Women show similar central and peripheral fatigue to men after half-marathon*

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(Article begins on next page)
Women show similar central and peripheral fatigue to men after half-marathon

ABSTRACT

Purpose: Women are known to be less fatigable than men in single joint exercises, but fatigue induced by running has not been well understood. Here we investigated sex differences in central and peripheral fatigue and in rate of force development (RFD) in the knee extensors after a half-marathon run.

Methods: Ten male and eight female amateur runners (aged 25 to 50 years) were evaluated before and immediately after a half-marathon race. Knee extensors forces were obtained under voluntary and electrically evoked isometric contractions. Maximal voluntary isometric contraction (MVC) force and peak RFD were recorded. Electrically doublet stimuli were delivered during the MVC and at rest to calculate the level of voluntary activation and the resting doublet twitch.

Results: After the race, decreases in MVC force (males: -11%, effect size (ES) 0.52; females: -11% ES 0.33), voluntary activation (males: -6%, ES 0.87; females: -4%, ES 0.72), and resting doublet twitch (males: -6%, ES 0.34; females: -8%, ES 0.30) were found to be similar between males and females. The decrease in peak RFD was found to be similar between males and females (males: -14%, ES 0.43; females: -15%, ES 0.14).

Conclusions: Half-marathon run induced both central and peripheral fatigue, without any difference between men and women. The maximal and explosive strength loss was found similar between sexes. Together, these findings do not support the need for sex-specific training interventions to increase the tolerance to neuromuscular fatigue in half-marathoners.

- Women are known to be less fatigable than men in single-joint exercises, but it still not clear if this is valid in running as well.
- We investigated the origins and effects of fatigue induced on knee extensors by a half-marathon race on male and female amateur runners.
- The loss of maximal strength and rate of force development was found to be similar between men and women. These force capacity reductions were associated with central and peripheral fatigue, without any difference between men and women.
- On the basis of these results, there is not a need for sex-specific training interventions focused on the tolerance of neuromuscular fatigue in half-marathoners.

Keywords:
Neuromuscular fatigue; explosive strength; sex differences; endurance running.
INTRODUCTION

Muscle fatigue can be defined as an exercise-induced decrease in the capacity to generate force (Gandevia, 2001). The mechanisms of muscle fatigue can be broadly separated into central (i.e. within the central nervous system) and peripheral (i.e. within the muscle) components. Central fatigue reflects a reduction in voluntary activation (VA) (Gandevia, 2001). Peripheral fatigue refers to the processes occurring at (or distal to) the neuromuscular junction and reflects a reduction of sarcolemma excitability, contractile properties, and excitation-contraction coupling (Allen, Lamb, & Westerblad, 2008). The extent to which peripheral and central processes contribute to fatigue is dependent on the nature, the duration, and the intensity of the exercise task. In general, the available literature suggests that higher-intensity, shorter duration exercise is primarily limited by peripheral fatigue and central fatigue is exacerbated as the exercise bout is prolonged (Lepers, Maffiuletti, Rochette, Brugniaux, & Millet, 2002; Place, Lepers, Deley, & Millet, 2004; Thomas et al., 2015).

Over the past years several studies have measured muscle fatigue (defined as decrease in muscle force) induced by prolonged level and graded running (Giandolini et al., 2016; Millet & Lepers, 2004; Place, Yamada, Bruton, & Westerblad, 2010). In general, strength loss increases non-linearly with duration of exercises (Giandolini et al., 2016; Millet & Lepers, 2004; Place et al., 2010). For example, mean strength loss was found to be 15% after a 20 km laboratory time trial (Ross, Goodall, Stevens, & Harris, 2010), 22% after an official marathon (42.195 km)(Petersen, Hansen, Aagaard, & Madsen, 2007), and 40% after a 24 h laboratory time trial (Martin et al., 2010). Even though the half marathon (21.097 km) run is even more popular than marathon race (Knechtle et al., 2014), to date no data are available for fatigue induced by running this distance.

