Sex Differences in Fatigability and Recovery Following a 5 KM Running Time Trial in Recreationally Active Adults

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Sex differences in fatigability and recovery following a 5 km running time trial in recreationally active adults

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ABSTRACT
Females demonstrate greater fatigue resistance compared to males in tasks ranging from single-limb contractions to whole-body exercise, including running. Many of the studies investigating sex differences in fatigability following running, however, occur after long duration, low-intensity tasks and it is unknown whether there is a sex difference in fatigability following high-intensity tasks. This study compared fatigability and recovery following a 5 km running time trial in young males and females. Sixteen recreationally active participants (8 males, 8 females, age: 23 ± 4 years) completed a familiarisation and experimental trial. Knee-extensor maximal voluntary contractions (MVCs) were performed before and up to 30 min after a 5 km time trial on a treadmill. Heart rate and rating of perceived exertion (RPE) were recorded after every kilometre during the time trial. Although not significantly different, males completed the 5 km time trial 15% faster than females (p = 0.095). Heart rate (p = 0.843) and RPE (p = 0.784) were similar between the sexes during the trial. Prior to running, males had larger MVCs (p = 0.014). The relative decrease in MVC force was less in females than males immediately post-exercise (−4.6 ± 2.4% vs. −15.1 ± 3.0%, p < 0.001) and at 10-minutes post-exercise (p = 0.018). At 20- and 30-minutes recovery, however, relative MVC force was not different between the sexes (p ≥ 0.129). These data demonstrate that females experienced less fatigability of the knee extensors than males following a high-intensity 5 km running time trial. The findings highlight the need to understand responses to exercise in both sexes and have implications for recovery from training and exercise prescription.

Highlights
- Data regarding sex differences in fatigability following high-intensity running is relatively sparse.
- Therefore, this study quantified the decrease in knee-extensor maximum voluntary contraction force (MVC) following a 5-km self-paced running time trial.
- Despite similar heart rates and ratings of perceived exertion, the percentage decrease in MVC was three times greater in males compared to females.
- Relative MVCs remained greater in females compared to males until 20 min post-exercise.

Introduction
The influence of biological sex in human research can be substantial, however, females remain under-represented in studies, especially in the exercise sciences. A recent audit demonstrated that females only account for 34% of participants included in sport and exercise science research between 2014-2020; indeed, only 6% of studies were conducted on exclusively females (Cowley et al., 2021). The result of the male bias in testing is that the collective understanding of how females respond to acute and chronic exercise is poor relative to males (Ansdell et al., 2020b).

In laboratory studies where exercise intensity is strictly controlled, females frequently demonstrate a greater resistance to fatigue of limb muscles than males (for review see Hunter, 2016a). Fatigability is quantified as an exercise-induced reduction of expected force, and classically measured as the reduction in maximal force (Hunter, 2018). During tasks such as intermittent single-limb contractions at a constant intensity, females typically exhibit a longer time to task failure than males (Ansdell et al., 2017; Hunter et al., 2004), primarily due to a greater preservation of contractile function (Ansdell et al., 2019a). Additionally, recovery
in the immediate post-exercise period appears to be faster for females compared with males (Ansdell et al., 2019a; Senefeld et al., 2018). These findings are typically attributed to the greater proportional area of type I muscle fibres observed in female skeletal muscles such as the vastus lateralis (Hunter, 2016a; Staron et al., 2000), which is associated with a greater oxidative capacity (Cardinale et al., 2018), capillarisation (Ropes-torff et al., 2006), and vasodilatory response (Parker et al., 2007). However, whilst the single-limb studies allow mechanistic insight into the sex differences in fatigability, their findings are task-specific; for instance, contraction velocity influences the magnitude of sex difference (Hunter, 2016b). Collectively, this suggests that the conclusions from single-limb studies may not translate to a whole-body model of locomotion.

Compared to the number of single-limb sex comparisons, there are fewer studies investigating fatigability following whole-body locomotive tasks (Hunter, 2016b). Following two hours of constant intensity running (Glacé et al., 1998) and cycling (Glacé et al., 2013) at the ventilatory threshold (determined during incremental exercise), males experienced greater losses in maximal voluntary contraction force (MVC) and contractile function of the knee extensors. These conclusions are supported by recent studies demonstrating that females experience greater preservation of contractile function of the knee extensors following high-intensity cycling (Ansdell et al., 2020a; Azevedo et al., 2021). Constant-load tasks permit mechanistic insight into the sex difference in fatigability, however, do not replicate the “real-world” demands of competitive endurance exercise as do self-paced tasks. Fluctuations in exercise intensity between the start, middle and end of events mediate the development of fatigue (Azevedo et al., 2019), therefore the aforementioned studies investigating sex differences in fatigability following constant-load tasks may not necessarily inform self-paced tasks.

