# Sex Differences in Muscle Fatigue Following Isokinetic Muscle Contractions

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**Research**

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# Abstract

Muscle fatigue is a limiting factor of human performance. It is unclear whether sex-based differences in fatigability exist during dynamic exercise of varying velocities of contraction. We aimed at exploring sex differences in muscle fatigue elicited by maximal isokinetic muscle contractions performed at different angular velocities. Twenty-six healthy participants (13 men: 23.2 ± 1.5; 13 women: 21.9 ± 3.0 years) were tested for knee-extension at slow, moderate and fast angular velocity (60, 180 and 300º.$s^{-1}$, respectively). The impact of sex on fatigue resistance and consecutive recovery for each isokinetic condition was explored by calculating the percent change in maximal voluntary isometric contraction (MVIC) and in rate of torque development (RTD), from pre- to post-isokinetic exercise. The isokinetic fatigue index was also determined. No sex differences were obtained in response to isokinetic contractions completed at 60º.$s^{-1}$. After performing muscle contractions at 300º.$s^{-1}$, women had a significantly greater loss in MVIC than men (-18.4 ± 5.5 vs. -12.9 ± 3.8%; p = 0.009) and larger decreases in work output during isokinetic exercise (-34.2 ± 8.9 vs -27.5 ± 10.6 %; p = 0.017). Recovery of initial MVIC strength was greater for women post-exercise at 180º.$s^{-1}$ (6.7 ± 9.5 vs. 15.6 ± 4.1%; p = 0.003). No differences were found between sexes in any condition for RTD from pre- to post- fatigue. These results suggest the presence of a sexually dimorphic fatigability in response to dynamic (isokinetic) contractions favouring men at higher velocities of contraction.

# Background

Fatigue has been one of the most studied topics in human physiology and yet one of the most controversial. As a fundamental parameter describing skeletal muscle function, fatigue can be defined as a loss of force or power in response to contractile activity [1]. Several mechanisms contribute to muscle fatigue, which depend not only on the specificities of the task and muscle group, but also on the physical characteristics of the individual, including sex [2, 3]. The impact of sex on fatigue is difficult to understand because the interaction between both is highly dependent on the nature of the motor task to be performed [4] .

Although some studies reported no differences in muscle fatigue between sexes, many others have shown that regardless of being stronger than women, men are often more fatigable for sustained and intermittent isometric exercise performed at similar relative intensity [5]. Men have also been shown to recover more slowly than women following isometric exercise (sustained and intermittent), and this is likely related to heightened central fatigue in men [6, 7], thus corroborating the concept that sex differences in muscle fatigue may extend well beyond the actual exercise period. Despite the current evidence, it is still unclear whether sex-differences in fatigability are present during dynamic motor tasks performed with different muscle groups, contraction velocities and loads. Also, it has not yet been determined which intrinsic factors may concur to a sexually dimorphic pattern during dynamic exercise. For instance, while blood flow restriction appears to be highly responsible for sex differences in fatigability favoring women during low-intensity contractions performed with the elbow flexors [8], this is not the case for knee-extension exercise [9]. Similar inconsistencies have been reported for isotonic contractions completed at different velocities and with different muscle groups. For instance, there are data showing that women are less fatigable than men during low-load dynamic exercise (20% of maximum voluntary isometric contraction (MVIC)) with the elbow flexors at slow, but not high-velocity contractions (i.e. ~ 60º.$s^{-1}$ vs. maximum velocity, respectively) [10, 11]. In contrast, for the knee-extensors, men show a similar reduction in maximal angular velocity as women while responding to muscle contractions performed as fast as possible at 20% MVIC. Yet, under these circumstances, men still exhibit a greater decline in MVIC torque immediately after exercise [10].

Nevertheless, as reported for the immediate post exercise period, women exhibit a faster rate of MVIC recovery after 120 maximal voluntary concentric contraction at 20% MVIC [7]. It was also shown that the mechanistic basis of such differences relies on sex differences at the peripheral level – with women showing contractile properties more compatible with a greater proportional area of fibers containing type I myosin heavy chain [7].

Despite the relevance of these findings, it is important to note that past research did not control for differences in maximal contraction velocity between sexes (men: 420 vs. women: 290º.$s^{-1}$), and this is an important limitation [7]. In addition, it should be emphasized that previous experimental designs focusing on dynamic muscle contractions were unable to ensure comparable conditions between sexes and this precludes drawing further conclusions. To discriminate the role of sex in muscle fatigue during dynamic exercise, it is critical to test both men and women at similar angular velocities. In one study that explored sex differences in muscle fatigue resulting from isokinetic exercise, the authors implemented a single velocity of exercise (i.e. 90º.$s^{-1}$) [12]. No differences were observed in torque or work decrement between sexes after 50 continuous cycles of maximal knee-extension exercise. Whether this occurs following knee-extension exercise performed at higher isokinetic angular velocity, is not known. Therefore, it remains to be unravelled whether fatigue follows a sexually dimorphic pattern in response to isokinetic muscle contractions completed at different angular velocities (i.e. slow vs. moderate vs. fast velocities).

Past research on the topic of sex differences in muscle fatigue approached this issue by quantifying the magnitude of post-exercise reduction in average/peak levels of torque, power or work output. However, one of the most critical aspects of sports performance and injury prevention is rate of torque development (RTD), which can be defined as the ability to increase force as quickly as possible during a rapid voluntary contraction from a low or resting level [13]. Sex may influence the ability for explosive force production because men clearly outperform women in absolute RTD [14]. Absolute strength, normalized motor-tendon unit stiffness, intrinsic contractile properties and agonist muscle activation most likely underlie this sexually dimorphic pattern [14–16]. Yet, only the first mechanism was unequivocally shown to provide a partial explanation for differences in absolute RTD between sexes [14]. When accounting for sex differences in maximal strength, men and women show similar force-generating capacity in response explosive muscle contractions [14]. Unfortunately, to our knowledge, no previous research has compared decreases in explosive force production between sexes after isokinetic fatiguing exercise performed at different angular velocities.

Considering all these aspects, this study aimed at determining the impact of sex on the decline, as well as on the recovery, of MVIC and RTD post-isokinetic knee-extension exercise performed at slow, moderate and fast angular velocities. We also intended to explore sex differences in the reduction of mechanical work output (fatigue index) during isokinetic exercise performed at each angular velocity. It was hypothesized that women would fatigue less than men after completing 30 maximal knee-extension isokinetic contractions at slow angular velocity. In addition, we hypothesized that both sexes would exhibit similar levels of fatigue in response to 30 maximal knee-extension isokinetic contractions performed at fast angular velocity. Finally, we hypothesized that women would recover at a faster rate than men after isokinetic exercise, and that this would be extensive to slow, moderate and fast angular velocities.

## Methods

# Participants

Twenty-six participants (13 men and 13 women) were included in this study (see Table 1). Physical activity levels were assessed using “The Aerobics Centre Longitudinal Study Physical Activity Questionnaire” [17]. Exclusion criteria included body mass index ≥ 25 $kg.m^{-2}$, participation in less than 150 min of moderate to vigorous physical activity per week and also any involvement in regular resistance training (frequency ≥ 2 exercise sessions/week) for the lower limb during the past 8 weeks before volunteering for this study. Participants were tested on their dominant limb, which was determined using the Waterloo limb-dominance questionnaire [18]. All participants were healthy and free from any musculoskeletal injury that would limit exercise performance. The risks of participation were carefully explained and informed consent was obtained from all participants. This study complied with the principles set forth in the Declaration of Helsinki and was approved by the Faculty’s Ethics Committee (CEFMH nº: 15/2019).

# Procedures

Each participant visited the laboratory on 4 different non-consecutive days to complete 1 familiarization session and 3 testing sessions (one at each angular velocity on a randomized fashion). All sessions were conducted between 12:00 and 17:00 h. Participants were tested for unilateral knee-extension exercise. They all completed the following tasks on each testing session: (1) knee-extension MVICs (2) isokinetic knee-extension fatigue protocol and (3) post-fatigue MVICs. Participants were also asked to avoid the consumption of alcohol, xanthine derivatives and engagement in any form strenuous lower-limb exercise before testing (24, 12 and 48 h, respectively).

