the pre-twitch).

For the isotonic contractions during the fatigue task, dependent variables included peak power (W), torque (Nm) and velocity (rad/s) at peak power, dynamic peak RTD (Nm/s) and peak rate of velocity development (RVD; rad/s^2). Peak power was calculated from the product of torque (Nm) and velocity (rad/s). RVD was calculated for the dynamic contractions as the peak linear slope, using a moving mean method (10 ms) of the velocity-time curve (Δvelocity (rad/s)/Δtime (s)) over the initial portion of contraction onset (Thompson et al., 2014). Baseline values for all measures used to analyze the dynamic contractions were averaged across the first 10 contractions

of the fatigue tasks; whereas the post-fatigue measures were taken as the average of the last 10 dynamic contractions of the fatigue task.

All data were analyzed using SPSS version 22 (IBM, Armonk, New York, USA). A two-way analysis of variance (sex × time) with repeated measures was used to analyze all data. Significance was set at $p \leq 0.05$. When significant main effects or interactions were present, a Bonferroni correction factor was used to determine where the significant differences occurred. All data are reported as means ± standard deviations.

Results

Baseline. Compared with females, the males showed a trend towards 16% and 14% greater values for MVC (p=0.06) and potentiation (p=0.08), respectively (Table 3). However, there were no detectable sex-related differences for Pt (p=0.73), normalized TPT (p=0.49), normalized HRT (p=0.37), MVC RTD (p=0.67), and voluntary activation (p=0.25; Table 3).

For the baseline data of the isotonic contractions, the males were 37% more powerful (p<0.05) with a 30% greater torque (p<0.05) and 9% faster velocity (p<0.05) at peak power than the females. Furthermore, dynamic RTD and RVD were 37% and 20% greater (p<0.05) for the males than females, respectively (Table 4).

Table 3. Baseline isometric plantar flexion values for females and males.

	MVC (Nm)	**MVC RTD (Nm/s)**	**Voluntary Activation (%)**	**Pt (Nm)**	**TPT (ms/Nm)**	**HRT (ms/Nm)**	**Potentiation (%)**
Female	161.1 ± 28.0	537.8 ± 225.5	95.8 ± 7.0	20.2 ± 3.9	6.6 ± 1.0	5.1 ± 1.2	118.5 ± 14.2

Male	189.2 ± 22.2*****	622.5 ± 274.2	98.5 ± 1.1	19.8 ± 3.8	6.9 ± 1.4	4.6 ± 1.2	137.3 ± 23.1*****

Maximal voluntary isometric contraction (MVC), peak rate of torque development of the MVC (MVC RTD), peak twitch torque (Pt), normalized time to peak torque (TPT), normalized half relaxation time (HRT). The males exhibited a trend towards a greater MVC amplitude and potentiation than the females (*$p \leq 0.08$). Values are means ± standard deviations.

Table 4. Baseline dynamic plantar flexion values for females and males.

	Power (W)	**Torque (Nm)**	**Velocity (Rad/s)**	**RTD (Nm/s)**	**RVD (rad/s^2)**
Female	117.4 ± 33.6	60.4 ± 12.4	1.9 ± 0.2	102.8 ± 31.4	54.5 ± 11.0
Male	160.7 ± 29.7*	78.6 ± 13.0*	2.0 ± 0.1*	130.7 ± 35.4*	68.4 ± 15.3*

Dynamic rate of torque development (RTD), rate of velocity development (RVD), peak power (Power), torque at peak power (Torque) and velocity at peak power (Velocity) were all greater for the males than females (*$p<0.05$). Values are means ± standard deviations.