Studies utilising self-paced tasks to compare fatigability between the sexes typically quantify the decline in neuromuscular function following endurance events. For example, Temesi et al. (2015) observed a lesser decrease in MVC force and contractile function in females compared to males following a 110 km ultra-endurance run. This sex difference following long distance running appears to be consistent in distances over 40 km (Besson et al., 2021), although the literature is not conclusive, with Boccia et al. (2018) demonstrating similar magnitudes of fatigability in males and females following a half marathon (21.1 km). The physiological demands of half marathon and ultra-distance running differ, with the latter taking place at lower intensities, for longer duration where other factors can have a large influence and could explain the incongruent results.

No known studies have investigated sex differences in the recovery of neuromuscular function following high-intensity running. Therefore, the present study aimed to address this gap in the literature and compare the magnitude of fatigue and rate of recovery following a 5 km running time trial in healthy, young males and females. It was hypothesised that females would experience a lesser decrease in MVC force, and a faster rate of recovery of maximal force than males.

Methods

Ethical approval

This study received institutional ethical approval from the Research Ethics Committee (submission reference: 40417) and was conducted according to all aspects of the Declaration of Helsinki. Participants volunteered for the study and provided written informed consent.

Participants

An a priori sample size calculation was conducted with G*Power (version 3.0.0) using the effect size for the sex difference in recovery from Ansdell et al. (2020a) and reliability data for maximum voluntary contractions from Ansdell et al. (2019b). With the parameters of $\alpha = 0.001$ and $1-\beta = 0.99$, the minimum sample size required was 12 participants (6 males and 6 females). To maximise statistical power and detect potential sex differences, we recruited 16 participants: 8 males (mean ± SD age: 24 ± 5 years; stature: 1.80 ± 0.10 m; mass: 71.6 ± 12.3 kg) and 8 females (mean ± SD age: 22 ± 2 years; stature: 1.66 ± 0.04 m; mass: 61.5 ± 4.6 kg).

A screening questionnaire was used to ensure all inclusion criteria were met for each participant, and also to quantify training and activity status. All participants reported accumulating at least 150 min of moderate-intensity activity (such as brisk walking or cycling); or 75 min of vigorous intensity activity (such as running) per week, as per the U.K. Chief Medical Officer’s guidelines.

Hormonal status was not an exclusion criterion for this study. Female participants were tested in any inclusion criteria were met for each participant, and also to quantify training and activity status. All participants reported accumulating at least 150 min of moderate-intensity activity (such as brisk walking or cycling); or 75 min of vigorous intensity activity (such as running) per week, as per the U.K. Chief Medical Officer’s guidelines.

Hormonal status was not an exclusion criterion for this study. Female participants were tested in any
reported using a monophasic oral contraceptive pill (Table 1), and two were naturally cycling.

**Experimental design**

All participants visited the laboratory twice to complete a familiarisation and experimental session. These sessions were separated by a minimum of 48 h to permit full recovery of any potential long lasting muscle fatigue (Carroll et al., 2017). To account for diurnal variations in maximal force-generating capacity, the testing sessions occurred at the same time of day. All visits were conducted in a laboratory facility where the temperature conditions were pre-set to 20°C. Participants were asked to arrive at the laboratory rested and hydrated, with strenuous physical activity avoided for 48 h, and caffeine and alcohol prohibited for 24 h.