Table 1
Characteristics of the participants.

| | Women (n = 13) | Men (n = 13) | p value |
|---|---|---|---|
| Age (years) | 21.9 ± 3.0 | 23.2 ± 1.5 | 0.088 |
| Height (cm) | 162.8 ± 6.6 | 175 ± 6.8 | < 0.001* |
| Body mass (kg) | 58.2 ± 6.0 | 73.7 ± 10.9 | < 0.001* |
| BMI (kg/m$^2$) | 22 ± 2.0 | 24 ± 3.1 | 0.061 |
| PA (MET-h/wk) | 41.3 ± 4.2 | 40.6 ± 5.0 | 0.701 |
| Values are mean ± SD | | | |
| Abbreviations: BMI, body mass index; PA, physical activity; MET, metabolic equivalent. | | | |
| *Sex difference at p < 0.05 | | | |

# Measurements

Participants remained seated on a Biodex System 3 Pro isokinetic dynamometer (Biodex Medical Systems, Shirley, NY) with a hip angle of 85º (supine position = 0º). For each knee-extension MVIC, the knee joint was fixated at 70º of knee extension [19]. For the isokinetic fatigue protocol, knee-extension range of motion was set at 90º (0º = maximum knee-extension). All torque readings were corrected for the effect of gravity on the lower limb. Velcro straps were placed across the trunk, hip and thigh to prevent extraneous movement. The axis of rotation of the dynamometer was aligned with the lateral epicondyle of the knee. The lower leg was also strapped to the knee extension/flexion attachment, which was placed at a standardized distance of 3 cm from the medial malleolus. Torque signal was obtained at 1000 Hz (MP150, BIOPAC Systems Inc., Goleta, CA). Data were collected and processed using the software AcqKnowledge 4.3.1 (BIOPAC Systems Inc., Goleta, CA). A 12 Hz low-pass filter (zero-phase shift 4th order Butterworth filter) was applied to torque signals, using a custom-built routine for analysis (MATLAB version R2018a).

# Protocol

Two days before testing, each participant underwent a familiarization session during which additional information was provided, along with completion of the questionnaires. Afterwards, the participants were submitted to a familiarization protocol including both isometric and isokinetic contractions performed at three different angular velocities (60, 180 and 300º.s$^{-1}$). This was done to minimize the learning effect associated with this specific motor task [20].

Each testing session began with a dynamic warm up, consisting of 5 min of submaximal cycle-ergometry set at 25 W. Then, participants performed 2 sets of 5–6 submaximal isokinetic repetitions (1 set at 120º.s$^{-1}$ and 1 set at speed test: 60, 180 or 300º.s$^{-1}$) with 30 s of pause between sets. This was followed by 4–5 submaximal isometric repetitions (with the knee at 70º of extension) at ~ 60–70% of participants' perceived maximum effort. The last repetition corresponded to a 5-s MVIC to promote post-activation potentiation [21]. A rest period of 4 min was allowed between the completion of warm up and testing procedures. Four maximal isometric 4-s voluntary knee extensions were then performed, with 1 min rest between trials. The participants were instructed to exert their maximum force "as fast and hard as possible", to obtain both maximal torque and RTD [13]. To ensure an accurate assessment of these variables, visual instantaneous feedback of the torque-time curve was provided to all participants during each trial. MVIC was defined as the highest peak torque (PT) obtained in response to these isometric contractions. This value was used as a measure of maximum isometric strength pre-fatigue (baseline). Another 5 maximal voluntary knee extensions were performed post-fatigue, with 1 min of interval between trials. The 1st (performed immediately post-exercise cessation) and 5th repetitions (post-fatigue.1 and post-fatigue.5, respectively) were then used to explore the magnitude of post-exercise recovery.

RTD was computed using different approaches. Sequential RTD was calculated using the torque-time curve slope (i.e. Δtorque/Δtime) and analysed in incremental epochs of 50 ms (0–50; 50–100; 100–150 ms). Peak RTD (pRTD), which corresponds to the highest torque-time curve slope, was calculated using 20-ms time windows [13]. Explosive torque (ETorque) was defined as the %MVIC attained at specific time points (50, 100, 150 and 200 ms). It represents a relative measure of explosive torque production and it translates the ability to recruit the individual torque reserve. The onset of torque development (start of contraction) was defined as the time point at which the torque curve exceeded the average baseline values by 3 N.m [13, 22]. Contractions associated with pre-tension or counter-movement were discarded, and another trial was performed. Torque, pRTD and sequential RTD were measured in absolute and normalized terms (relative to MVIC) i.e. relative pRTD was calculated as follows:

$$\frac{\mathrm{pRTD}_{(\mathrm{N.m.s}^{-1})} \times 100}{\mathrm{MVIC}_{(\mathrm{N.m})}}$$

For the isokinetic muscle contractions, testing involved a fatigue protocol consisting of 30 maximal repetitions performed in the concentric/passive mode at randomly pre-selected angular velocities - slow, moderate and fast (60, 180 and 300º.s$^{-1}$, respectively) [23]. Passive mode velocity was set at 90º.s$^{-1}$ for all conditions. Participants were instructed to exert maximal torque as fast and hard as possible during the concentric phase, corresponding to knee extension. Knee flexion was performed passively. The impact of sex on fatigue resistance at each isokinetic angular velocity was explored by calculating the percent change in MVIC and pRTD across time points (fatigue: $\mathrm{MVIC}_{\mathrm{loss}}$ and $\mathrm{pRTD}_{\mathrm{loss}}$ - from baseline to post-fatigue.1; recovery: $\mathrm{MVIC}_{\mathrm{rec}}$ and $\mathrm{pRTD}_{\mathrm{rec}}$ – from post-fatigue.1 to post-fatigue.5). Analysis on the impact of fatigue at the level of sequential RTD and ETorque were exclusively performed in transition from baseline to post-fatigue.1. Finally, we computed the modified isokinetic fatigue index for PT and work output to explore sex differences in the of decline muscle performance during isokinetic force production:

$$) \; \boldsymbol{Fatigue\ index\ (\%\ decrease)} = \frac{(\bar{x}\ 5\ highest\ consecutive\ repetitions - \bar{x}\ last\ 5\ repetitions)}{\bar{x}\ 5\ highest\ repetitions} \times 100$$

(1)

in which $\bar{x}$ , represents the mean value of PT or work output. This equation has been shown to be more accurate than the traditional isokinetic fatigue index (which accounts for the first 5 repetitions instead of the highest consecutive 5 repetitions) [24]. Work output was calculated as the area under the torque-angle curve during the isokinetic window of each velocity (angular acceleration = 0).

# Statistical Analysis

Descriptive and outcome statistics are presented as mean ± standard deviation (SD) in the text and as mean ± standard error of the mean (SEM) in the figures. Leg dominance was compared between sexes with the Mann-Whitney U, non-parametric test. Based on previous research, if the decrement in MVIC from pre- to post-dynamic knee-extension fatiguing tasks in men corresponds to 35.0 ± 13.4% and 23.1 ± 8.4% in women [7, 24], a sample size of 24 participants (12 men and 12 women) was estimated to achieve more than 80% power of correctly rejecting the null hypothesis. Therefore, 26 participants were recruited for this study. Independent samples t tests were used to explore sex differences in anthropometric characteristics, physical activity levels and in baseline measures of torque-related variables. Separate repeated-measures ANOVAs, with sex as a between-subject factor, were computed to compare changes in MVIC and pRTD over time (fatigue and recovery) during each testing session (60, 180 and 300º.s$^{-1}$). To assess the time effect of fatigue elicited by the dynamic muscle contractions, we compared data obtained at baseline with those obtained immediately after the cessation of exercise (baseline vs. post-fatigue.1). Additionally, we also explored between-sex differences in the magnitude of post-exercise recovery. This was done by comparing the time point immediately subsequent to the fatiguing task with that seen after 5 min of recovery (post-fatigue.1 vs. post-fatigue.5). Post hoc analyses were performed using independent samples t tests, with sex as the grouping variable. For variables calculated only at baseline and post-fatigue.1 (i.e. sequential RTD and ETorque), independent samples t tests (with sex as the grouping variable) were used to determine sex differences between time-points. To analyse changes resulting from the isokinetic fatiguing task (using the fatigue index based both on PT and work output), independent samples t tests were also used, with sex as the grouping variable. All data were tested for normality with the Kolmogorov–Smirnov test. For each ANOVA, data were tested for sphericity with Mauchly’s test. For independent-samples t tests, the Levene’s test for equality of variances was performed. Data were analysed using IBM SPSS Statistics (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) and significance was set $p < 0.05$.