Fatigue. Isometric values are shown as a percentage of the corresponding baseline values in Figure 2. The MVC showed a time effect ($p<0.01$), but no sex effect ($p = 0.13$) nor interaction ($p = 0.18$). The MVC value for both sexes decreased by 17% immediately following task termination. MVC RTD showed no time effect ($p=0.5$), sex effect ($p=0.17$), nor interaction ($p=0.18$) whereby the MVC RTD was unchanged compared with baseline following task termination for both sexes. For voluntary activation, there was an overall time effect ($p<0.05$) as both sexes decreased by 7%. For the Pt, there was a time effect ($P<0.01$), and a trend towards an interaction ($p=0.08$), but no sex effect ($p=0.69$). The Pt increased 26% following task termination for the males compared with baseline, but did not change following task termination for the females. There was a time effect ($p<0.01$) and an interaction ($p<0.01$), but no main effect for sex ($p=0.45$) for the normalized TPT. Thus, males had a 34% decrease in contraction time

of the twitch as indicated by the normalized TPT following task termination; whereas there were no detectable differences for the females. For normalized HRT, there was a main effect for time ($p<0.01$), but no effect for sex ($p=0.31$) nor interaction ($p=0.74$). For both sexes, normalized HRT decreased by 24% following task termination compared with baseline values. Finally, for potentiation, males decreased by 23% but females increased by 8%.

For peak power, there was a main effect for time ($p<0.01$), and sex ($p<0.05$), and an interaction ($p<0.05$), such that males exhibited a 34% decrease in peak power by task termination compared with baseline, but females only decreased by 22% (Figure 3). For dynamic torque, there were time ($p<0.01$) and sex ($p<0.05$) effects and a trend towards an interaction ($p=0.06$). Dynamic torque decreased by 26% in the males by task termination compared with baseline, but only decreased by 15% for the females whereby males exhibited 17% greater torque values than the females at task termination. For velocity at peak power, there was a main effect for time ($p<0.01$), but no main effect for sex ($p=0.09$) nor interaction ($p=0.17$). For both sexes, velocity decreased by 9% by task termination compared with baseline. For dynamic RTD, there was a time ($p<0.01$) and sex ($p<0.05$) effect with an interaction ($p=0.05$). Dynamic RTD decreased by 31% and 20% at task termination compared with baseline for the males and females, respectively. For RVD, there were main effects for time ($p<0.01$) and sex ($p<0.05$), but no interaction ($p=0.14$). Thus, RVD decreased by 23% and 16% by task termination compared with baseline, for the males and females, respectively ($p<0.05$).

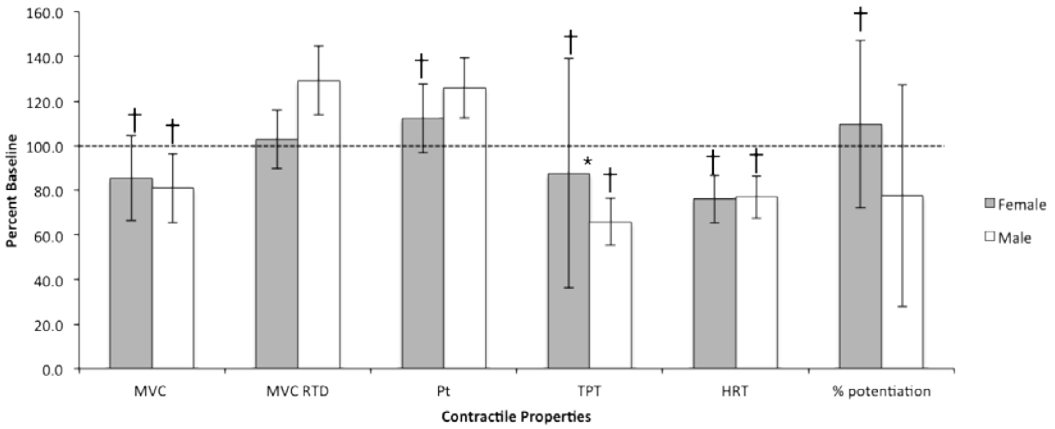

Figure 2. Isometric contractile properties shown as a post-fatigue value calculated as a percentage of the respective baseline value (fatigue/baseline ×100). Maximal voluntary isometric contraction (MVC), peak rate of torque development of the MVC (MVC RTD), peak twitch torque (Pt), normalized time to peak torque (TPT), normalized half relaxation time (HRT). The * indicates a difference between sexes and † indicates a difference for time. Values are means ± standard deviations.

