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Sex Comparison of Knee Extensor Size, Strength And Fatigue Adaptation to Sprint Interval Training

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Abstract

Background: Regular sprint interval training (SIT) improves whole-body aerobic capacity and muscle oxidative potential, but very little is known about knee extensor anabolic or fatigue resistance adaptations, or whether effects are similar for males and females. The purpose of this study was to compare sex-related differences in knee extensor size, torque-velocity relationship and fatigability adaptations to 12 weeks SIT.

Methods: Sixteen males and fifteen females (mean (SEM) age: 41 (±2.5) yrs) completed measurements of total body composition assessed by DXA, quadriceps muscle cross-sectional area (CSA_Q) assessed by MRI, the knee extensor torque-velocity relationship (covering 0 – 240°·sec^{-1}) and fatigue resistance, which was measured as the decline in torque from the first to the last of 60 repeated concentric knee extensions performed at 180°·sec^{-1}. SIT consisted of 4 x 20 second sprints on a cycle ergometer set at an initial power output of 175% of power at VO_2max, three times per week for 12 weeks.

Results: CSA_Q increased by 5% (p=0.023) and fatigue resistance improved 4.8% (p=0.048), with no sex differences in these adaptations (sex comparisons: p=0.140 and p=0.282, respectively). Knee extensor isometric and concentric torque was unaffected by SIT in both males and females (p>0.05 for all velocities).

Conclusions: 12 weeks SIT, totalling 4 minutes very intense cycling per week, significantly increased fatigue resistance and CSA_Q similarly in males and females, but did not significantly increase torque in males or females. These results suggest that SIT is a time-effective training modality for males and females to increase leg muscle size and fatigue resistance.

Keywords: Sprint Interval Training, Exercise, Skeletal Muscle, Fatigue, Torque-Velocity Relationship

INTRODUCTION

In recent years, there has been a resurgence of research interest in high intensity interval training and sprint interval training (SIT). Studies usually set out to understand the cellular regulation of training adaptations and to investigate the implementation of training practices to improve health status of various populations (5). However, the majority of research in these areas included only young, male participants, with females and middle-aged people being under-represented.

It should not be taken as a certainty that the findings from studies including only males will apply equally to females. Males have higher maximal skeletal muscle strength and power compared with females (28) and higher maximal power output during sprinting (14, 17). However, the superior performance does not lie entirely with males, since males fatigue more quickly than females during controlled isometric contractions of single muscle groups (23, 33) and during sprinting, while females recover faster during short rest periods between repeated sprinting bouts (14, 17).

Male advantage when producing maximal muscle force and power is in part due to the higher relative muscle mass (7), larger muscles (26) and larger fibre cross-sectional areas in males than females (16). Any sex-related comparisons for muscle force and power should therefore normalise values to muscle size ('normalised' force and power), sometimes termed as "muscle quality" in the literature (20, 28). However, it is not only muscle mass that exhibits a sex-related difference, but also the contractile and metabolic characteristics. For instance, males have been reported to have higher concentrations of glycolytic enzymes and faster rates of contraction and relaxation than females (33). Males may use relatively more carbohydrates during sub-maximal aerobic exercise than females (43), shift to anaerobic metabolism at lower relative intensity during incremental exercise (37) and during maximal sprinting higher glycolytic contributions were reported in males compared with females (15).

Skeletal muscle characteristics such as these that affect energetics may also confer sex differences in fatigability and may influence adaptations to SIT.

Few studies directly examine sex-related differences in adaptations to SIT. We recently reported sex differences for the changes to maximal rate of oxygen uptake (VO_2max) and body fat after 12 weeks SIT (REF TO BE ADDED AFTER REVIEW). Focussing on peak power output, Esbjörnsson-Liljedahl et al. (16) showed that females increased their power output more than males after 4 weeks SIT, but another study looking at adaptation to just 6 SIT sessions reported similar gains in peak power for males and females (4).

Increased power output could in theory be due to changes to neural activation, but the results from Esbjörnsson-Liljedahl et al. (16) allude to proportionally larger gains in vastus lateralis fibre cross sectional area (particularly Type IIx) in females than males as a mechanism. This would suggest that females have a greater hypertrophic adaptation to SIT than males, but there is little evidence to this effect because muscle-specific hypertrophy has been largely overlooked in studies of SIT. Hypertrophy follows a net increase in anabolic signalling over time, and in this regard Fuentes et al. (2012) found no sex-related differences in their anabolic responses to a single SIT session (18). Another study, however, reported approximately 150% higher rates of muscle protein synthesis 48 hours following 3 weeks of SIT in males than females (38). This is in conflict with the previous report of higher increases in Type IIx muscle fibre CSA in females than males (16), although it should be noted that type IIx fibres typically account for approximately 10% of vastus lateralis fibres (42). Irrespective of the conflicting reports, neither of these cross-sectional studies of acute training adaptation examined changes to muscle size after several weeks SIT. Measurements of total body lean mass by DEXA are contradictory in this area. Heydari et al. observed a 2% significant increase after 12 weeks HIIT in young, overweight males (22), whereas Trapp et al. (utilising the same protocol but over 15 weeks) saw no change in total body lean mass in young females (19). These studies taken together suggest that the muscle hypertrophic response to SIT may be sex-specific, but the contradictory results highlight the need for further evidence.