Most of the research investigating the influence of fatigue induced by prolonged running on force capacity has focused on the decline in maximal voluntary contraction (MVC) force (MVCF) (Millet & Lepers, 2004). However, the effect of fatigue on the ability to produce force rapidly, also referred to as explosive strength, has received less attention despite its importance for the production of force in running. The rate of force development (RFD) calculated over the first 150 ms of contraction is considered functionally more informative than MVCF (Maffiuletti et al., 2016). RFD reflects indeed the ability to quickly increase muscle force during a rapid voluntary contraction starting from a low level of force or from rest. In endurance running, the vertical ground reaction force quickly increases from foot strike to the first peak in less than 100-150 (Bigouette, Simon, Liu, & Docherty, 2016; Kluitenberg, Bredeweg, Zijlstra, Zijlstra, & Buist, 2012). In this short time, the loading rate is controlled by knee extensors muscles that act rapidly to absorb the shock of the impact (Novacheck, 1998). Thus, when muscle fatigue impairs the capacity to increase force rapidly (Buckthorpe, Pain, & Folland, 2014) running performances could be negatively influenced (Maffiuletti et al., 2016; Rodriguez-Rosell, Pareja-Blanco, Aagaard, & Gonzalez-Badillo, 2017). Remarkably, both central and peripheral mechanisms appeared to contribute to impaired RFD after fatiguing exercise (Boccia et al., 2016; Buckthorpe et al., 2014; Penailillo, Blazevich, Numazawa, & Nosaka, 2015). Recently, we demonstrated that the relationship between MVCF and RFD impairment induced by prolonged running may not be straightforward (Boccia et al., 2017).

It is recognised that women are less fatigable than men for sustained and intermittent isometric contractions at the same relative intensity (Hunter, 2014). It has been suggested that the
proportion of fatigue attributable to peripheral and central mechanisms may vary between males and females (Hunter, 2014). Nevertheless, most studies which have evaluated the sex differences in fatigability have been based on single-joint tasks (Hunter, 2016; Senefeld, Pereira, Elliott, Yoon, & Hunter, 2018). Findings from single-joint protocols may not be applicable to the type of fatigue experienced by endurance athletes in racing situations such as cycling and running (Hunter, 2016; Marongiu & Crisafulli, 2015). Indeed, during locomotor exercises, muscles contract at relatively low intensity, over the course of many hours, are likely to deplete glycogen stores, and the exercise is not associated with the occlusion of blood flow seen in high intensity contraction (Place et al., 2010). There is a scarcity of studies that examine sex differences in the origins of fatigue, i.e., central versus peripheral, during prolonged endurance exercise. Recently, Temesi and colleagues (2015) showed that after 110-km ultra-trail-running race the females showed lower strength loss in knee extensors, but with similar central and peripheral fatigue. To the best of the authors’ knowledge, no studies are available showing sex differences in shorter level running races, particularly a half-marathon. It is worth noting that female amateur runners are less likely to slow down during a marathon compared to their male counterpart (Deaner, Carter, Joyner, & Hunter, 2015). This difference may be driven by subtle changes of muscular fatigue throughout the race (Hunter, 2016).

Thus, the primary aim of this study was to quantify the central and peripheral fatigue induced by a half-marathon run. We hypothesized that a half-marathon race would induce a substantial central and peripheral fatigue. The secondary aim of the study was to investigate sex differences in neuromuscular fatigue induced by half-marathon. We hypothesized that neuromuscular fatigue would be lower in women than in men. We furthermore hypothesized that this difference may be caused by lower peripheral fatigue as suggested for single joint exercises.