## Results

# Demographics and baseline measures

As shown in Table 1, men and women were of similar age and attained similar levels of weekly physical activity ($p > 0.05$). They did not differ for body mass index, however men were heavier (sex main effect, $F = 20.0$, $p < 0.001$) and taller than women (sex main effect, $F = 21.1$, $p < 0.001$). There were no sex-differences in leg dominance ($p > 0.05$). Tables 2, 3 and 4 depict the differences between sexes in torque-related variables at each angular velocity. Overall, knee-extension absolute MVIC torque was 34% higher in men compared to women (men: 330.5 ± 43.6 vs. women: 216.6 ± 49 N.m; sex main effect, $F = 29.1$, $p < 0.001$). Men also exhibited 38% higher levels of absolute pRTD (1750.3 ± 330.6 vs. 1077.2 ± 267.3 N.m.s$^{-1}$; sex main effect, $F = 30.9$, $p < 0.001$). Finally, they also showed enhanced absolute values of sequential RTD (50 ms epochs) (40% difference $RTD_{0-50}$; 35% difference $RTD_{50-100}$; 30% difference $RTD_{100-150}$; sex main effect, $F = 30.6$, $p < 0.001$). However, after normalizing pRTD and sequential RTD to MVIC, sexual dimorphism in all these variables was dissipated ($p > 0.05$, for all comparisons). No sex differences were found for ETorque across time points in either condition ($p > 0.05$).

Table 2
Relative change in mechanical variables from pre- to post-isokinetic contractions and during recovery from exercise performed at different angular velocities.

| | **60º.s$^{-1}$** | | **180º.s$^{-1}$** | | **300º.s$^{-1}$** | |
|---|---|---|---|---|---|---|
| **Variables** | MEN | WOMEN | MEN | WOMEN | MEN | WOMEN |
| MVICloss (%) | -24.8 ± 9.19 | -27.2 ± 10.4 | -15.2 ± 6.85 | -18.8 ± 10.4 | -12.9 ± 3.81 | -18.4 ± 5.52* |
| MVICrec (%) | 16.1 ± 7.3 | 17.6 ± 9.3 | 6.7 ± 9.5 | 15.6 ± 4.12* | 8.03 ± 6.6 | 13.04 ± 6.4 |
| Absolute pRTDloss (%) | -41.8 ± 21.2 | -39.3 ± 19.8 | -22.3 ± 25 | -26.5 ± 11.9 | -15.8 ± 15.8 | -12.6 ± 14.5 |
| Absolute pRTDrec (%) | 22.6 ± 28.8 | 21.3 ± 29.8 | 12.5 ± 22.5 | 16.3 ± 14.6 | -2.3 ± 30.6 | 4.33 ± 9.5 |
| Relative pRTDloss (%) | -235 ± 125.6 | -207 ± 105.6 | -135 ± 113.3 | -135 ± 67.7 | -82 ± 85.9 | -86 ± 105.7 |
| Relative pRTDrec (%) | 105 ± 103.2 | 88.8 ± 105.7 | 74 ± 105.4 | 74 ± 67.7 | 16.4 ± 125.9 | 36 ± 71.7 |

Values are mean ± SD.

Abbreviations: $MVIC_{loss}$, relative change in maximal voluntary isometric contraction from baseline to immediately after fatigue; $pRTD_{loss}$, relative change in peak rate of toque development from baseline to immediately after fatigue; $MVIC_{rec}$, relative change in maximal voluntary isometric contraction from immediately after fatigue to 5-min post-exercise cessation; $pRTD_{rec}$, relative change in peak rate of torque development from immediately after fatigue to 5-min post-exercise cessation.

*Sex difference at $p < 0.05$.

Table 3
Comparison of absolute rate of torque development from pre- to post- fatigue in both sexes.

| **VARIABLES** | ***$60^{o}.s^{-1}$*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **pre-exercise** | | **post-exercise** | | **p value** | **Δ (%)** | | |
| Absolute RTD (N.m/$s^{-1}$) | MEN | WOMEN | MEN | WOMEN | | MEN | WOMEN | P value |
| 0–50 ms | 1310 ± 342 | 787 ± 197 | 548 ± 168 | 384 ± 100 | < 0.001* | -53.9 ± 19.9 | -48.8 ± 15.4 | 0.500 |
| 50–100 ms | 1378 ± 318 | 951 ± 206 | 826 ± 247 | 565 ± 109 | < 0.001* | -38.1 ± 17.4 | -37.7 ± 18.9 | 0.956 |
| 100–150 ms | 932 ± 238 | 619 ± 112 | 620 ± 0.256 | 477 ± 124 | < 0.001* | -30.5 ± 27.7 | -22.7 ± 16.7 | 0.447 |
| **VARIABLES** | $180^{o}.s^{-1}$ | | | | | | | |
| | pre-exercise | | post-exercise | | p value | Δ (%) | | |
| Absolute RTD (N.m/$s^{-1}$) | MEN | WOMEN | MEN | WOMEN | | MEN | WOMEN | P value |
| 0–50 ms | 1191 ± 354 | 722 ± 274 | 704 ± 341 | 473 ± 274 | < 0.00* | -48.3 ± 2.7 | -22.6 ± 43.7 | 0.095 |
| 50–100 ms | 1431 ± 363 | 924 ± 294 | 1033 ± 471 | 687 ± 182 | < 0.001* | -28.9 ± 29.9 | -21.5 ± 22.1 | 0.503 |
| 100–150 ms | 949 ± 141 | 679 ± 145 | 888 ± 268 | 569 ± 122 | 0.055 | -3.76 ± 31.6 | -14.7 ± 16.4 | 0.299 |
| **VARIABLES** | $300^{o}.s^{-1}$ | | | | | | | |
| | pre-exercise | | post-exercise | | p value | Δ (%) | | |
| Absolute RTD (N.m/$s^{-1}$) | MEN | WOMEN | MEN | WOMEN | | MEN | WOMEN | P value |
| 0–50 ms | 1292 ± 347 | 757 ± 0.26 | 1109 ± 377 | 567 ± 115 | < 0.001* | -13.6 ± 19.1 | -17.8 ± 26.3 | 0.660 |
| 50–100 ms | 1473 ± 304 | 925 ± 226 | 1342 ± 291 | 838 ± 164 | 0.006* | -7.9 ± 13.7 | -7.39 ± 14.0 | 0.918 |
| 100–150 ms | 924 ± 187 | 658 ± 172 | 893 ± 191 | 615 ± 162 | 0.188 | -1.7 ± 18.1 | -5.3 ± 17.2 | 0.626 |

Values are mean ± SD.

Abbreviations: RTD, Rate of torque development

* Difference from pre- to post-exercise at $p < 0.05$.