Thus, the aim of the present study was to compare sex-related differences in muscle size, knee extensor torque-velocity relationship and fatigability (occurring after 60 maximal voluntary concentric knee extensions), and their adaptation to 12 weeks SIT. It was hypothesised that 12 weeks cycling SIT would promote knee extensor hypertrophy, increased torque and fatigue resistance. Based on the limited available data indicating larger gains in type IIx fibre CSA in females than males, females were hypothesised to have a greater hypertrophic adaptation compared with males. Assuming no change to the muscle quality, it was further hypothesised that females would increase maximal torque more than males in line with the greater hypertrophic adaptation.

METHODS

Experimental Approach to the Problem

To determine the effect of SIT on knee extensor hypertrophy, torque production and fatigue resistance, 16 males and 15 females were recruited from the general population through advertisement in local and national newspaper articles, a local gym and campus advertisement. The participants reported to the laboratory and completed measurements of knee extensor cross sectional area (Magnetic Resonance Imaging, MRI), total body composition (Dual Energy X-ray Absorptiometry, DXA) and knee extensor torque and fatigue (Unilateral Knee Extension Dynamometry). The participants then completed 12 weeks of SIT in a local gym or in the laboratory before returning to repeat the measurements.

Subjects

The study conformed to the latest revisions of the Declaration of Helsinki (45) and was approved by the Ethics Committee at Manchester Metropolitan University. Volunteers provided written, informed consent prior to participation. Those with a history of cardiovascular, neuromuscular or metabolic disease were excluded as well as people whom had suffered a leg fracture within the past two years. Participants who were involved in competitive sports or cycled for more than 15 minutes per day for three or more days per week were also excluded. The included participants were from the same group as previously reported in (REF TO BE ADDED AFTER REVIEW). Included participants ranged from 20 to 69 years. Although not reported in the present manuscript, the mean VO_2max values (43 and 34 $mL \cdot kg \cdot min^{-1}$ for males and females, respectively) previously reported for the study group (REF TO BE ADDED AFTER REVIEW) were at around the 60th percentile of population-based values (2, 9, 44). A total of 31 participants completed the 12-week SIT intervention and the primary outcome measurements for this study were changes to: quadriceps cross-sectional area (CSA_Q), knee extensor maximal isometric and concentric torque, and fatigue resistance. Participant characteristics are shown in *Table 1*.

TABLE 1 AROUND HERE

Procedures

Total body and leg lean mass were assessed by dual-energy x-ray absorptiometry (DXA: Lunar Prodigy Advance; GE Medical; EnCore version 10.50.086) using the same procedures as previously reported by our group (REF TO BE ADDED AFTER REVIEW), and thigh lean mass was also recorded (REF TO BE ADDED AFTER REVIEW). The test-retest variation in measurement for this equipment has been determined in our laboratory as 1% (*unpublished)*.

Magnetic resonance imaging (MRI) was used to measure peak quadriceps cross-sectional area (CSA_Q) using a T1-weighted turbo 3D sequence (256x256 matrix, Repetition Time 40ms, Echo Time 16ms) on a 0.25-T scanner (G-scan, Esaote, Genoa, Italy) with the participant supine and hips and knees fully extended. The scanning coil was positioned over the thigh of the dominant leg and contiguous transverse-plane slices of 6 mm thickness were collected with no gap between slices. Images were analysed using OsiriX imaging software (OsiriX medical imaging, OsiriX, Atlanta, USA) by manually tracing the quadriceps muscles and avoiding any visible fat deposits in the muscle. Slices at 24mm apart were analysed and the slice with the highest quadriceps anatomical cross-sectional area was recorded. Analyses were carried out by the same investigator. Using the same equipment and measurement techniques, our laboratory previously reported a co-efficient of variation of 0.43, 0.35, 0.30 and 0.31% for repeated measurements of *Vastus Lateralis, Rectus Femoris, Vastus Medialis* and *Vastus Intermedius* muscles, respectively (REF TO BE ADDED AFTER REVIEW). The scanning procedure was repeated after 12 weeks of SIT.

The knee extensor torque-velocity relationship and fatigue resistance were assessed in 16 males and 15 females using unilateral extensions on a Cybex Norm Dynamometer (Cybex, division of Lumex Inc, Ronkonkoma, New York, USA). Participants were seated upright (hip angle of 85^0) with straps secured firmly around the upper body and the hips to limit extraneous body movements. The torque lever was strapped 2 cm above the ankle malleolus of the dominant leg (as determined by the participant) and the centre of knee rotation was aligned with the point of rotation of the dynamometer lever arm. A brief warm up included six isokinetic contractions at $180°\cdot sec^{-1}$ using approximately 60-70% of maximal effort. The maximal voluntary isometric torque (MVC) was assessed three times with 60 seconds of rest between efforts at a knee angle of 90°. The highest torque value was recorded. Following a 3 minute rest, isokinetic torque was assessed over two efforts separated by 60 seconds rest between efforts at any velocity at 60, 120, 180, 240°·sec^{-1} in a random order, blinded from the participant, with a 60 second rest between velocities. Each trial started with the leg flexed as far as possible and participants made two maximal efforts at each velocity through the full range of movement until the leg reached full extension. The peak torque occurring at any point during the concentric contraction was recorded. A rest of 30 seconds was given between maximal efforts and strong verbal encouragement was given throughout. The data obtained from MRI scanning was then combined with the data from the isokinetic torque production to measure 'normalized torque', that is, torque produced per cm^2 of CSA_Q, in order to give an indication of muscle quality before and after SIT:

$$\textit{Normalized Torque} = \textit{Isokinetic Torque (Nm) at a given velocity} \ (°\cdot\mathrm{sec}^{-1}) \div CSA_Q \ (cm^2)$$