**METHODS**

**General overview**

The study was performed during a specific initiative called Run For Science, hosted by the University of Verona (Italy) in April 2015, for details see (Lippi & Schena, 2017). In this initiative participants competed in a half-marathon with official athletic federation timing. The days before and after the event the amateur athletes underwent anthropometric, biomechanical, physiological, and biochemical testing performed by different scientific groups (Lippi & Schena, 2017). Each athlete participates in only one scientific project. Start waves were assigned to participants based on the estimated race time, to avoid many participants arriving simultaneously in a testing station.

In this particular study, the assessments consisted in a series of voluntary and electrically evoked contractions of the knee extensors. Participants were involved in two measurement sessions: the first was performed the day before the race (PRE), and the second immediately after the race (POST). During this first session, participants were familiarised with the MVC and muscle electrical stimulation procedures. For that purpose, participants repeated a two or three trials of the test procedures until they were able to produce consistent results. The optimal placements of stimulation electrodes over the muscles were found during this session. In the PRE session participants performed 15 min of standardised warm-up (details are given below) before neuromuscular testing. In the POST session the neuromuscular assessment started within 7 – 15 minutes after the race. A researcher was positioned at the finishing line to conduct the runners to the
testing site, which was located about 50 m from the finishing line. The testing session at POST lasted about 6 minutes.

Participants

For this study 21 amateur runners (11 males and 10 females, age 36±8, body mass 74±10 kg, height 1.73±0.08 m) were recruited. This sample size is in accordance with previous studies on neuromuscular fatigue using similar measurement techniques (Glace, Kremenic, & McHugh, 2013; Temesi et al., 2015). Participants were recruited through printed and electronic media, advertising the possibility to be a subject for scientific study within the event Run for Science, for details see (Lippi & Schena, 2017). Inclusion criteria were to be regularly engaged in recreational running (mean training regimen of 220 min/week), to have finished a half-marathon in the previous two years, and to be free from clinical evidences of cardiovascular, neuromuscular, or joint diseases. Participants were instructed to refrain from performing strenuous physical activity in the 24 h before the first experimental session. All participants provided their written informed consent before participation in the experiments. The study was approved by the local Ethical Committee (Department of Neurological and Movement Sciences, University of Verona) and performed in accordance with the Helsinki Declaration.

The warm-up at PRE consisted of 15-min of outdoor running at an incremental intensity from 75% to 90% of the predicted maximal heart rate. The duration of the warm-up was chosen based on previous studies showing that muscle temperature rises rapidly after 5 min and reaches an equilibrium after 15 min (Bishop, 2003). Immediately after the warm-up, as well as after the race, the oral temperature was measured using single-use chemical thermometer (tempa.DOT, 3M, Minnesota, USA) to control the core temperature (Van den Bruel, Aertgeerts, De Boeck, & Buntinx, 2005).

Set-up

Participants were seated on a custom-made chair that allowed the assessment of the knee extensors, and straps were fastened across the chest and hips to avoid undesired lateral and frontal trunk displacements. During the testing, participants’ knee and hip were flexed at 90° from full extension and they were instructed to maintain the arms crossed on the chest. The knee extensors mechanical response was recorded with a strain gauge load cell (546QD- 220kg; DSEurope, Milan, Italy), fixed with non-compliant straps level with the external malleolus. All measurements were taken from the participants’ right limbs (which was the dominant limb for 19 out of 21 participants). The force signals were sampled at 2048 Hz, low-pass filtered with a cut-off frequency of 20 Hz, and converted to digital data with a 12-bit A/D converter (EMG-USB, OT Bioelettronica, Turin, Italy).