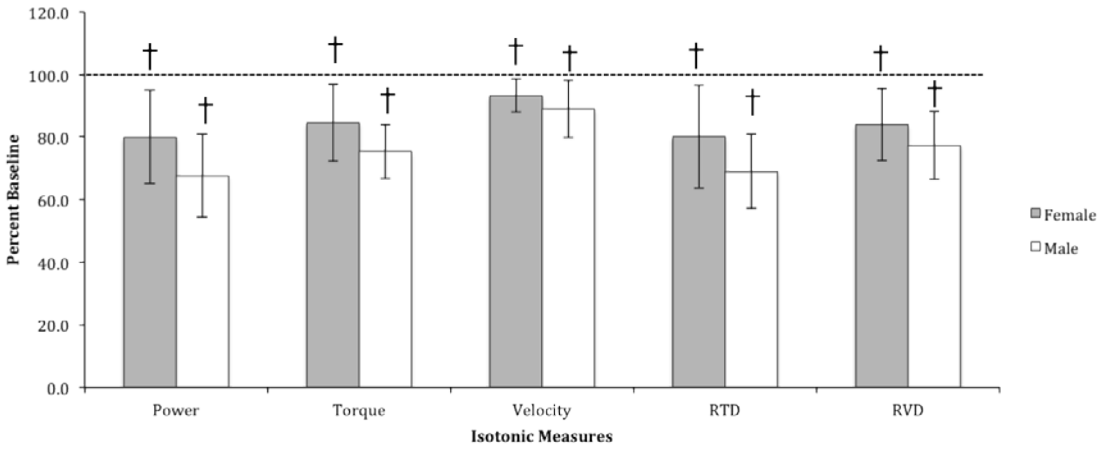

Figure 3. Isotonic contraction properties shown as a post-fatigue value calculated as a percentage of the respective baseline value (fatigue/baseline ×100). All variables are dynamic. Rate of torque development (RTD) and rate of velocity development (RVD). The * indicates difference between sexes and † indicates a difference for time. Values are means ± standard deviations.

Discussion

The purpose of this experiment was to investigate the sex-related differences of fatigue associated with isotonic maximal-effort concentric contractions of the plantar flexors at 30% MVC. It was hypothesized that males would show greater fatigue, quantified as greater reductions in power during the fatigue task, and this is supported by my results as males decreased by 34% and females by 22%.

Baseline. Although there were trends towards males having greater values for MVC and potentiation, there were no significant sex-related differences at baseline for these isometric measures. Previously, most studies have found that males have greater MVC values than females, because they, on average, have a greater muscle mass and cross-sectional area (Hunter 2014). In my study, however, the subjects were inadvertently strength-matched as there was no significant sex-related difference between MVC baseline values. It has been hypothesized that males may fatigue more

because they have higher MVC baseline values than females (Hunter 2014), but this was not a factor in my study due to the non-significant difference in MVC baseline values between sexes.

For dynamic measures at baseline, males had higher values in peak power owing to higher values for dynamic torque, velocity, RTD, and RVD compared with females. This is in agreement with a previous study of knee extensors and elbow flexors in which measures of power, torque, and velocity were also shown to be higher for males than females at baseline (Senefeld et al. 2013). RTD and RVD, however, are novel to this study so there is no previous literature to compare baseline values between sexes. One interesting aspect to note is that while the isometric MVC showed no sex difference, the dynamic torque value at peak power was 30% higher in males than females, implying that dynamic torque production may involve different physiological mechanisms than isometric torque production. One possible difference is that more torque is produced with an accompanying shortening velocity due to factors of cross-bridge cycling and the force-length relationship of the sarcomere in which peak force occurs at a neutral length.