Isokinetic torque as a percentage of isometric torque produced was assessed by:

$$\textit{\%Isometric Torque} = \textit{Isokinetic Torque (Nm) at a given velocity} \ (°\cdot\mathrm{sec}^{-1}) \div \textit{Isometric Torque measured at } 90° \textit{ (Nm)}$$

Knee extensor fatigue resistance was assessed after a 3 minute rest. The test started with the knee flexed as far as possible and participants performed 60 maximal-effort isokinetic contractions over 2 minutes (one every 2 seconds, as timed by a metronome), moving through the full range of knee extension at a velocity of 120°·sec^{-1} and returning to the fully flexed knee angle between contractions. The highest torque produced during the first 3 contractions was recorded as the highest contraction torque during the test and in all cases the lowest torque was produced during the final contraction and this was recorded as the lowest torque. The fatigue index was calculated using the formula:

$$\textit{Fatigue Index} = \textit{(Torque Produced in final contractions} \div \textit{Torque Produced in First Contractions)} \times 100$$

In this instance, a higher value indicates greater fatigue resistance, *i.e*. the percentage of muscle torque output maintained after 60 contractions relative to the first contraction.

The isometric MVC ICC using these techniques is 0.854 with isokinetic variation ICC of 0.819 at 60°·sec^{-1}, 0.810 at 120°·sec^{-1}, 0.850 at 180°·sec^{-1}, 0.836 at 240°·sec^{-1}.

Sprint Interval Training

Participants completed an incremental cycling test to establish the workload at the maximal rate of oxygen uptake (VO_2max), as previously described (REF TO BE ADDED AFTER REVIEW) and this was used to determine the SIT workload. SIT was completed on cycle ergometers (Cateye, Japan). The training consisted of 2 minutes of warm-up at a self-selected moderate intensity. This was followed by four bouts of 20 seconds maximal effort sprints at a workload (in Watts) that was set at a power output corresponding to 175% of the workload attained in the VO_2max test at the initial laboratory visit. This target workload was increased every two weeks by 5%, reaching 200% of the workload attained in the VO_2max test at the initial laboratory visit after 12 weeks (a standard incremental cycling test was used to determine the VO_2max, as described previously (REF TO BE ADDED AFTER REVIEW). Each of these bouts was separated by 2 minutes of very low intensity cycling (a workload of 20% of that attained in the initial VO_2max test). This training protocol was chosen due to its brevity, as well as previous studies yielding significant changes in physiological measurements in short time periods (10, 34). Thus, each training session lasted less than 10 minutes and only 80 seconds was completed at an intensity that would be expected to influence the primary outcome variables: knee extensor size, maximal torque and fatigue resistance.

The first training session for each participant was supervised by the research team in the research laboratory and participants received clear instructions on the use of the cycle ergometers and the training regimen. Participants were then instructed to train three times per week for 12 weeks (36 sessions in total) using the ergonomic cycles (Cateye, Japan) that we provided in a local gym or at our laboratory. Participants completed on average 33 (±2) sessions over 12 weeks, with males and females completing similar numbers of sessions (Table 2). Exercise instructors at the local gym were fully informed of the research and training protocols, they were available to provide a safe training environment and to assist participants if needed during training sessions. The exercise instructors were not involved in the data collection process or in the interpretation of data. Participants maintained a training logbook to record workloads during training sessions and were otherwise asked to maintain their usual dietary and exercise habits throughout the intervention period.

Statistical Analyses

The primary outcome measurements were: peak quadriceps muscle cross sectional area (CSA_Q); torque measured at the different velocities; and fatigue index after 60 maximal effort concentric contractions. A secondary outcome measurement was lean mass measured by DXA. The differences between pre- and post- 12 weeks SIT were calculated and sex-related differences in adaptation were compared. All data were tested for normality of distribution using the Kolmogorov-Smirnov test. Independent samples t-test was used to examine sex-related differences in the number of training sessions completed (*Sex effect*, *Table 1*) and baseline sex-related differences in all recorded measurements. If no sex difference was found at baseline, a two-factor repeated measures ANOVA was used to assess sex differences in training adaptation and between isokinetic velocities. If a baseline sex difference was found, a two-factor repeated measures ANCOVA was used with baseline values as a co-variate. In examining sex-related differences over the training intervention, the sex x time interaction effect refers to sex-related differences as a result of the training intervention (pre- to post-training intervention). Three-Factor repeated measures ANOVA was used to assess sex- and time related differences in the force-velocity profile. Relationships between measurement outcomes and participant age were examined using partial correlation coefficients controlling for sex. The data were analysed using SPSS (v.20 IBM) and statistical significance was accepted at $p<0.05$. Data are presented as mean ± standard error of mean (SEM).

Results

No significant correlations were found between participant age and the adaptations to SIT for any of the outcome variables (all $p>0.200$).

Body composition and knee extensor muscle size

Table 1 shows variables relating to body composition and skeletal muscle size in males and females. Total body lean mass was unchanged after training (p=0.147), with no sex difference in this adaptation (sex x time interaction: p=0.067). Analysis of leg lean mass and thigh lean mass from DXA scans showed no significant changes after training. However the more detailed analysis of CSA_Q from MRI showed a significant increase of 3.25 cm^2 after SIT (p=0.023), with both males and females increasing CSA_Q similarly after training (sex x time interaction: p=0.140).