Procedure

RFD measurements were obtained during two short (< 1 s) isometric MVCs, with a 1-min rest between contractions. The participants were instructed to contract their muscles as fast and hard as possible. Great emphasis was therefore given to the velocity of muscle contraction. Visual feedback of the force output signal was provided as a real-time display on a computer screen. If any countermovement was evident on force signal to the operator, the measurements were rejected and an additional MVC was measured.
One minute after the second MVC, two further MVCs with superimposed supramaximal doublet, that is paired stimuli at high stimulation frequency (100 Hz, 10 ms inter-stimulus interval), were performed. During these contraction participants were requested to reach their MVC progressively and maintain the maximal contraction for almost 3 s. The electrical doublet stimulation was delivered during the isometric force plateau. Electrically induced doublet during MVC produced an interpolated twitch. Two other doublet stimulations were then delivered to the relaxed muscle. One in a potentiated state (within 2 s after the contraction) to generate a resting doublet twitch (Db100) and another one 5 s later at low stimulation frequency (10 Hz, 100 ms interstimulus interval, Db10). The set of voluntary and electrically evoked contraction (MVC + interpolated doublet; doublet at 100 Hz; doublet at 10 Hz) was repeated twice with 1 min of rest between sets.

**Electrical stimulation**

Electrical stimulations were applied percutaneously to the muscles via self-adhesive electrodes. Two aluminium foil electrode pads (5 x 10 cm in size) coated with conductive gel were customised to each subject. The cathode was placed over the proximal section of the quadriceps muscle, and the anode was placed over the distal part of the quadriceps muscle. A constant current stimulator (Digitimer DS7A, Hertfordshire, United Kingdom) was used to deliver a square-wave stimulus of 1 ms duration with maximal voltage of 400 V. To ensure that stimulation was primarily to the tested muscle, electrically evoked single stimulations were progressively increased in stimulation intensity at the start of the testing procedure until the resting twitch reached a plateau. If the resting twitch force decreased with an increase in stimulation intensity, the electrode pads were repositioned, or a different size of electrode was used until a plateau in resting twitch was achieved with increasing stimulation intensity. The stimulation intensity (range: 120 – 300 mA) was then increased by 15% to assure supramaximal stimulus (115% of optimal intensity) and kept constant throughout the experiment. The position of the electrodes was marked on the skin with an indelible marker so that they could be located in the same place after the race.

**Data analysis**

All data were analysed by custom-written software in MATLAB R2014a (Mathworks, Natick, Massachusetts). The onset of force production was visually defined by an operator blinded to the condition. If a countermovement, i.e. a visible drop in force, was performed before the force onset, the contraction was discarded from the analysis of RFD. Peak of RFD (RFD\text{peak}) was determined using a moving 20-ms window throughout the force-time curve as the highest RFD value at any time during the contraction. The RFD were quantified in absolute terms (N/s) and normalized to the maximal force (relative RFD\text{peak}) recorded within the same contraction (%/s).

The amplitude of the resting doublet twitches (Db100 and Db10) were analysed and the average values computed from the two sets was considered. The level of VA during each MVC was calculated as VA(%)=100(1 – interpolated doublet/doublet)×100 (Merton, 1954). A correction was consistently applied to this equation when the superimposed doublet was elicited slightly before or after the actual peak force during a MVC (Strojnik & Komi, 1998). The Db10:Db100 ratio was used as a surrogate measure of low-frequency fatigue, which is usually associated with a failure in the excitation-contraction coupling (Millet, Martin, Martin, & Verges, 2011; Verges et al., 2009).
Statistical analysis

Data are presented as mean ± standard deviation (SD). Kolmogorov-Smirnov normality test was used to assess distributions normality. If the data were not normally distributed were log-transformed before statistical analysis and back-transformed to obtain descriptive statistics. Data were assessed for practical significance using a magnitude-based inferences approach (Batterham & Hopkins, 2006; Hopkins & Batterham, 2016), on a modified statistical spreadsheet (Hopkins, 2006). Standardized differences \( d \) were calculated using the pooled data PRE SDs (Cohen, 1988), and the precision of estimates was indicated with 90% confidence limits (CL). Threshold values for the magnitude of difference were: \( \leq 0.2 \), trivial; \( > 0.2 \), small; \( > 0.6 \), moderate; \( > 1.2 \), large; \( > 2.0 \), very large (Batterham & Hopkins, 2006). For between-sex comparisons, the chances that the (true) changes for females were greater than the smallest practically important effect, or the smallest worthwhile change (0.2 × the between-subject SD), unclear or smaller than these for the males were calculated. When the effect size (ES) crossed the threshold of ±0.2 the difference was deemed unclear. Otherwise, we interpreted that change as the observed chance (Batterham & Hopkins, 2006).