Table 4
Comparison of normalized values of sequential rate of torque development from pre- to post-fatigue in both sexes.

| **VARIABLES** | ***60º.s$^{-1}$*** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **pre-exercise** | | **post-exercise** | | **p value** | **Δ (%)** | | |
| Relative RTD (%MVIC) | MEN | WOMEN | MEN | WOMEN | MEN | WOMEN | p value | |
| 0–50 ms | 412 ± 116 | 376 ± 101 | 237 ± 98 | 257 ± 74 | < 0.001* | -160.3 ± 133 | -119.7 ± 87.3 | 0.394 |
| 50–100 ms | 422 ± 65 | 445 ± 54 | 337 ± 72 | 373 ± 72 | < 0.001* | -77.5 ± 103 | -72.2 ± 78.2 | 0.889 |
| 100–150 ms | 286 ± 67 | 294 ± 53 | 249 ± 74 | 313 ± 75 | 0.644 | -34.1 ± 79.6 | 18.8 ± 44.4 | 0.069 |
| **VARIABLES** | 180º.s$^{-1}$ | | | | | | | |
| | pre-exercise | | post-exercise | | p value | Δ (%) | | |
| Relative RTD (%MVIC) | MEN | WOMEN | MEN | WOMEN | | MEN | WOMEN | p value |
| 0–50 ms | 370 ± 123 | 342 ± 105 | 255 ± 120 | 290 ± 140 | 0.002* | -114 ± 106 | -51.6 ± 129 | 0.204 |
| 50–100 ms | 430 ± 83 | 434 ± 79 | 369 ± 142 | 403 ± 71 | 0.096 | -60 ± 173.2 | -30.5 ± 73.8 | 0.584 |
| 100–150 ms | 290 ± 50 | 326 ± 60 | 318 ± 83 | 335 ± 49 | 0.247 | 29 ± 87.9 | 8.9 ± 69.7 | 0.542 |
| **VARIABLES** | 300º.s$^{-1}$ | | | | | | | |
| | pre-exercise | | post-exercise | | p value | Δ (%) | | |
| Relative RTD (%MVIC) | MEN | WOMEN | MEN | WOMEN | | MEN | WOMEN | p value |
| 0–50 ms | 396 ± 115 | 352 ± 114 | 380 ± 105 | 334 ± 110 | 0.297 | -15.4 ± 76.1 | -17.7 ± 79.2 | 0.944 |
| 50–100 ms | 443 ± 59 | 424 ± 65 | 463 ± 62 | 473 ± 50 | 0.008* | 19.9 ± 62.1 | 49.2 ± 53.1 | 0.227 |
| 100–150 ms | 282 ± 68 | 301 ± 48 | 311 ± 69 | 345 ± 59 | 0.001* | 28.7 ± 46.4 | 44.1 ± 49.1 | 0.435 |

Values are mean ± SD.

Abbreviations: RTD, Rate of torque development

* Difference from pre- to post-exercise at $p < 0.05$.

Baseline data (MVIC, pRTD, sequential RTD and ETorque), obtained in each condition, were similar between visits (60, 180 and 300º.s$^{-1}$). Importantly, this occurred similarly for both men and women.

# Isometric torque production (fatigue and recovery)

## MVIC and pRTD

For all conditions, in both sexes, MVIC and pRTD were reduced from baseline to immediately post-isokinetic exercise ($MVIC_{loss}$; time main effect, $F = 181.8$, $p < 0.001$; $pRTD_{loss}$; time main effect, $F = 48.8$, $p < 0.001$). Then, MVIC increased throughout the 5 min of recovery ($MVIC_{rec}$; time main effect, $F = 103.0$, $p < 0.001$; $pRTD_{rec}$; time main effect, $F = 10.1$, $p = 0.004$) (Table 2). Although $MVIC_{loss}$ and $MVIC_{rec}$ were similar between men and women at 60º.$s^{-1}$, significant interactions were obtained at 180 and 300º.$s^{-1}$ (sex x time interaction, $F = 6.7$, $p = 0.016$ and $F = 6.1$, $p = 0.021$, respectively). For $MVIC_{loss}$ at 180º.$s^{-1}$, while both sexes had identical decrements over time ($p = 0.187$), women had a greater $MVIC_{rec}$ than men ($p = 0.007$). Additionally, at 300º.$s^{-1}$ women had a greater $MVIC_{loss}$ than men ($p = 0.009$), while $MVIC_{rec}$ was similar for both sexes ($p = 0.186$) (Fig. 1). The $pRTD_{loss}$ and $pRTD_{rec}$ response was similar between sexes in all conditions, both for absolute and normalized values ($p > 0.05$).

*insert Table 2 here*

*insert Fig. 1 here*

## Sequential RTD and ETorque

Absolute and normalized values of sequential RTD and ETorque are shown in Tables 3 and 4, as well as in Fig. 2, respectively (these variables were only calculated for fatigue). Isokinetic knee-extension exercise performed at all angular velocities (60, 180 and 300º.$s^{-1}$) was effective in reducing sequential RTD (both absolute and normalized values) and ETorque in both sexes. However, this was not extensive to all time intervals (see Tables 3 and 4). Comparisons between sexes revealed that the magnitude of change in sequential $RTD_{loss}$ (absolute and normalized) and $ETorque_{loss}$ was similar between men and women in all conditions ($p > 0.05$).

*insert Fig. 2 here*

## Fatigue during isokinetic exercise

During isokinetic exercise, dynamic PT and work output decreased from the start to the end of the protocol in all conditions (Fig. 3). No sex differences were found in PT fatigue index during isokinetic exercise at any angular velocity ($p > 0.05$). However, for the work-based fatigue index, although no differences between sexes were found at 60 or 180ºs.1 ($p > 0.05$), women fatigued 7% more than men while responding to the exercise performed at 300ºs.$^{-1}$ (women: -34.2 ± 8.9 vs. men: -27.5 ± 10.6%; $p = 0.017$) (Fig. 3).

*insert Fig. 3 here*

*insert Table 3 here*

*insert Table 4 here*

## Discussion

The aim of this study was to explore whether sex differences in muscle fatigue are sustained during and after maximal isokinetic knee-extension exercise performed at different angular velocities. Our results indicate that different velocities of contraction have a distinct impact on muscle performance, and that sex interacts with the relationship between contraction velocity and muscle fatigue. We unravelled that men exhibit smaller work output decrement and better isometric muscle performance post-fatigue induced by isokinetic knee extensions performed at faster angular velocities (300º.$s^{-1}$). Additionally, we found that women only recover faster than men after isokinetic exercise completed at moderate velocities of contraction (180º.$s^{-1}$). These findings are in partial agreement to those hypothesized.

We chose to use an isokinetic approach to investigate muscle fatigue because, under these conditions, muscle contractions are performed at maximal intensity throughout the entire range of motion, regardless of the selected velocity [12]. Despite being a non-natural condition for real-life muscle performance, it provides insight into the individual single-limb exercise capacity at maximal intensity, but limited velocity. As confirmed by our data, under these circumstances, muscle fatigue manifested itself differently from that seen after isotonic contractions in both sexes [9, 12].

### Isokinetic and isometric fatigue

## MVIC, dynamic PT and work output

First, since MVIC and RTD decreased from pre- to post-exercise in all conditions, it can be confirmed that isokinetic contractions were effective in eliciting muscle fatigue (loss of torque/power) [1]. Our data provide evidence that there is no sexual dimorphism in torque decrement or muscle performance in response to isokinetic fatiguing exercise performed at slow velocity (60º.$s^{-1}$). In line with our findings, previous reports have shown no sex differences in PT decrease or relative work output when performing 150 and 50, respectively, isokinetic knee-extensions at 90º.$s^{-1}$ [25]. Contrary to that seen in the present study using isokinetic contractions, it has been shown that during isotonic slow-velocity contractions (~ 60º.$s^{-1}$) women are more fatigue-resistant than men because they perform more repetitions for low-intensity knee-extension (20% MVIC) [9]. Additionally, further corroborating these data, women have been shown to attain a longer time to failure in response to low-intensity dynamic elbow-flexion exercise (20% MVIC) (Yoon et al. 2015). It is generally believed that this is secondary to sex-related differences in contractile mechanisms regulating the changes in peak rates of muscle relaxation [15]. The lack of sex differences in muscle fatigue after slow velocity isokinetic muscle contractions is likely explained by the maximal intensity of each repetition completed using this specific mode of exercise. This notion is supported by past research showing that sex differences in muscle fatigue are virtually negligible during dynamic contractions performed at higher intensities [26]. High intensity muscle contractions heighten the recruitment of type II muscle fibers [27, 28] and this likely offsets the typical female-associated reliance on type I fibers for muscular work (performed slowly at submaximal intensity on an isotonic fashion).