Knee extensor maximal torque and fatigue resistance

Males had higher isometric torque than females at baseline (*Table 2*), but both sexes generally showed similar percentage decline in torque as contraction velocity increased, with torque at all velocities ($°\cdot sec^{-1}$) relative to isometric MVC being similar for males and females (sex x velocity interaction; p=0.374) (*Figure 1a*). When normalising torque to CSA_Q, males had higher values than females at $180°\cdot sec^{-1}$ (*Figure 1b*), with sex-related difference in the decrease in torque per cross-sectional area of muscle approaching significance (sex x velocity interaction; p=0.051). There were no significant sex-related differences in the torque-velocity profile after SIT (sex x time x velocity interaction; p=0.425).

FIGURE 1a AND 1b ABOUT HERE

The fatigue index (proportion of torque that remained after 60 maximal effort concentric contractions) showed no sex-related differences at baseline (*Table 2*). Fatigue index improved overall by 4.8% after training ($p=0.048$), with no sex differences in this adaptation (sex x time interaction; $p=0.127$) (*Table 2*).

TABLE 2 ABOUT HERE

Discussion

This SIT programme included only 4 minutes per week of very high intensity exercise and led to significant increases to fatigue resistance and CSA_Q, but no change to knee extensor concentric torque. The training effects were similar for males and females. These findings advance previous studies of physiological adaptation to SIT which typically focussed on aerobic and metabolic adaptation in young adult males and females separately.

Muscle size

There are two contradictory reports in the literature concerning the possible sex differences in hypertrophic responses to sprint interval or high intensity interval training. Esbjornsson-Liljedhal et al., reported that females increased Type IIx fibre CSA more than males after 4 weeks of SIT (16), while another study reported lower skeletal muscle anabolic response to training in females compared with males (38), but this latter work was based only on acute responses and did not follow up after a period of training. In the present study, we found that males and females showed similar increases in CSA_Q, which are agonist muscles during cycling (6). This could be expected since sprint interval exercise activates Type I and IIx fibres similarly in males and females (15, 39), suggesting motor unit recruitment and therefore the training stimulus received by the IIx fibres, is similar for males and females.

A review of the literature indicated that the extent of hypertrophy may depend on the length of the training programme: training 6-weeks or less did not cause significant changes to fibre cross-sectional areas (36). However, longer term training of 7-weeks or more generally increased fibre cross-sectional areas, although it should be noted that studies in this area included only small sample sizes (*n* = 8 to 13) and none of them compared sex-related differences in adaptation (36). For example, a six-week SIT protocol caused a non-significant increase of fibre CSA by 6-12% in 11 untrained males (mean age= 23±5 years) (1). However, 8 months SIT increased fibre CSA by 8-16% in 13 athletes (8 males and 5 females, mean age= 17±1 years), although sex comparisons were not possible due to small sample sizes and the females in the study were trained in sprinting prior to the intervention whilst the males were not (11).

Total body lean mass measured by DXA was unchanged by SIT, with no sex difference in this adaptation (*Table 1*). The leg lean mass and thigh lean mass measured using DXA, also showed no significant changes after training. It is not clear why the DXA detected no significant changes with training, while the MRI clearly showed significant hypertrophy of the quadriceps muscles. The problem is not due to lack of consistency of repeated scans, since Kiebzak et al. (27) observed a 1% variance in lean mass with repeated DXA scans on the same participants over consecutive days and in previous pilot work we determined the test-retest variation to be 1% from our scanner over 4 weeks (*unpublished*). Disparity between MRI and DXA for measuring muscle size has been reported previously, with DXA also failing to reveal the full extent of muscle loss with ageing (30, 31). So it is possible that the DXA is not suitable for detecting these relatively small changes to muscle tissue.

Muscle maximal torque

The higher values in males compared with females across the concentric torque-velocity relationship are mainly due to the larger muscle mass of males, but there was a clear trend for the torque per muscle cross-sectional area to be higher in males than in females and this was significant at $180°\cdot sec^{-1}$. Torque decreased with increasing knee extension velocity (*Figure*

1b). These findings fit with previous estimations of torque per muscle cross sectional area, sometimes described as "muscle quality" in the literature. Lindle et al. (28) observed in 346 males and 308 females aged 20-90 that males have a 9% higher concentric peak torque per muscle cross sectional area than females. Similarly, Goodpaster et al. (20) observed approximately 17% higher muscle quality in older males compared with older females (mean age= 73±3 years) during isokinetic contractions, suggesting that this sex difference is maintained throughout the lifespan. Previous studies examining sex differences after SIT in muscle strength characteristics have been significantly shorter, not lasting more than 4 weeks (4, 16).

The increase in quadriceps muscle size in the present study did not lead to gains in knee extension maximal torque in either males or females. A previous study that measured torque before and after SIT (repeated Wingate tests over 3 weeks) also found no significant changes to knee extensor MVC in 11 males or 9 females (3). It is possible that the mode of exercise training (cycling) might not have trained the neural control needed for isolated knee extensions, as was suggested when the converse was observed when knee extension training did not increase cycling power output (13).