RESULTS

Out of the 21 initially recruited participants, three (one male and two females) did not perform the POST session because they dropped out of the race. Thus, data are reported for 18 participants (10 males and 8 females). The race time was largely shorter for males 1h42±15 min than for females 1h58min±13 min. The oral temperature was not different from PRE (36.5±0.5 °C) to POST (36.7±0.8 °C).

Table 1 reports the PRE and POST values and the statistics for both groups. Figure 1 briefly shows the percent (mean±SD) decrements from PRE to POST. In general, the maximal force showed a small decrease in both groups, however the ES of the decrease was possibly lower in females. Voluntary activation showed a moderate decreased in both groups. The decrease of Db10 was small in both groups and the decrease in Db10:Db100 was large in both groups. The decrease of all these variables was not different between groups.

The decrease in RFD\(_{\text{peak}}\) was similar between males and females. On the contrary the decrease in relRFD\(_{\text{peak}}\) was possibly more pronounced in females (small decrease) than in males (trivial decrease).

DISCUSSION

The main purpose of this study was to explore the origins and effects of fatigue induced on knee extensors by a half-marathon race on male and female amateur runners. The race induced a small loss of maximal force in both males and females, and a small decrease in the rate of force development. These force capacity reductions were associated with central and peripheral fatigue. However, the origin of fatigue seemed to be independent of sex. The main innovation of this study was the assessment of the origins of fatigue induced by a popular type of running event, the half-
marathon. Moreover, the measurements performed in an actual race allowed the study of fatigue in an ecological setting and ensured that participants were very motivated to perform optimally over the distance. Finally, focusing the attention on the effects of fatigue on the capacity to quickly increase force, rather than producing maximal force, increased the meaningful of the study.

After the half-marathon the maximal force showed a small decrease (≈11%) in both groups, confirming that the prolonged running induced fatigue in knee extensor muscles. The decrease in maximal force is a common finding after endurance running in actual race conditions (Giandolini et al., 2016; Millet & Lepers, 2004; Place et al., 2010). The amount of maximal force loss varies between 10 – 40 % depending on the details of the task and on the delay between the end of exercise and the force measurement (Place et al., 2010; Temesi et al., 2015). The maximal force loss recorded in this study is found near the lower bound of the range reported by the literature (≈11%) (Place et al., 2010; Temesi et al., 2015). This is an expected result since the previous studies that reported more pronounced strength loss have investigated running races of longer distance: -22% of maximal force was recorded after a marathon race (42.2 km) (Petersen et al., 2007); -24% after 30 km running race (Millet, Martin, Lattier, & Ballay, 2003); -30% after 65 km running race (Millet et al., 2002); -37% after 55 km running race (Gaque et al., 2006). The comparison with other available laboratory based studies are difficult because the time delay between the end of exercise and the measurements is much lower in laboratory (1-3 min) with respect to a real competition setting (5-20 min)(Place et al., 2010). During this period the recovery process occurs and thus the extent of muscle fatigue may be underestimated in actual race than in laboratory based settings (Place et al., 2010).

Our results did not show clear difference between women and men in muscle fatigue, defined as maximal force loss. On the basis of this finding, which rely on a small group of recreational runners, the hypothesis that women may be more fatigue resistant than men cannot be supported. In a study of comparable duration but different task, i.e. 2 h of cycling, Glace and colleagues (2013) showed that the knee extensors strength loss was similar between women and men. On the contrary, Temesi and colleagues (2015) found that the fatigue induced by 110 km of trail running was greater for men than women in the knee extensors (but similar between groups in plantar flexor muscles). However, the extreme duration and challenge of ultra-trail races may be less applicable to shorter distance running. In another study based on repeated sprint cycling, greater fatigue recorded in men was likely to be a consequence of their greater absolute initial-sprint performance, rather than a sex difference in fatigue resistance per se (Billaud & Bishop, 2012).