**Familiarisation visit**

On arrival, participants’ stature (cm) (Seca 213 Stadiometer, Medisave UK Ltd, Dorset) and body mass (kg) (Seca Scales, Seca Ltd Birmingham) were recorded. Participants then performed a 5-minute warm-up on the treadmill (Woodway ELG 55, USA) where they were able to control the speed. For the warm-up, participants were instructed to maintain a heart rate less than 80% of age-predicted maximum. Following the warm-up, pre-exercise maximal voluntary contractions (MVCs) of the knee-extensors were performed (see MVC Procedure). The participants then performed the 5 km time trial, during which heart rate (Polar Electro, Finland), RPE, and treadmill speed were recorded at every km. The RPE was recorded using the 6–20 scale (Borg, 1982), with 6 being no exertion at all and 20 being maximal exertion. The treadmill was set to a constant incline of 1% throughout the trial to compensate for the lack of air resistance (Jones & Doust, 1996) but participants were allowed to freely increase/decrease their speed at any point during the trial. Participants were instructed to complete the 5 km run as fast as possible and in the least time as possible, strong verbal encouragement was provided throughout. During the time trial, participants were informed of the distance completed and elapsed time at the end of each kilometre. Immediately after completion of the time trial (<30 s), participants performed post-exercise MVCs.

**Experimental trial**

Other than the recording of stature and body mass, the experimental trial was performed in an identical manner to the familiarisation trial. Following the completion of the 5 km time trial and immediate post-exercise MVCs, participants performed further MVCs at 10-, 20-, and 30-minutes post exercise.

**MVC procedure**

Participants were seated on a custom-built chair, with hip and knee angles kept constant at 90° flexion. Force (N) was measured using a calibrated load cell (MuscleLab force sensor 300, Ergotest Technology, Norway) attached via a non-compliant cuff to the participant’s dominant leg, 2 cm superior to the ankle malleolus. The force transducer height was adjusted to ensure a direct line with the applied force for each participant. At each time point, three knee-extensor MVCs were performed with 30 s between measurements. Participants were not provided with visual feedback of MVC force, however were informed of the peak force value during each contraction. The MVC force was determined as the peak force achieved during the largest of the 3 MVCs at each time point.

**Statistical analysis**

Data are presented as mean ± SD within the text and figures. Normal Gaussian distribution of data was confirmed using the Kolmogorov–Smirnov test. The significance level for all statistical tests was set at p < 0.05. Participant characteristics and time trial completion time were compared between sexes with independent samples t tests. To account for the sex difference in maximum strength, fatigability was quantified by comparing the post-exercise MVC, expressed as a percentage (%) of baseline, with an independent samples t test. MVC force (% baseline) was then compared between sexes with a two-way (2 × 4) repeated measures ANOVA to
assess recovery during the 30-minute post-exercise period. Heart rate, RPE, and treadmill speed during the time trial were compared between sexes with a two-way (2 × 5) repeated measures ANOVA. If a significant sex, time, or interaction effect were observed, these were followed up by post hoc Bonferroni-corrected pairwise comparisons.

Test-retest reliability was quantified for key outcome variables from the familiarisation and experimental visits for each sex using paired samples t-tests, coefficient of variation (CV%: [standard deviation ÷ mean] × 100) and intraclass correlation coefficients (ICC); the latter were rated poor (< 0.5), moderate (0.5-0.75), good (0.75-0.9) or excellent (>0.9), according to Koo and Li (2016). Time taken to complete the 5-km TT demonstrated excellent reliability (p ≥ 0.274, ICC ≥ 0.903, CV% ≤ 3.0%), whilst pre-exercise MVC force demonstrated good reliability (p ≥ 0.810, ICC ≥ 0.735, CV% ≤ 9.6%).

Results

Participant characteristics

Participant characteristics are reported in Table 2. There was no difference in age (p = 0.392) or self-reported physical activity time per week (p = 0.310), however males were taller (p = 0.002) and had greater body mass (p = 0.048).

Time trial performance & physiological responses

Time taken to complete the 5 km time trial was not statistically different between sexes, despite a mean difference of ~15% whereby males completed the time trial faster (29.46 ± 3.39 vs. 34.89 ± 7.87 min, p = 0.095, Figure 1).

There was a main effect of time (F_{1.6},_{22.3} = 56.9, p < 0.001, ηp^2 = 0.803) indicating that heart rate rose during the 5 km time trial (Figure 2(A)), however there were no sex or sex × time interaction effects (p ≥ 0.337). Similarly, there was a main effect of time (F_{1.8},_{24.8} = 109.2, p < 0.001, ηp^2 = 0.886) on RPE (Figure 2(B)) during the 5 km time trial, but no sex or sex × time interaction effects (p ≥ 0.188). Treadmill speed at each km interval (Figure 2(C)) demonstrated a main effect of time (F_{1.6},_{22.3} = 10.8, p < 0.001, ηp^2 = 0.436), but no sex or sex × time interaction effect (p ≥ 0.167).