Fatigue. Compared with baseline, males displayed a greater reduction in peak power by task termination than females. Specifically, peak power was reduced in males by 34% and only 22% for females. As my criterion of fatigue, this supports my hypothesis that males fatigue more than females during an isotonic maximal-effort fatiguing task of the plantar flexors. This contradicts Senefeld et al. (2013) who found no sex-related difference in power reduction following 90 unconstrained-velocity isotonic shortening contractions of both the knee extensors and elbow flexors.

Conversely, my results match those of a study involving isokinetic contractions of the knee extensors and flexors in which males saw greater reductions in power and torque (Pincivero et al. 2003). For dynamic torque, males decreased by 26% and females by 15%. This shows that a part of the males' greater decrease in power can be attributed to the greater loss in dynamic torque for males than females. Velocity, however, showed no sex-related difference in reduction after task termination. As power is the product of torque and velocity, this indicates that velocity had minimal effect on the greater reduction of peak power in males than females. Thus, dynamic torque-generating capacity is a key contributor in the greater fatigability in males than females during shortening contractions.

Furthermore, dynamic RTD decreased in males by 31% and 20% in females, showing a greater reduction in males after task termination. RVD decreased in males and females by 23% and 16%, respectively, showing that RVD also decreased more in males than females. These measures are important, however, because it shows that each contraction developed torque and velocity at slower rates. RTD is an integral component of explosive movements and are thought to be strongly correlated with some intrinsic contractile properties such as muscle fiber type and cross-bridge cycling (Andersen & Aagaard 2005). RVD has been shown to consistently peak before RTD which may imply that RVD contributes more to the initial power production than RTD (Andersen et al. 2005). Overall, coupled with decreased values of power and torque, it is plausible that the reductions in RTD and RVD of each contraction strongly affected the males' ability to produce power to a greater extent than that of the females.

The final variable to show greater reduction after task termination is normalized TPT in which males decreased by 34% and females showed no detectable decrease. Normalized HRT, however, did not show any sex-related differences, indicating that there is a physiological mechanism of contraction that may cause sex-related differences but that it does not significantly affect muscle relaxation.

These variables (power, torque, RTD, RVD, and TPT) could be affected by several physiological mechanisms including factors of differing muscle fiber types, excitation-contraction coupling, or a neural factor. A neural factor could involve inhibition of the motor neuron due to metabolite buildup (Reference here). Although the lack of sex-difference in voluntary activation would indicate that neural drive is likely not a contributing factor, there are other variable that may support this theory. In addition, factors of differing muscle fiber types and excitation-contraction coupling could contribute to these sex-related differences.