Together, these findings suggest that women do not experience less muscle fatigue than men in whole body endurance exercise (e.g. < 2 h duration), contrary to what occurs in single joint exercises (Hunter, 2014). However, the scarcity of research on muscle fatigue induced by whole body exercise cannot allow to draw a definitive conclusion.

The half marathon induced a trivial-small decrease in the peak RFD both in women and men (13 – 14%). This finding indicated that prolonged running impaired the force capacity in early phase of muscle contraction, that is the phase of force raising. This is an original finding since most previous studies investigating the effects running-induced fatigue on muscle force, focused mainly on the maximal aspect of force, i.e. the plateau (Giandolini et al., 2016; Millet & Lepers, 2004; Place et al., 2010). However, investigating the force rising phase of muscle contraction is functionally important (Maffiuletti et al., 2016). Indeed, runners must repeatedly cope with the transient of the vertical ground reaction force within the first 100-150 ms of stance (Lieberman et
al., 2010), which is much less than the time needed to reach the maximal force during voluntary contraction (>300ms) (Maffioletti et al., 2016). Thus, the impaired capacity of muscle force production in the early phase of contraction could have consistently affected the running mechanics during the race by decreasing the available force during the early part of stance. Few studies found that contact time increases during the course of prolonged running (Chan-Roper, Hunter, J, D, & M, 2012; Schena et al., 2014), this may be possibly induced by lower capacity to generate force quickly. However, whether a small-trivial decrease in knee extensors RFD is a meaningful change, and can thus generate an impairment in the profile of ground reaction force is still to be determined (Zadpoor & Nikooyan, 2012) and it is beyond the possibility of this study. Future research should address this gap by measuring both knee extensors RFD and ground reaction force and leg stiffness in fatigued runners. Even if the trivial-small decrease in RFD might seem a negligible change, it must be noted that the delay between the end of the race and testing procedures likely allowed for a partial recovery of RFD (see methodological limitations later). Thus, the impairment in RFD at the end of the race, when this RFD possibly influenced most the running mechanics, was likely larger than that herein reported.

The decrement in RFD was not different between sexes, suggesting that the running performance of men was similarly impaired compared to women. However, when we compared the relative RFD, i.e. when RFD is normalized to maximal force, a possibly greater reduction was recorded in women (≈11%, small) than men (≈2%, trivial). Consequently, the decrease in relative RFD in women cannot be explained on the basis of a lower maximal force, but it was specific alteration of the explosive phase of contraction. However, the running mechanics is possibly more influenced by actual absolute rather than relative RFD capacity. Overall, these findings highlight the importance of assess the raising phase of muscle contraction when testing neuromuscular fatigue in runners.

Men and women runners underwent similar moderate decrease of voluntary activation (≈4-6%), indicating a comparable reduced capacity to voluntarily activate the knee extensors. Central fatigue could reflect the existence of a common central mechanism aimed at reducing neural drive to the working muscles to limit the level of exhaustion (Millet et al., 2002). It may nevertheless be activated at spinal level or by peripheral feedback from the muscle (Taylor, Todd, & Gandevia, 2006). Central fatigue is widely reported in endurance events and is overall greater for bouts of long-duration exercise (>2 h) than for shorter, more intense bouts of Martin et al., 2010; Millet & Lepers, 2004; Millet, Tomazin, et al., 2011). However, the evidence of central fatigue in the present study confirm the possible presence of this mechanism also in exercises rather shorter than 2 h (Ross et al., 2010). The lack of differences between the magnitude of central fatigue between the two groups is in accordance with two previous studies that showed similar central fatigue in males and females after prolonged 110 km of trail running (Temesi et al., 2015) and 2 h of cycling (Glace et al., 2013). Furthermore, since we did not found difference in maximal force loss, the non-different central fatigue was a convincing result.