Fatigue resistance

The majority of studies into sex differences in muscle fatigue during controlled exercise of individual muscle groups utilised isometric contractions (23, 24) and the results from such studies generally indicate that females have superior fatigue resistance compared with males (33, 40). Some studies involving concentric contractions also suggest superior fatigue resistance of females compared with males (23, 35, 46). However, fatigability, measured in the present study as the decline in torque after 60 maximal-effort unilateral moderate-velocity concentric knee extensions, was similar in males and females at baseline, with torque during the final contractions dropping to 55% of the first 3 contractions. A possible explanation for why our findings differ from other previous studies is that other studies tended to include young adults or older adults, whereas we included a range of young and middle aged adults. Differences between studies in the velocity of contraction might also influence the fatigability and it is interesting to note that a study utilising maximal velocity contractions at a load equal to 20% of the participant's MVC also reported similar fatigue in males and females during knee extension (40).

There are reports that fatigue characteristics of individual muscle groups are unaffected by sprint training in males (21), but no previous studies compared chronic training adaptation of males and females. Fatigue resistance improved after 12-weeks SIT in the present study. When examining isokinetic contractions, previous work suggests a sex dimorphism in muscle fatigue, with males fatiguing significantly faster than females when velocity is controlled. However, when examining as a product of exercise intensity (i.e., a percentage of maximal power or 1-repetition maximum, not a controlled velocity), a sex difference is no longer observed (32). When matched for initial sprinting mechanical work, males and females see similar decline in muscle power after repeated sprint exercise (8, 41), similar to isokinetic contractions which are matched to initial power output, suggesting that the mechanism for increased fatigue resistance in females seen when measuring power output in repeated sprint exercise is an initial higher power output in males (23). In the present study, where training was normalised to cycling power at VO_2Max, it was observed that males and females increased their resistance to fatigue similarly after SIT when measured as a product of contraction velocity (sex x time interaction: $p=0.127$). Taken together, this could suggest that differing prescription of exercise training (i.e., normalised to initial power output versus velocity or body mass etc.) may have sex-related differences in muscle fatigue. The physiological mechanisms underlying the training-induced improvement to fatigue cannot be identified from the present study, but are likely to be associated with increases in mitochondrial concentrations (and therefore improvements in skeletal muscle metabolism) (29) and capillary density (12) that have been found after SIT and collectively improve muscle oxidative energy recovery during the brief rest intervals between contractions.

Limitations

The design of the training programme, being performed in a local gym or the research laboratory, gave exercise volunteers more control and although this is the case in real-life situations, it may confer less commitment or obligation to training compared with typical fully supervised laboratory-based programmes and we were not able to directly record the power output completed by the study volunteers during training. It was not possible to control for physical activities outside of the training programme and dietary intake was not monitored throughout the training programme. Instead, participants were asked to maintain their usual patterns of food and drink consumption. Finally, there was no control for menstrual cycle variations, which potentially limits the interpretation of some aspects of the data relating to sex-related differences in adaptation. In this regard however, all female participants should equally have completed 3 full menstrual cycles before returning to the laboratory for post-training measurements. Furthermore, evidence points toward there being no change in the muscle parameters measured in this study (25).

Practical Applications

The novel aspects of this research were that we examined maximal knee extensor torque, size and fatigue resistance in males and females ranging from young through to middle-aged adults before and after a period of cycling SIT. Although knee extension torque across a wide range of velocities did not change with training, fatigue resistance and CSA_Q were improved in males and females. Practitioners can use these findings as evidence that SIT is a time-effective option to increase muscle size and resistance to fatigue.

References

1. Allemeier CA, Fry AC, Johnson P, Hikida RS, Hagerman FC, and Staron RS. Effects of sprint cycle training on human skeletal muscle. *J Appl Physiol (1985)* 77: 2385-2390, 1994.
2. American College of Sports Medicine. *ACSM's guidelines for exercise testing and prescription.* Lippincott Williams & Wilkins, 2013.
3. Astorino TA, Allen RP, Roberson DW, and Jurancich M. Effect of high-intensity interval training on cardiovascular function, VO2max, and muscular force. *J Strength Cond Res* 26: 138-145, 2012.
4. Astorino TA, Allen RP, Roberson DW, Jurancich M, Lewis R, McCarthy K, and Trost E. Adaptations to high-intensity training are independent of gender. *Eur J Appl Physiol* 111: 1279-1286, 2011.
5. Batacan RB, Jr., Duncan MJ, Dalbo VJ, Tucker PS, and Fenning AS. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. *Br J Sports Med*, 2016.
6. Bijker KE, de Groot G, and Hollander AP. Differences in leg muscle activity during running and cycling in humans. *Eur J Appl Physiol* 87: 556-561, 2002.
7. Bijlsma AY, Meskers MC, Molendijk M, Westendorp RG, Sipilä S, Stenroth L, Sillanpää E, McPhee JS, Jones DA, Narici M, Gapeyeva H, Pääsuke M, Seppet E, Voit T, Barnouin Y, Hogrel JY, Butler-Browne G, and Maier AB. Diagnostic measures for sarcopenia and bone mineral density. *Osteoporos Int* 24: 2681-2691, 2013.
8. Billaut F and Bishop DJ. Mechanical work accounts for sex differences in fatigue during repeated sprints. *Eur J Appl Physiol* 112: 1429-1436, 2012.
9. Bouchard C, An P, Rice T, Skinner JS, Wilmore JH, Gagnon J, Perusse L, Leon AS, and Rao DC. Familial aggregation of VO(2max) response to exercise training: results from the HERITAGE Family Study. *J Appl Physiol* 87: 1003-1008, 1999.
10. Burgomaster KA, Howarth KR, Phillips SM, Rakobowchuk M, Macdonald MJ, McGee SL, and Gibala MJ. Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. *J Physiol* 586: 151-160, 2008.
11. Cadefau J, Casademont J, Grau JM, Fernández J, Balaguer A, Vernet M, Cussó R, and Urbano-Márquez A. Biochemical and histochemical adaptation to sprint training in young athletes. *Acta Physiol Scand* 140: 341-351, 1990.
12. Cocks M, Shaw CS, Shepherd SO, Fisher JP, Ranasinghe AM, Barker TA, Tipton KD, and Wagenmakers AJ. Sprint interval and endurance training are equally effective in increasing muscle microvascular density and eNOS content in sedentary males. *J Physiol* 591: 641-656, 2013.
13. Erskine RM, Jones DA, Maffulli N, Williams AG, Stewart CE, and Degens H. What causes in vivo muscle specific tension to increase following resistance training? *Exp Physiol* 96: 145-155, 2011.
14. Esbjörnsson-Liljedahl M, Bodin K, and Jansson E. Smaller muscle ATP reduction in women than in men by repeated bouts of sprint exercise. *J Appl Physiol (1985)* 93: 1075-1083, 2002.
15. Esbjörnsson-Liljedahl M, Sundberg CJ, Norman B, and Jansson E. Metabolic response in type I and type II muscle fibers during a 30-s cycle sprint in men and women. *J Appl Physiol (1985)* 87: 1326-1332, 1999.