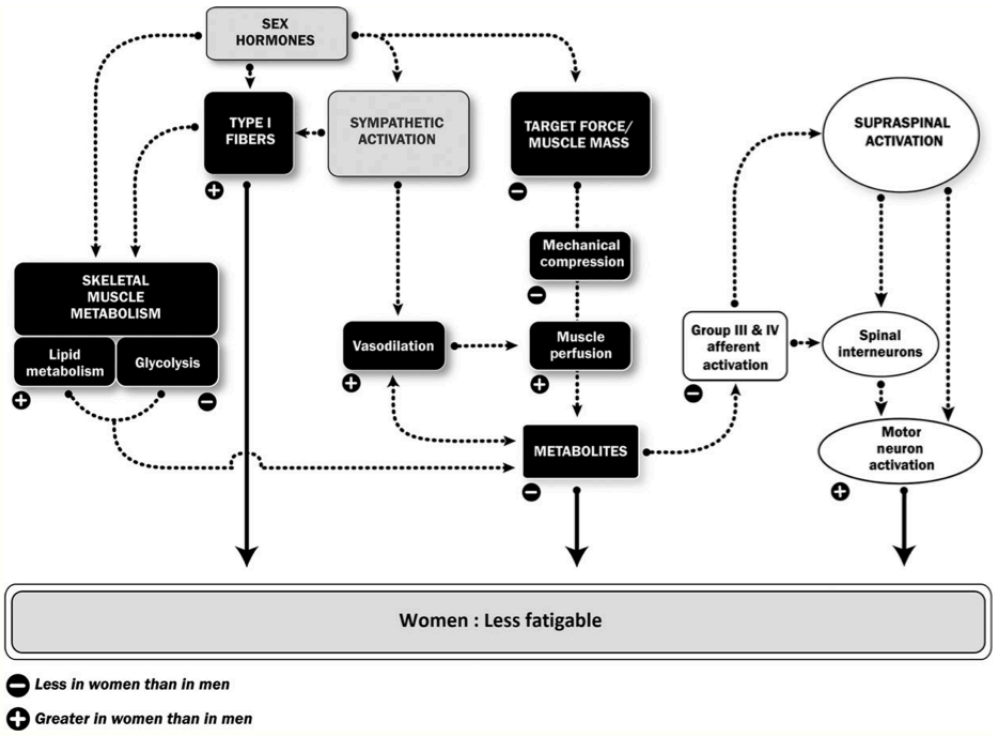

Figure 4. A flowchart adapted from Hunter et al. (2014) showing the potential factors responsible for sex-related differences of muscle fatigue.

Figure 4 highlights the sex-related differences associated with a higher number of type I fibers in females, as compared to males. Type I fibers are more reliant on oxidative metabolism as opposed to glycolysis to produce ATP for use in the muscle contraction (Binnert et al. 2000). Accompanied by greater vasodilation in females than males (Yoon et al. 2009), this leads to less metabolic byproducts, which results in less interference of the excitation-contraction coupling process and less excitation of the Group III and IV afferents (Martin et al. 2008). With a reduced amount of Group III and IV activation, the supraspinal activation of the spinal interneurons and motor neurons remains uninhibited, leading to greater activation during subsequent contractions (Martin et al. 2006). In addition, the cross-bridge cycling process may be weakened

during the binding of actin and myosin if enough metabolites are accumulated (Russ & Kent-Braun 2003). As shown in figure 4, glycolysis (mostly used by type II fibers) seems to produce a greater number of metabolites than does oxidative metabolism (mostly used by type I fibers) (Kent-Braun et al. 2002). Thus, due to their higher proportion of type II fibers, males tend to produce more metabolites than females, which may be another source of greater fatigability for the males. Although in the current study, I did not measure muscle fiber composition, fiber type seems to be a likely factor in sex-related differences of fatigue. This explanation could rationalize the greater decreases in torque, RTD, and RVD in males, as compared to females because the males' muscle contractions may be more inhibited.

HRT is not affected by the muscle contractile properties because it is a variable of the muscle's ability to relax. Muscle relaxation is dependent on the detachment of actin and myosin, controlled by rate of ATP use, and on the rate of Ca^{2+} reuptake into the sarcoplasmic reticulum (Allen et al. 2008). The result of no sex-related difference in HRT shows that these physiological mechanisms may not have a role in the sex-related differences of fatigue, as shown here.

One interesting result is that the Pt increased in males after task termination by 26% but females showed no change. This may be related to phosphorylation of the myosin light chains from the fatigue task as the actin and myosin are brought closer together due to a rise in Ca^{2+} concentration from muscle activity in a process called potentiation (Rassier 2000). This phosphorylation only affects a submaximal contraction such as a twitch, and does not affect contractions such as MVCs, which may be why there is no sex-related difference in MVC results, but there is in Pt.

General Summary

Overall, this study supports the theory that males are more fatigable (as quantified by reduction in peak power) than females during a maximal-effort isotonic shortening task involving the plantar flexors. This is important because this type of activity is utilized not only during workouts that involve running, but also general activities of daily living. Males and females often receive the same generalized workout plan but this study supports the engagement of sex-based training programs to employ the sex-related differences of physiological mechanisms involved in activity.

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