Both men and women presented small amount of peripheral fatigue, as indicated by the decrease in the double twitch amplitude of about 6-8%. The reduction in electrically evoked force can be attributed to muscle excitability or to the impairment of the excitation-contraction coupling mechanism (Bellinger et al., 2008; Place et al., 2010). Since we did not measure the electromyographic responses to electrically elicited stimulation we cannot distinguish between these two mechanisms. However, since the amount of low-frequency fatigue (Db10:Db100, ≈7-10%) was
similar to that of twitch amplitude, we can speculate that the failure of excitation-contraction coupling was the main contributor to peripheral fatigue. The amount of peripheral fatigue found in this study was similar to that previously reported after 30 km running race (≈9%). Even more pronounced peripheral fatigue (≈18-20%) was recorded after longer duration running (>65 km) (Millet et al., 2002; Place et al., 2004).

Regarding sex comparison in peripheral fatigue, men and women showed similar outcome in our study. The literature about that is scarce and partly conflicting. Temesi and colleagues (Temesi et al., 2015), did not found statistically significant difference in signs of peripheral fatigue of knee extensors after a 110 km trail running, but they found greater peripheral fatigue in men than women in plantar flexors. Whereas Glace and colleagues (Glace et al., 2013) after 2 h of cycling found signs of peripheral fatigue only in men but not in women. Thus, more research is needed to clarify if females are more resistant to the peripheral fatigue than males during whole body endurance exercise.

Overall, our results did not support the hypothesis of different origins of fatigue on male compared to female runners (Hunter, 2014). Nevertheless, numerous studies have suggested that the proportion of fatigue attributable to peripheral and central mechanisms may vary between men and women (Hunter, Butler, Todd, Gandevia, & Taylor, 2006). However, the sex difference in fatigability differ according to the contraction type, speed and intensity, the involved muscle group, and environmental conditions (Hunter, 2009). It is worth noting that much of the previous work investigating peripheral versus central mechanisms of fatigue used protocols based on single joint contractions with relatively high intensity and short duration (Hunter, 2014). Differently, in endurance exercise, thousands of contractions are performed at low intensities, and the mechanisms leading to fatigue may be different from those mechanisms which contribute to fatigue during exercise requiring orders of magnitude fewer shortening cycles (Glace et al., 2013). Thus, we advocate that more studies are needed to assess possible sex-differences in neuromuscular fatigue during endurance exercises.

The main limitation of the study are the small sample sizes, especially for women (N=8). Thus, future research on this topic are warranted to increase the sample size and the precision of the estimates. The methodological limitations of this study are the followings. First, the delay (7 – 15 minutes) between the end of the race and the beginning of the testing in this study probably allowed a partial recovery of both central fatigue (Gruet et al., 2014), and peripheral fatigue (Froyd, Millet, & Noakes, 2013). Indeed, it has been shown that substantial central and peripheral recovery occurs in the first 1-2 minutes after task completion. Thus, the central and peripheral fatigue at the end of the race, that is when fatigue possibly influenced most the running performance, were likely greater than that recorded in the measurements. As a consequence, the impairment that we found in maximal strength and RFD were likely underestimated as well. Second, for practical reasons we did not measure the electromyographic responses during voluntary and elicited contractions. This lack partially lessens the possibility to distinguish between muscle excitability and failure in excitation-contraction coupling.

**PRACTICAL APPLICATIONS AND CONCLUSIONS**

These findings demonstrate that amateur male and female runners experienced moderate central and small peripheral fatigue during a half-marathon race. Since the amount of fatigue was
similar between men and women, sex-specific interventions to delay or attenuate fatigue cannot be supported on the basis of these results. Furthermore, after the race runners showed a decrease in the peak rate of force development. However, also in this case the impairment was similar between sexes. Thus, on the basis of these results, there is not a need for sex-specific training interventions focused on the tolerance of rapid contraction.