16. Esbjörnsson Liljedahl M, Holm I, Sylvén C, and Jansson E. Different responses of skeletal muscle following sprint training in men and women. *Eur J Appl Physiol Occup Physiol* 74: 375-383, 1996.
17. Froese EA and Houston ME. Performance during the Wingate anaerobic test and muscle morphology in males and females. *Int J Sports Med* 8: 35-39, 1987.
18. Fuentes T, Guerra B, Ponce-González JG, Morales-Alamo D, Guadalupe-Grau A, Olmedillas H, Rodríguez-García L, Feijoo D, De Pablos-Velasco P, Fernández-Pérez L, Santana A, and Calbet JA. Skeletal muscle signaling response to sprint exercise in men and women. *Eur J Appl Physiol* 112: 1917-1927, 2012.
19. Gillen JB, Percival ME, Ludzki A, Tarnopolsky MA, and Gibala MJ. Interval training in the fed or fasted state improves body composition and muscle oxidative capacity in overweight women. *Obesity (Silver Spring)* 21: 2249-2255, 2013.
20. Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, Schwartz AV, Simonsick EM, Tylavsky FA, Visser M, and Newman AB. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci* 61: 1059-1064, 2006.
21. Harridge SD, Bottinelli R, Canepari M, Pellegrino M, Reggiani C, Esbjörnsson M, Balsom PD, and Saltin B. Sprint training, in vitro and in vivo muscle function, and myosin heavy chain expression. *J Appl Physiol (1985)* 84: 442-449, 1998.
22. Heydari M, Freund J, and Boutcher SH. The effect of high-intensity intermittent exercise on body composition of overweight young males. *J Obes* 2012: 480467, 2012.
23. Hunter SK. Sex differences in human fatigability: mechanisms and insight to physiological responses. *Acta Physiol (Oxf)* 210: 768-789, 2014.
24. Hunter SK. Sex differences in fatigability of dynamic contractions. *Exp Physiol*, 2015.
25. Janse de Jonge XA, Boot CR, Thom JM, Ruell PA, and Thompson MW. The influence of menstrual cycle phase on skeletal muscle contractile characteristics in humans. *J Physiol* 530: 161-166, 2001.
26. Janssen I, Heymsfield SB, Wang ZM, and Ross R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. *J Appl Physiol (1985)* 89: 81-88, 2000.
27. Kiebzak GM, Leamy LJ, Pierson LM, Nord RH, and Zhang ZY. Measurement precision of body composition variables using the lunar DPX-L densitometer. *J Clin Densitom* 3: 35-41, 2000.
28. Lindle RS, Metter EJ, Lynch NA, Fleg JL, Fozard JL, Tobin J, Roy TA, and Hurley BF. Age and gender comparisons of muscle strength in 654 women and men aged 20-93 yr. *J Appl Physiol (1985)* 83: 1581-1587, 1997.
29. Little JP, Safdar A, Wilkin GP, Tarnopolsky MA, and Gibala MJ. A practical model of low-volume high-intensity interval training induces mitochondrial biogenesis in human skeletal muscle: potential mechanisms. *J Physiol* 588: 1011-1022, 2010.
30. MacDonald AJ, Greig CA, and Baracos V. The advantages and limitations of cross-sectional body composition analysis. *Curr Opin Support Palliat Care* 5: 342-349, 2011.
31. Maden-Wilkinson TM, Degens H, Jones DA, and McPhee JS. Comparison of MRI and DXA to measure muscle size and age-related atrophy in thigh muscles. *J Musculoskelet Neuronal Interact* 13: 320-328, 2013.
32. Maughan RJ, Harmon M, Leiper JB, Sale D, and Delman A. Endurance capacity of untrained males and females in isometric and dynamic muscular contractions. *Eur J Appl Physiol Occup Physiol* 55: 395-400, 1986.