As above-mentioned, not many previous experimental designs have controlled for contraction velocity, especially during isotonic contractions (i.e. slow velocity was set for 60º.$s^{-1}$ and fast velocity for “as fast as possible”). Therefore, few studies have explored sex differences at moderate velocities of contraction, in this case 180º.$s^{-1}$. Our data support those of past studies showing that no sex differences exist in muscle fatigue during isokinetic exercise at slow velocities [25] and contrast with the findings of others focusing on moderate velocities [24, 29]. Wretling & Henriksson-Lársen (1998) found no differences between men and women in mechanical output following 150 knee-extension isokinetic contractions at 90º.$s^{-1}$. In contrast, Pincivero et al. (2000) found a sexually dimorphic pattern in peak work output favouring women after 30 maximal isokinetic knee-extensions performed at 180ºs.$^{-1}$. Unfortunately, the authors did not normalize their data to MVIC and this limits further interpretations. In another study, the same authors reported a higher rate of quadriceps femoris muscle fatigue in men than in women. Fatigue was calculated in response to 30 isokinetic knee-extensions at 180º.$s^{-1}$ using the modified fatigue index [24]. Accordingly, even though our methods were relatively similar to those of past reports (number of repetitions, angular velocity, isokinetic variable and fatigue quantification), we found no sex differences in fatigue index for PT or work output. We therefore provide evidence that the magnitude of MVIC reduction is not different between sexes after isokinetic exercise at 180ºs $^{-1}$ (moderate velocity). During contractions at 180ºs.$^{-1}$ vs. 60º.$s^{-1}$, the work-to-rest ratio decreases along with time under tension (concentric phase lasting 1.5 s at 60º.$s^{-1}$ and 0.5 s at 180ºs.$^{-1}$). Despite this, the physiological mechanisms that likely explain the onset of fatigue and absence of difference between men and women at 60º.$s^{-1}$ are possibly the same as those underlying such differences at 180º.$s^{-1}$ (i.e. decrement in maximal torque production).

Contrary to what has previously been reported in the literature, our data suggest that men are less fatigable than women during and after isokinetic exercise completed at an angular velocity of 300º.$s^{-1}$. Some studies reported that women exhibit less fatigue than men at high velocities of contraction for the knee extensors [7, 10], but not for the elbow flexors [10]. Our data show that men are more resistant than women during isokinetic exercise at 300º.$s^{-1}$ (7% less decrease in work output) and that they also experience an attenuated reduction in MVIC following this specific motor task (5.5% less fatigue). There is a great level of inconsistency between studies at this particular level and this is likely secondary to the methodological differences of past reports. For instance, in the study conducted by Senefeld et al. (2018), each isotonic contraction performed at maximal velocity was completed at 20% MVIC. Conversely, in our study all contractions were completed at maximal intensity in respect to each angular velocity, due to the isokinetic condition. Not surprisingly, our results contrast with the aforementioned study because, while women outperform men during low-intensity dynamic contractions potentially due to heightened vasodilatory response [30, 31], this state of enhanced blood supply to the working muscles cannot be sustained during maximal contractions [26]. Also, when asked to perform the task “as fast as possible”, the velocity of isotonic maximal concentric contractions is inevitably different between sexes. To our knowledge, this is the first study to explore sex differences in muscle fatigue using high-velocity isokinetic exercise. Because the concentric phase at 300º$s^{-1}$ only lasts 0.3 s, the greater fatigue resistance of men at this velocity is likely related with their ability to generate force at high velocities under a time constraint. In this case, the rate-limiting mechanisms of maximal velocity of fiber contraction (speed of cross-bridge cycling and $Ca^{2+}$ kinetics in the fiber) may well explain our findings [1]. It has been shown that the potentiation of twitch force in response to maximal muscle contraction is greater in men compared to women, irrespectively of age [32]. This corroborates the notion that men exhibit a greater increase in actin-myosin $Ca^{2+}$ sensitivity in response to high intensity muscle contractions [32]. Moreover, in women, contractile properties are typically characterized by longer half-relaxation time and lower evoked-twitch force than men [32, 33]. This slowing is consistent with women exhibiting a higher level of type I fibers [34] involved in torque production throughout the entire range of motion (work). The sexual dimorphism in phenotypic muscle fiber-type expression might explain why men were more capable of resisting fatigue during fast-velocity isokinetic contractions. This condition implicates the additional recruitment of high-threshold motor units, in which type II muscle fibers predominate (with higher rates of force production and relaxation) [3, 35]. It is possible to assume that the phenotypic traits associated with muscle fiber type expression in women might exert a negative impact in their ability to delay fatigue in response to high-velocity contractions. Since our data indicate a statistically significant sex difference in MVIC decrement of 5.5%, this may well be the case.

## pRTD, sequential RTD and ETorque

This is the first study that explored sex differences in RTD following the onset of fatigue resulting from isokinetic exercise performed at different velocities. Our data show that each velocity has a different impact in the ability to produce force rapidly. We also explored whether RTD is differently affected between sexes in response to each condition (velocity). We found that the fatigue-induced reduction of pRTD, sequential RTD and ETorque does not follow a sexually dimorphic pattern after isokinetic exercise performed at 60, 180 or 300º.$s^{-1}$. Importantly, this was sustained when data were analysed both in an absolute and normalized terms.

Explosive strength was here defined as the ability to increase force as quickly as possible during a fast voluntary contraction from a low or resting level [13]. Our findings are in accordance with those of Hannah et al. (2012), thus corroborating the concept that both sexes present a similar ability to express the available force-generating capacity, despite men outperform women in absolute values.

Neural determinants, intrinsic contractility and contractile capacity assume different preponderance during early and late stages of explosive force production [13, 16]. Previous studies examining explosive knee-extensor force production found that, in absolute terms, agonist electromyographic (EMG) activation greatly determines force production from the early to mid-phase of force production (up to ~ 50 ms) [13, 16]. Conversely, contractile properties more closely related with force production from 50 to 100 ms and MVIC largely determined force-generating capacity beyond 75 ms [16]. It is interesting to note that, despite both sexes exhibit a dissimilar reduction in MVIC and mechanical work output after completing high-velocity isokinetic exercise, this does not seem to impair fast force production to a different extent between men and women in either condition (post-30 repetitions at 60, 180 or 300º.$s^{-1}$). Previous studies have related the decline in explosive torque production with a reduction of EMG activity [16, 36]. Since agonist EMG is an important determinant of explosive torque [16], the lack of sex differences in neural activation following the completion of the fatiguing dynamic protocols may possibly explain why men and women have similar losses in pRTD, sequential RTD and ETorque, regardless of the contraction velocity.

## Post-exercise recovery

The present findings are in line with that reported in the existent literature supporting that women recover to a greater extent than men [7, 37]. However, this was only seen at moderate velocities. Women have consistently been shown to recover at a faster rate than men following isometric (sustained and intermittent) [7, 38] and dynamic contractions [7, 11]. Yet, the mechanisms of recovery differ depending on the type of contraction elicited during exercise. While central mechanisms of fatigability are more strongly associated with sexual dimorphism in recovery from isometric contractions, contractile mechanisms and differences in metabolic substrate largely explain why men recover slower than women following dynamic contractions [7]. These differences in metabolic substrate utilization resulting from muscle fatigue have been previously described by Kent-Braun et al. (2012). The authors found that during an exercise bout of increasing intensity, women have smaller increases in inorganic phosphate (Pi) and dihydrogen phosphate ($H_2PO_4^-$) and less decrease in intracellular pH than men [7, 32]. This indicates that women rely more on oxidative pathways for the supply of adenosine triphosphate for muscle contractions [39]. The greater accumulation of the aforementioned metabolic by-products (Pi, $H_2PO_4^-$, hydrogen ions ($H^+$)) in men most likely impairs their ability to recover faster because of a greater demand for metabolite clearance. However, our results do not reveal a sex difference in recovery at $60^\circ.s^{-1}$, and this is may be related to the greater extent to which both sexes fatigued on that particular condition, the limited time-course of recovery assessment (5-min post-exercise cessation) and the isokinetic condition per se.