Future research should increase the sample size of this study and expand on other muscle group than can affect running mechanics, such as the plantar flexors. Moreover, the fatigue-induced decline in rate of force development should be compared with the consistency of absorbing ground impacts, in order to assess the relevance of rate of force development on long-distance running mechanics.

REFERENCES


Figure Caption

**Figure 1.** Percentage changes of neuromuscular variables measured PRE vs POST half marathon run in males and females. Magnitude based statistics are reported in Table 1. MVC, maximal voluntary contraction force; VA, voluntary activation; Db100, twitch evoked by the doublet at 100 Hz; Db10:Db100, ratio between the twitches evoked with doublets at 10 to 100 Hz; RFDpeak, peak of rate of force development.
Table 1 – Magnitude based statistics of PRE vs POST comparisons

<table>
<thead>
<tr>
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<th>Males</th>
<th>Females</th>
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<tr>
<td></td>
<td>PRE</td>
<td>POST</td>
<td>PRE vs POST (%)</td>
<td>PRE</td>
<td>POST</td>
<td>PRE vs POST (%)</td>
<td>PRE</td>
<td>POST</td>
<td>PRE vs POST (%)</td>
<td>PRE vs POST (%)</td>
<td>Difference between sex (d)</td>
<td>% chances (negative/trivial/positive)</td>
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<tr>
<td>MVCF (N)</td>
<td>345±84</td>
<td>304±79</td>
<td>-11±6</td>
<td>221±39</td>
<td>196±35</td>
<td>-11±7</td>
<td>-0.33±0.20</td>
<td>0.20±0.22</td>
<td>0/50/50</td>
<td>Possibly positive</td>
<td></td>
<td></td>
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<tr>
<td>VA (%)</td>
<td>87±6</td>
<td>82±8</td>
<td>-6±6</td>
<td>93±7</td>
<td>89±10</td>
<td>-4±5</td>
<td>-0.72±0.82</td>
<td>0.16±0.74</td>
<td>46/33/21</td>
<td>Unclear</td>
<td></td>
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<tr>
<td>Db100 (N)</td>
<td>127±23</td>
<td>119±31</td>
<td>-6±15</td>
<td>84±11</td>
<td>76±12</td>
<td>-8±7</td>
<td>-0.30±0.28</td>
<td>0.04±0.50</td>
<td>21/50/29</td>
<td>Unclear</td>
<td></td>
<td></td>
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<tr>
<td>Db10:Db100 (%)</td>
<td>84±7</td>
<td>76±10</td>
<td>-10±7</td>
<td>86±12</td>
<td>79±9</td>
<td>-7±8</td>
<td>-0.71±0.76</td>
<td>0.13±0.62</td>
<td>18/40/42</td>
<td>Unclear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RFDpeak (kN)</td>
<td>1.81±0.75</td>
<td>1.51±0.52</td>
<td>-14±20</td>
<td>1.01±0.27</td>
<td>0.80±0.12</td>
<td>-15±20</td>
<td>0.14±0.42</td>
<td>0.15±0.39</td>
<td>8/51/41</td>
<td>Unclear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative RFDpeak (%)</td>
<td>520±140</td>
<td>510±110</td>
<td>-2±25</td>
<td>480±170</td>
<td>400±70</td>
<td>-11±25</td>
<td>-0.50±0.83</td>
<td>0.50±0.82</td>
<td>74/19/8</td>
<td>Possibly negative</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend. MVCF, maximal voluntary contraction force; VA, voluntary activation; Db100, twitch evoked by the doublet at 100 Hz; Db10:Db100, ratio between the twitches evoked with doublets at 10 to 100 Hz; RFDpeak, peak of rate of force development; relative RFDpeak, RFDpeak normalized to MVCF.