33. Mcphee JS, Maden-Wilkinson TM, Narici MV, Jones DA, and Degens H. Knee extensor fatigue resistance of young and older men and women performing sustained and brief intermittent isometric contractions. *Muscle Nerve* 50: 393-400, 2014.
34. Metcalfe RS, Babraj JA, Fawkner SG, and Vollaard NB. Towards the minimal amount of exercise for improving metabolic health: beneficial effects of reduced-exertion high-intensity interval training. *Eur J Appl Physiol* 112: 2767-2775, 2012.
35. Pincivero DM, Gandaio CM, and Ito Y. Gender-specific knee extensor torque, flexor torque, and muscle fatigue responses during maximal effort contractions. *Eur J Appl Physiol* 89: 134-141, 2003.
36. Ross A and Leveritt M. Long-term metabolic and skeletal muscle adaptations to short-sprint training: implications for sprint training and tapering. *Sports Med* 31: 1063-1082, 2001.
37. Russ DW and Kent-Braun JA. Sex differences in human skeletal muscle fatigue are eliminated under ischemic conditions. *J Appl Physiol (1985)* 94: 2414-2422, 2003.
38. Scalzo RL, Peltonen GL, Binns SE, Shankaran M, Giordano GR, Hartley DA, Klochak AL, Lonac MC, Paris HLR, Szallar SE, Wood LM, Peelor FF, Holmes WE, Hellerstein MK, Bell C, Hamilton KL, and Miller BF. Greater muscle protein synthesis and mitochondrial biogenesis in males compared with females during sprint interval training. *The FASEB Journal* 28: 2705-2714, 2014.
39. Scribbans TD, Edgett BA, Vorobej K, Mitchell AS, Joanisse SD, Matusiak JB, Parise G, Quadrilatero J, and Gurd BJ. Fibre-specific responses to endurance and low volume high intensity interval training: striking similarities in acute and chronic adaptation. *PLoS One* 9: e98119, 2014.
40. Senefeld J, Yoon T, Bement MH, and Hunter SK. Fatigue and recovery from dynamic contractions in men and women differ for arm and leg muscles. *Muscle Nerve* 48: 436-439, 2013.
41. Smith KJ and Billaut F. Tissue oxygenation in men and women during repeated-sprint exercise. *Int J Sports Physiol Perform* 7: 59-67, 2012.
42. Staron RS, Hagerman FC, Hikida RS, Murray TF, Hostler DP, Crill MT, Ragg KE, and Toma K. Fiber type composition of the vastus lateralis muscle of young men and women. *J Histochem Cytochem* 48: 623-629, 2000.
43. Venables MC, Achten J, and Jeukendrup AE. Determinants of fat oxidation during exercise in healthy men and women: a cross-sectional study. *J Appl Physiol* 98: 160-167, 2005.
44. Wang CY, Haskell WL, Farrell SW, Lamonte MJ, Blair SN, Curtin LR, Hughes JP, and Burt VL. Cardiorespiratory fitness levels among US adults 20-49 years of age: findings from the 1999-2004 National Health and Nutrition Examination Survey. *Am J Epidemiol* 171: 426-435, 2010.
45. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *Jama* 310: 2191-2194, 2013.
46. Yoon T, Doyel R, Widule C, and Hunter SK. Sex differences with aging in the fatigability of dynamic contractions. *Exp Gerontol* 70: 1-10, 2015.

Figure 1a: Isokinetic knee extensor torque relative to isometric MVC plotted as a function of contraction velocity at baseline (Pre-SIT). Data are mean ± SEM and plotted separately for males (n=16, circles) and females (n=15, triangles). *indicates statistically significant sex-related difference ($p<0.05$)

Figure 1b: Isokinetic knee extensor torque normalised to knee extensor cross sectional area plotted as a function of contraction velocity at baseline (Pre-SIT). Data are mean ± SEM and plotted separately for males (n=16, circles) and females (n=15, triangles). *indicates statistically significant sex-related difference ($p<0.05$)

Table 1. Participant characteristics and muscle size in males (n=16) and females (n=15) before and after 12 weeks SIT.