# Perspectives And Significance

This is the first study to compare muscle fatigue and recovery between men and women following isokinetic exercise performed at different angular velocities. Our results show that young men and women fatigue to a similar extent during slow and moderate isokinetic velocities. In contrast, at high contraction velocities, there is a sex difference in muscle fatigue favouring men. Rate of torque development was similarly affected in both sexes across all conditions. In addition, women recovered at a faster rate than men when exercising at moderate isokinetic velocities, confirming previous results. These findings corroborate the notion that sexual dimorphism in muscle fatigue is dependent on the specificities of the motor task and on the velocity of contraction. We also provide an important insight into sex differences in neuromuscular function and fatiguing exercise. Specifically, it may be contended that men and women likely respond in a distinctive manner to training and rehabilitation for knee extension isokinetic conditions. In specific, according to our data, at higher velocities men have to perform more repetitions than women to achieve a certain level of fatigue. Conversely, women need less time to recover than men after moderate and fast isokinetic exercise. This urges for the need of a sex-based individualization of exercise prescription and recovery.

## Limitations

Our study has at least three important limitations. First, we did not control for the impact of the menstrual cycle on the outcome variables. There is little evidence that the menstrual cycle and related monthly fluctuations in sex hormones negatively impact performance in fatigability of young women [40]. Thus, we believe this limitation is unlikely to have affected our results. Second, the participants recruited for this study were students from a Sports Science Faculty. Some of them reported to be assiduous (although amateur) practitioners of activities that require fast and explosive knee-extension movements (e.g. soccer). However, the number of male and female practitioners in this experimental design was very similar and therefore we do not believe that this limitation affected the key aspects of our study. Third, we were unable to record surface EMG from the quadriceps femoris of the participants. The ability for maximal and explosive muscular contractions is highly dependent on the neural drive to the agonist muscles [16], and the presence or absence of sex differences in agonist EMG activation following isokinetic fatigue at different angular velocities could provide an insight into the potential mechanisms that may explain our results. Therefore, this is an important limitation to our study.

## Abbreviations

$Ca^{2+}$ Calcium

ETorque Explosive Torque

EMG Electromyography

$H^+$ Hydrogen ions

$H_2PO_4^-$ Dihydrogen phosphate

MVIC Maximum voluntary isometric contraction

PA Physical activity

Pi Inorganic phosphate

pRTD Peak rate of torque development

PT Peak torque

RTD Rate of torque development

# Declarations

### Ethics approval and consent to participate

Ethical approval for this study was obtained from Conselho de Ética da Faculdade de Motricidade Humana (CEFMH nº: 15/2019).

### Consent for publication

Not applicable.

### Availability of data and materials

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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### Author’s contributions

M.G., P.C. and G.V.M. conceived and designed the research. M.G. and P.S. conducted experiments. P.P.C. provided equipment for data collection. M.G, P.S. and P.C. analysed data. M.G., P.P.C. and G.V.M. wrote the manuscript. All authors read and approved the final manuscript.

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# References

1. Kent-Braun JA, Fitts RH, Christie A. Skeletal muscle fatigue. Compr Physiol. 2012;2:2:997-1044; doi:10.1002/cphy.c110029.
2. Dearth DJ, Umbel J, Hoffman RL, Russ DW, Wilson TE, Clark BC. Men and women exhibit a similar time to task failure for a sustained, submaximal elbow extensor contraction. Eur J Appl Physiol. 2010;108:6:1089-98; doi:10.1007/s00421-009-1323-z.
3. Hunter SK. The Relevance of Sex Differences in Performance Fatigability. Med Sci Sports Exerc. 2016;48:11:2247-56; doi:10.1249/MSS.0000000000000928.
4. Hunter SK. Sex differences in fatigability of dynamic contractions. Exp Physiol. 2016;101:2:250-5; doi:10.1113/EP085370.
5. Hunter SK, Critchlow A, Shin IS, Enoka RM. Fatigability of the elbow flexor muscles for a sustained submaximal contraction is similar in men and women matched for strength. J Appl Physiol (1985). 2004;96:1:195-202; doi:10.1152/japplphysiol.00893.2003.
6. Hill EC, Housh TJ, Smith CM, Cochrane KC, Jenkins NDM, Cramer JT, et al. Effect of sex on torque, recovery, EMG, and MMG responses to fatigue. J Musculoskelet Neuronal Interact. 2016;16:4:310-7.
7. Senefeld J, Pereira HM, Elliott N, Yoon T, Hunter SK. Sex Differences in Mechanisms of Recovery after Isometric and Dynamic Fatiguing Tasks. Med Sci Sports Exerc. 2018;50:5:1070-83; doi:10.1249/MSS.0000000000001537.
8. Mendonca GV, Borges A, Teodosio C, Matos P, Correia J, Vila-Cha C, et al. Muscle fatigue in response to low-load blood flow-restricted elbow-flexion exercise: are there any sex differences? Eur J Appl Physiol. 2018;118:10:2089-96; doi:10.1007/s00421-

018-3940-x.