Maximal strength: fatigability & recovery

At baseline, males had greater MVC force than females (676 ± 180 N vs. 473 ± 98 N, p = 0.014). Thereafter, the percentage decrease in MVC force from pre to post 5-km time trial was greater for males compared to females (−15.1 ± 3.0% vs. −4.6 ± 2.4%, Figure 3, p < 0.001).

During the 30-minute post-exercise recovery period, a main effect of sex (F_{1.14} = 9.7, p = 0.008, ηp^2 = 0.410) was observed, however there was no main effect of time (p = 0.081) or sex × time interaction effects (p = 0.064) for MVC force. Post hoc tests revealed that females had greater MVC force (% baseline) than males at 10 min (p = 0.018), but not 20 (p = 0.129) or 30 min (p = 0.227) post time trial.

Discussion

This study compared fatigability and recovery of the knee extensor muscles between sexes following a 5 km running time trial. The novel findings were that females experienced lesser reductions in MVC force immediately and up to 10 min after the 5 km time trial. The lesser reduction in female MVC force was despite both sexes exhibiting similar heart rates and RPE values throughout, and the sex difference in running performance within the anticipated 10-20% range for sex differences in endurance performance (Joyner, 2017). Together, these findings have implications for high intensity exercise prescription in both sexes.

Sex differences in fatigue & recovery

Following running time trials of similar distances, studies with male-only cohorts have shown a 7–15% decrease in

Table 2. Characteristics of the male and female participants.

<table>
<thead>
<tr>
<th></th>
<th>Males (n = 8)</th>
<th>Females (n = 8)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24 ± 5</td>
<td>22 ± 2</td>
<td>0.392</td>
</tr>
<tr>
<td>Stature (cm)</td>
<td>180 ± 10</td>
<td>166 ± 4</td>
<td>0.002</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>71.6 ± 12.3</td>
<td>61.5 ± 4.6</td>
<td>0.047</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>22.0 ± 2.6</td>
<td>22.2 ± 2.2</td>
<td>0.660</td>
</tr>
<tr>
<td>Physical activity (h/week)</td>
<td>6 ± 3</td>
<td>8 ± 4</td>
<td>0.310</td>
</tr>
</tbody>
</table>

![Figure 1](https://example.com/figure1.png)
knee extensor MVC force (Nummela et al., 2008; Wüthrich et al., 2014) which corroborates data from the male group in the present study (15.1% decline). As Wüthrich et al. (2014) demonstrated, the decline in MVC force following high-intensity running is a result of a combination of muscular mechanisms (reduced contractile force) and a reduced ability of the central nervous system to activate the working muscles. Whilst the present study did not make a distinction between muscular and neural contributors, previous studies indicate females have more fatigue resistant muscle than males, with minimal sex differences in activation of the central nervous system, during high-intensity whole-body fatiguing tasks such as cycling (Ansdell et al., 2019a; Azevedo et al., 2021). Therefore, it is likely that the lesser decline in MVC for females was due to contractile differences within the knee extensors.

It is well established that the characteristics of skeletal muscle impact metabolism and fatigability during exercise. Previous research has demonstrated that males experience greater pH decreases (Russ et al., 2005) and greater phosphate accumulation (Esbjörnsson-Liljedahl et al., 2002) following high-intensity exercise, both of which are implicated in exercise-induced reduction in contractile function. Given that 5 km time trial running involves a near-maximal cardiovascular response (i.e. final heart rates of ∼190 bpm, Figure 2(A)), and likely takes place predominantly within the severe intensity domain (above the maximal sustainable intensity), this task would elicit substantial disruption of muscle metabolic homeostasis. Therefore, it is likely that the aforementioned sex differences within muscle contractile apparatus occurred in the present study and were contributing factors to the lesser decrease in MVC for females.