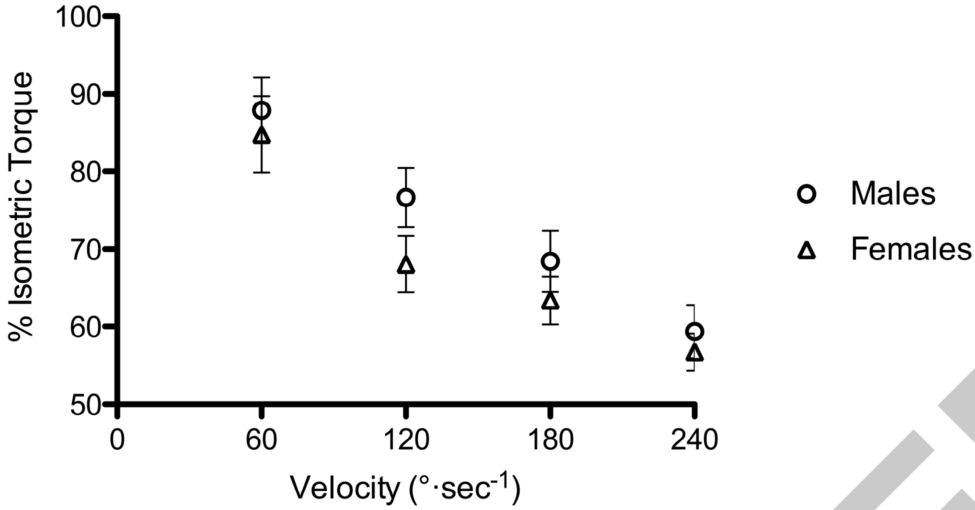
	Males (Pre)	Males (Post)	Females (Pre)	Females (Post)	Time effect (p-value)	Sex effect (p-value)	Sex x Time interaction (p-value)
Age (yrs)	40.8 (3.2)		40.9 (3.9)				
SIT Sessions		32 (2)		34 (2)		0.602	
VO_2max ($L\cdot min^{-1}$)	3.5 (0.2)	3.6 (0.2)	2.0 (0.1)	2.4 (0.1)	**0.032**	**<0.001**	0.595
VO_2max ($mL\cdot kg\cdot min^{-1}$)	43.7 (2.1)	45.8 (1.7)	34.3 (2.3)	40.8 (2.4)	**0.001**	**0.013**	0.815
Total body mass (kg)	80.0 (2.2)	79.2 (2.1)	62.5 (2.6)	62.1 (2.5)	**0.039**	**<0.001**	0.207
Height (m)	1.75 (0.02)		1.66 (0.01)				
Body Mass Index ($kg\cdot m^2$)	25.9 (0.9)	25.8 (0.9)	21.8 (0.7)	21.8 (0.7)	0.055	**0.001**	0.495
Body Fat (%)	22.5 (1.4)	21.3 (1.4)	30.4 (1.4)	29.9 (1.3)	0.807	**<0.001**	0.133
Total body lean mass (kg)	60.4 (1.6)	61.1 (1.6)	39.1 (0.9)	39.2 (1.0)	0.147	**<0.001**	0.067
Leg lean mass (kg)	21.6 (0.7)	21.0 (0.7)	13.6 (0.3)	13.0 (0.4)	0.992	**<0.001**	0.990
Right thigh lean mass (kg)	5.0 (0.2)	5.1 (0.2)	3.4 (0.1)	3.5 (0.2)	0.547	**<0.001**	0.880
CSA_Q (cm^2)	86.2 (3.3)	89.7 (3.1)	56.7 (1.9)	60.0 (1.6)	**0.023**	**<0.001**	0.140

Data are shown as mean (SEM). Knee Extensor CSA (cm^2) is measured in 15 males and 10 females due to equipment maintenance.

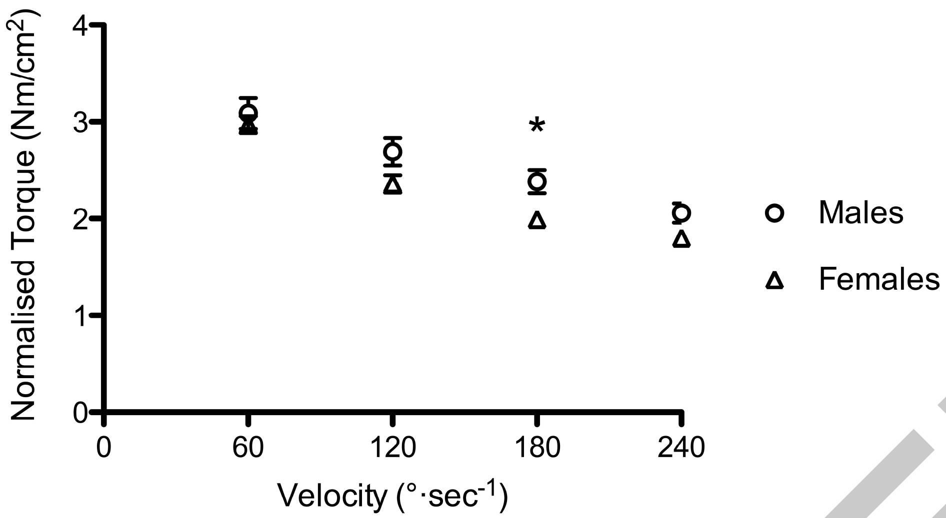
Table 2. Knee extensor torque in males and females before and after 12 weeks SIT

	Males (Pre)	Males (Post)	Females (Pre)	Females (Post)	Time effect	Sex effect	Sex x Time interaction
Isometric MVC (Nm)	314.32 (21.86)	322.98 (23.10)	193.33 (9.43)	204.20 (9.65)	0.079	**<0.001**	0.385
Isometric MVC ($Nm{\cdot}cm^2$)	3.65 (0.21)	3.57 (0.24)	3.23 (0.09)	3.23 (0.11)	0.712	0.248	0.705
$60°{\cdot}sec^{-1}$	260.25 (13.78)	265.89 (16.45)	161.23 (9.64)	175.66 (6.45)	0.080	**<0.001**	0.548
$120°{\cdot}sec^{-1}$	227.01 (12.27)	231.29 (13.42)	128.98 (6.34)	145.22 (4.03)	0.066	**<0.001**	0.806
$180°{\cdot}sec^{-1}$	199.55 (8.70)	201.50 (11.03)	120.11 (5.05)	120.54 (3.04)	0.495	**<0.001**	0.522
$240°{\cdot}sec^{-1}$	173.93 (8.22)	172.73 (9.91)	107.57 (3.93)	107.19 (3.25)	0.552	**<0.001**	0.659
Fatigue Index (%)	52.40 (2.52)	56.42 (3.27)	55.92 (3.56)	64.80 (2.26)	**0.048**	0.282	0.127

Data are shown as mean (SEM). Males (n=16), Females (n=15)



100
90
80
70
60
50
% Isometric Torque
0
60
120
180
240
Velocity (°·sec-1)
Males
Females


Normalised Torque (Nm/cm²)
4
3
2
1
0
0
60
120
180
240
Velocity (°·sec⁻¹)
*
Males
Females