9. Labarbera KE, Murphy BG, Laroche DP, Cook SB. Sex differences in blood flow restricted isotonic knee extensions to fatigue. J Sports Med Phys Fitness. 2013;53:4:444-52.
10. Senefeld J, Yoon T, Bement MH, Hunter SK. Fatigue and recovery from dynamic contractions in men and women differ for arm and leg muscles. Muscle Nerve. 2013;48:3:436-9; doi:10.1002/mus.23836.
11. Yoon T, Doyel R, Widule C, Hunter SK. Sex differences with aging in the fatigability of dynamic contractions. Exp Gerontol. 2015;70:1-10; doi:10.1016/j.exger.2015.07.001.
12. De Ste Croix MB, Deighan MA, Ratel S, Armstrong N. Age- and sex-associated differences in isokinetic knee muscle endurance between young children and adults. Appl Physiol Nutr Metab. 2009;34:4:725-31; doi:10.1139/h09-064.
13. Maffiuletti NA, Aagaard P, Blazevich AJ, Folland J, Tillin N, Duchateau J. Rate of force development: physiological and methodological considerations. Eur J Appl Physiol. 2016;116:6:1091-116; doi:10.1007/s00421-016-3346-6.
14. Hannah R, Minshull C, Buckthorpe MW, Folland JP. Explosive neuromuscular performance of males versus females. Exp Physiol. 2012;97:5:618-29; doi:10.1113/expphysiol.2011.063420.
15. Westh E, Kongsgaard M, Bojsen-Moller J, Aagaard P, Hansen M, Kjaer M, et al. Effect of habitual exercise on the structural and mechanical properties of human tendon, in vivo, in men and women. Scand J Med Sci Sports. 2008;18:1:23-30; doi:10.1111/j.1600-0838.2007.00638.x.
16. Buckthorpe M, Pain MT, Folland JP. Central fatigue contributes to the greater reductions in explosive than maximal strength with high-intensity fatigue. Exp Physiol. 2014;99:7:964-73; doi:10.1113/expphysiol.2013.075614.
17. Stofan JR, DiPietro L, Davis D, Kohl HW, 3rd, Blair SN. Physical activity patterns associated with cardiorespiratory fitness and reduced mortality: the Aerobics Center Longitudinal Study. Am J Public Health. 1998;88:12:1807-13; doi:10.2105/ajph.88.12.1807.
18. Elias LJ, Bryden MP, Bulman-Fleming MB. Footedness is a better predictor than is handedness of emotional lateralization. Neuropsychologia. 1998;36:1:37-43; doi:10.1016/s0028-3932(97)00107-3.
19. Pincivero DM, Salfetnikov Y, Campy RM, Coelho AJ. Angle- and gender-specific quadriceps femoris muscle recruitment and knee extensor torque. J Biomech. 2004;37:11:1689-97; doi:10.1016/j.jbiomech.2004.02.005.
20. Tredinnick TJ, Duncan PW. Reliability of measurements of concentric and eccentric isokinetic loading. Phys Ther. 1988;68:5:656-9; doi:10.1093/ptj/68.5.656.
21. Skurvydas A, Jurgelaitiene G, Kamandulis S, Mickeviciene D, Brazaitis M, Valanciene D, et al. What are the best isometric exercises of muscle potentiation? Eur J Appl Physiol. 2019;119:4:1029-39; doi:10.1007/s00421-019-04092-y.
22. Aagaard P, Simonsen EB, Andersen JL, Magnusson P, Dyhre-Poulsen P. Increased rate of force development and neural drive of human skeletal muscle following resistance training. J Appl Physiol (1985). 2002;93:4:1318-26; doi:10.1152/japplphysiol.00283.2002.
23. Valamtos M, Mil-Homens, P., Pinto, R. Avaliação Isocinética da Força. In: P. Pezarat Correia PM-H, G. V. Mendonça, editors. Treino da Força – Avaliação, Planemanento e Aplicações. Cruz Quebrada: Edições FMH; 2017. p. 39-62.
24. Pincivero DM, Gandaio CM, Ito Y. Gender-specific knee extensor torque, flexor torque, and muscle fatigue responses during maximal effort contractions. Eur J Appl Physiol. 2003;89:2:134-41; doi:10.1007/s00421-002-0739-5.
25. Wretling ML, Henriksson-Larsen K. Mechanical output and electromyographic parameters in males and females during fatiguing knee-extensions. Int J Sports Med. 1998;19:6:401-7; doi:10.1055/s-2007-971936.
26. Maughan RJ, Harmon M, Leiper JB, Sale D, Delman A. Endurance capacity of untrained males and females in isometric and dynamic muscular contractions. Eur J Appl Physiol Occup Physiol. 1986;55:4:395-400; doi:10.1007/BF00422739.
27. Li M, Larsson L. Force-generating capacity of human myosin isoforms extracted from single muscle fibre segments. J Physiol. 2010;588:Pt 24:5105-14; doi:10.1113/jphysiol.2010.199067.
28. Mendell LM. The size principle: a rule describing the recruitment of motoneurons. J Neurophysiol. 2005;93:6:3024-6; doi:10.1152/classicessays.00025.2005.
29. Pincivero D, Gear W, Sterner R, Karunakara RAJ. Gender Differences in the Relationship Between Quadriceps Work and Fatigue During High-Intensity Exercise. The Journal of Strength & Conditioning Research. 2000;14; doi:10.1519/00124278-200005000-

00014.

30. Kellawan JM, Johansson RE, Harrell JW, Sebranek JJ, Walker BJ, Eldridge MW, et al. Exercise vasodilation is greater in women: contributions of nitric oxide synthase and cyclooxygenase. Eur J Appl Physiol. 2015;115:8:1735-46; doi:10.1007/s00421-015-3160-6.
31. Parker BA, Smithmyer SL, Pelberg JA, Mishkin AD, Herr MD, Proctor DN. Sex differences in leg vasodilation during graded knee extensor exercise in young adults. J Appl Physiol (1985). 2007;103:5:1583-91; doi:10.1152/japplphysiol.00662.2007.
32. Kent-Braun JA, Ng AV, Doyle JW, Towse TF. Human skeletal muscle responses vary with age and gender during fatigue due to incremental isometric exercise. J Appl Physiol (1985). 2002;93:5:1813-23; doi:10.1152/japplphysiol.00091.2002.
33. Wust RC, Morse CI, de Haan A, Jones DA, Degens H. Sex differences in contractile properties and fatigue resistance of human skeletal muscle. Exp Physiol. 2008;93:7:843-50; doi:10.1113/expphysiol.2007.041764.
34. Jeon Y, Choi J, Kim HJ, Lee H, Lim JY, Choi SJ. Sex- and fiber-type-related contractile properties in human single muscle fiber. J Exerc Rehabil. 2019;15:4:537-45; doi:10.12965/jer.1938336.168.
35. Hoh JF. Muscle fiber types and function. Curr Opin Rheumatol. 1992;4:6:801-8.
36. Boccia G, Dardanello D, Tarperi C, Festa L, La Torre A, Pellegrini B, et al. Fatigue-induced dissociation between rate of force development and maximal force across repeated rapid contractions. Hum Mov Sci. 2017;54:267-75; doi:10.1016/j.humov.2017.05.016.
37. Fulco CS, Rock PB, Muza SR, Lammi E, Cymerman A, Butterfield G, et al. Slower fatigue and faster recovery of the adductor pollicis muscle in women matched for strength with men. Acta Physiol Scand. 1999;167:3:233-9; doi:10.1046/j.1365-201x.1999.00613.x.
38. Hill EC, Housh TJ, Smith CM, Schmidt RJ, Johnson GO. Gender- and Muscle-Specific Responses During Fatiguing Exercise. J Strength Cond Res. 2018;32:5:1471-8; doi:10.1519/JSC.0000000000001996.
39. Hicks AL, Kent-Braun J, Ditor DS. Sex differences in human skeletal muscle fatigue. Exerc Sport Sci Rev. 2001;29:3:109-12; doi:10.1097/00003677-200107000-00004.
40. Janse de Jonge XA. Effects of the menstrual cycle on exercise performance. Sports Med. 2003;33:11:833-51; doi:10.2165/00007256-200333110-00004.