Following the 5 km time trial, a main effect of sex, but no sex × time interaction effect was observed. Post-hoc tests showed that females demonstrated greater relative MVC force (% baseline, Figure 3) up to 10 min post-exercise, but were similar to males from 20 to 30 min post-exercise. This mirrors previous data from single-limb exercise following isometric and dynamic knee-extensor contractions (Ansdell et al., 2019a; Senefeld et al., 2018). This sex difference in recovery of MVC force could be due to intramuscular factors, such as a faster restoration of calcium homeostasis (Carroll et al., 2017), which would agree with previous evidence that demonstrated a sex difference in Ca²⁺-ATPase activity in female skeletal muscle (Harmer et al., 2014). In addition, the restoration
of high-energy intramuscular phosphate stores is thought to be dependent on oxidative phosphorylation and pH-dependent mechanisms, therefore the greater oxidative capacity of female skeletal muscle (Cardinale et al., 2018) and lesser pH decline following exercise (Russ et al., 2005) could also contribute to MVC recovery in the 10 min post-time trial. Despite this, caution should be exercised when interpreting the present recovery data, given male experienced a far greater decrease in MVC force post-exercise. To investigate this further, future studies should match the degree of fatigue between sexes before observing the rates of recovery.

In addition to contractile and metabolic mechanisms underpinning the sex differences in fatigability after the 5 km run, Besson et al. (2022) recently outlined other factors that may contribute to sex differences in endurance running. For example, biomechanical differences such as a lower ground contact time, and therefore lower duty cycle in females than males at high-speeds could contribute (Nelson et al., 1977). In addition, sex differences in muscle activation strategies during the gait cycle result in females using the vastus medialis less but hip extensors and plantar flexors more during the weight acceptance phase, and the rectus femoris less during the swing phase (Santuz et al., 2022). Collectively, this sex difference in muscle activation could reduce the involvement of the knee-extensors in the gait cycle and be a contributing factor in the lesser MVC decline observed in the present study.

**Experimental considerations**

This study was the first to compare fatigability between sexes following high-intensity running, however there are considerations that the reader must be wary of. Firstly, we ensured of homogenous sample of participants by recruiting recreationally active, yet untrained, university students and staff. However, it is established that the magnitude of fatigue experienced following equivalent exercise is less in professionally trained athletes compared to moderately trained individuals (Ducrocq et al., 2021). Therefore, the present data may not translate to elite athletes and cannot be generalised to inform athletic preparation, further investigation in this population should be undertaken.

Matching training status between males and females was not explicitly performed in the present study, and future investigations should perform cardiopulmonary exercise testing to quantify physiological markers of training status (i.e. maximal oxygen uptake, VO$_{2\text{max}}$) prior to comparing fatigability. However, the self-reported weekly physical activity of participants was similar between sexes (Table 2), and the sex difference in time to complete the 5 km time trial was 15%. The latter fits with the expected sex difference in performance of endurance tasks (Joyner, 2017); for instance, data from 2004 demonstrated a 14.1% sex difference in 5000 m running times (Cheuvront et al., 2005). This therefore indirectly implies that the males and female cohorts in the present study were of similar training status. Additionally, given that heart rate and RPE were similar (Figure 1), it can be assumed that the equivalently trained males and females exercised at similar intensities, and the observed sex difference in fatigability was a result of intrinsic physiological differences.

The present study quantified the magnitude of fatigue experienced by males and females using knee-extensor MVCs. This measure provides an assessment of the state of the entire neuromuscular pathway and is influenced by neural drive to the muscle, as well as the contractile apparatus. Future investigation should employ techniques such as electrical nerve stimulation and/or transcranial magnetic stimulation to distinguish between the relative contributions of neural and contractile contributions to the MVC decline following the 5 km time trial. Discerning the aetiology of the observed sex difference in fatigue will permit practitioners to adjust athletic preparation accordingly. For instance, the intention of high-intensity exercise is often to elicit adaptation by inducing a state of contractile dysfunction in the working muscles. Therefore, if females experience greater preservation of contractile function following an acute bout of high-intensity running, this might impair long-term adaptation to a training protocol (Ansdell et al., 2020b).

Finally, the present study did not observe a significant difference in 5 km time trial performance, despite a mean difference between males and females of 5.43 min (15%). This is likely as the study was adequately powered to detect a sex difference in fatigability (see Methods) rather than a sex difference in performance.

**Conclusion**

This study is the first to quantify the sex differences in fatigue and recovery following a 5 km running time trial. During the time trial, females and males exercised at similar intensities, with equivalent heart rates and RPE, however, immediately following the time trial, less fatigue was observed in female knee extensors compared to males. Females also maintained greater relative MVC force up to 10 min post-exercise. These findings add to the growing evidence base regarding sex differences in the response to exercise and raise the importance of tailoring exercise prescription to the
individual, instead of using previously established male-only data.

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**Disclosure statement**

No potential conflict of interest was reported by the author(s).

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