## Figures

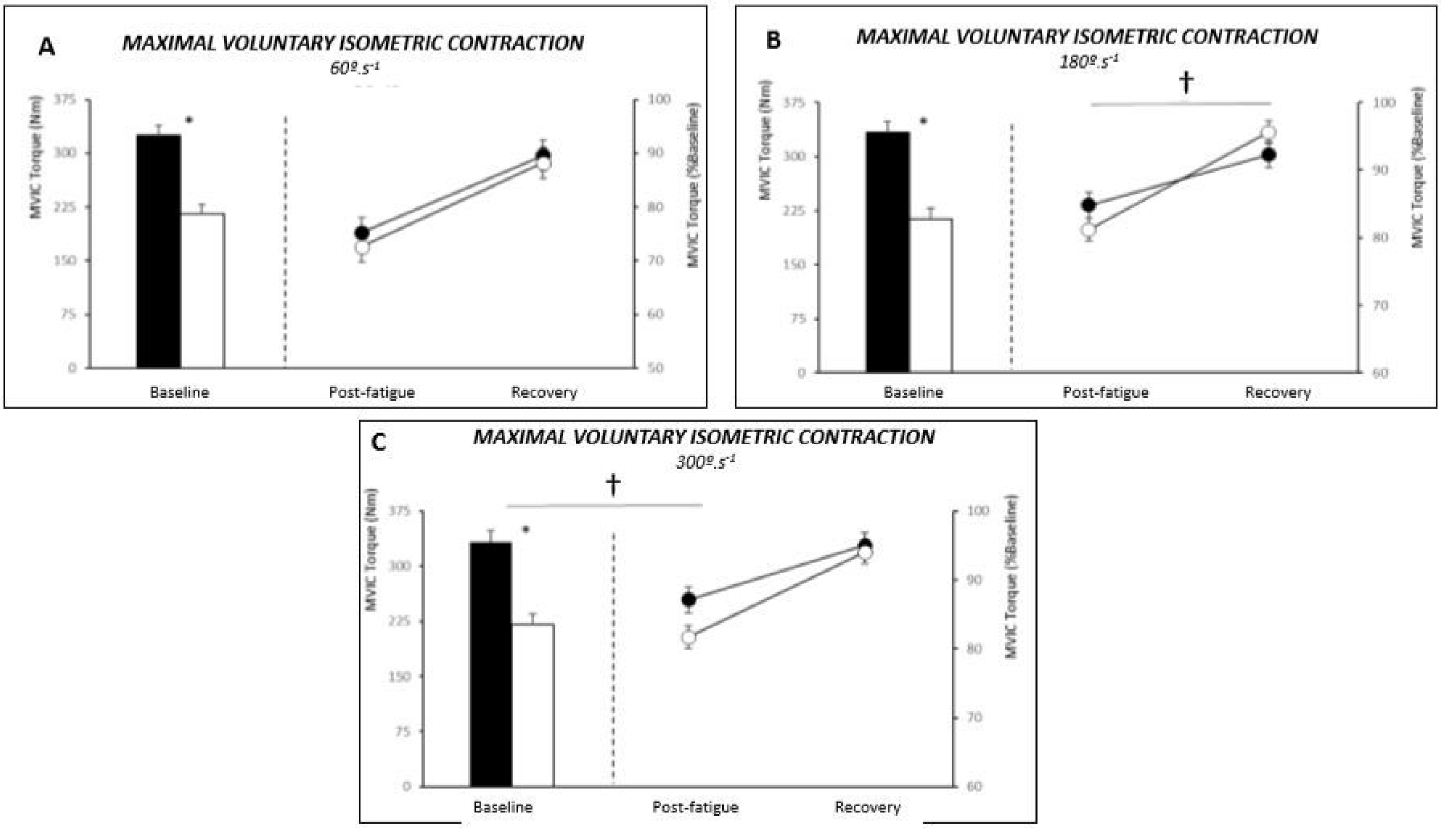
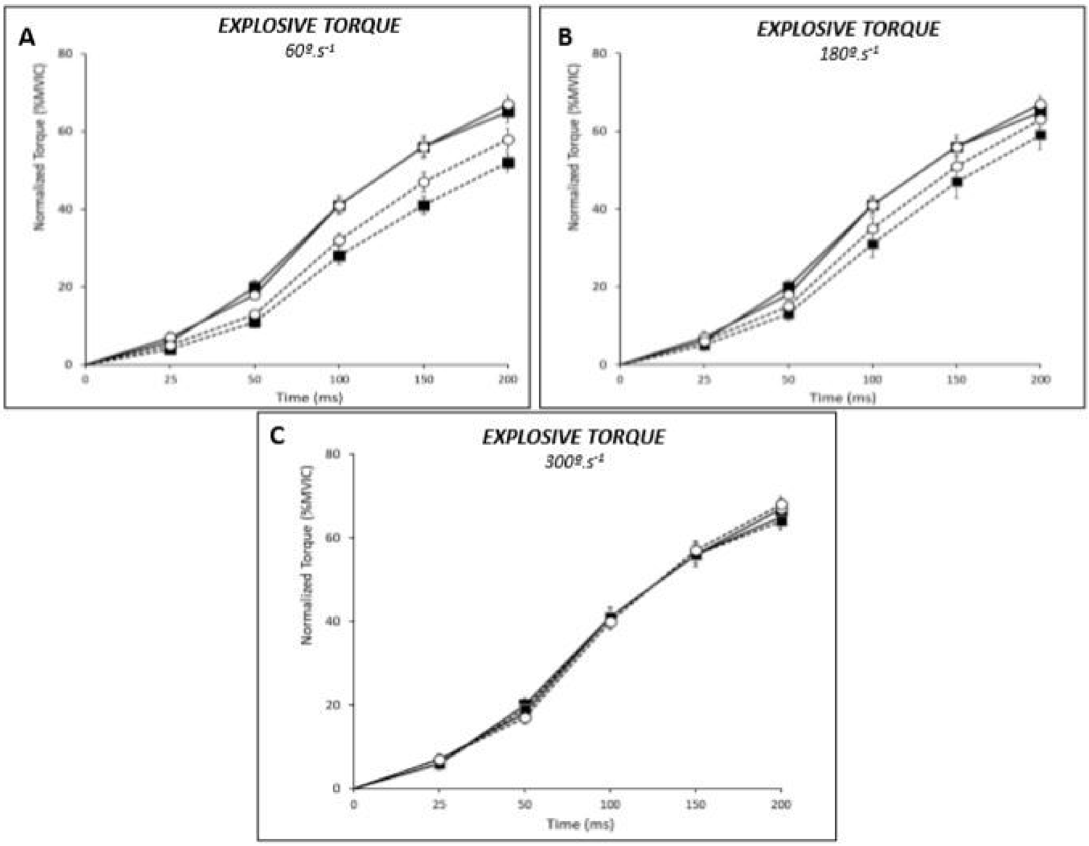


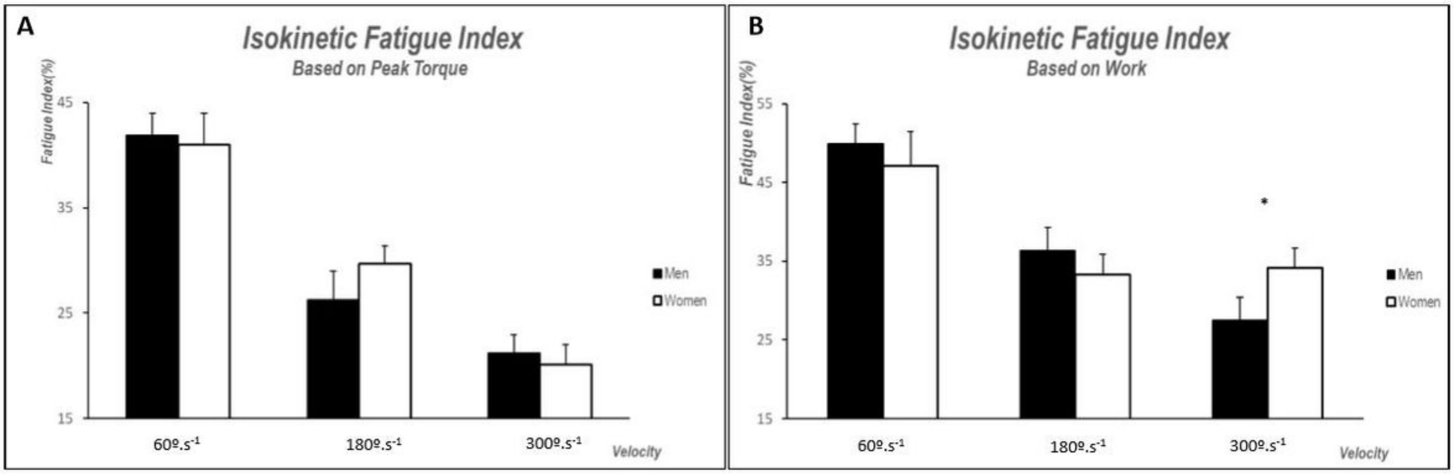
**Figure 1**

Maximal voluntary isometric contraction (MVIC) at pre-, post-exercise and during recovery from isokinetic knee-extensions performed in each condition (A: 60º.s-1; B: 180º.s-1; C: 300º.s-1). Men are represented by the black (filled) bars and circles and women by the white and open bars and circles. Baseline, measurements were taken before exercise; post-fatigue.1 measurements were taken immediately after exercise and Post-fatigue.5 measurements were taken 5 min after exercise cessation. *Sex difference at specific time-point ($p < 0.05$); † sex difference in the delta between time-points (fatigue or recovery) ($p<0.05$)



## Figure 2

Comparison of explosive torque between men and women from pre- to post-exercise in each condition (A: 60º.s-1; B: 180º.s-1; C: 300º.s-1). Men are represented by the black (filled) squares and women by the white circles. Pre- exercise data are represented by the continuous line and post-exercise data are represented by the dash line. MVIC, maximal voluntary isometric contraction



## Figure 3

Isokinetic fatigue index based on peak torque (A) and work output (B). Men are represented by the black (filled) bars and women by the white bars. *Sex difference at ($p < 0.05$)