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Abstract

New Findings

- **What is the topic of this review?**
  Women are usually less fatigable than men for isometric fatiguing contractions of similar intensity, but whether this occurs for dynamic tasks is less clear. This review presents evidence that the sex difference in muscle fatigue of repeated dynamic contractions is specific to the task requirements, including the velocity of shortening and the muscle group involved.
- **What advances does it highlight?**
  Contractile mechanisms are responsible for the sex differences in muscle fatigue for slow-velocity and low-load dynamic tasks. The variability of the sex difference in fatigability among dynamic tasks has implications for fatiguing contractions prescribed in training and rehabilitation to men and women.

Women are usually less fatigable than men during single-limb isometric contractions, primarily because of sex-related differences in contractile mechanisms. It is less clear whether these sex differences in muscle fatigue occur for dynamic fatiguing tasks. This review highlights new findings that the sex difference in fatigability for dynamic shortening contractions with a single limb is dependent on the contraction velocity and the muscle group involved.

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Recent studies demonstrate that women are less fatigable than men for a dynamic task as follows: (i) the elbow-flexor muscles at slow- but not high-velocity contractions; and (ii) the knee-extensor muscles when muscle fatigue was quantified as a reduction in the maximal voluntary isometric contraction force after the dynamic fatiguing task. Contractile mechanisms are responsible for the sex difference in muscle fatigue of the dynamic contractions, with no evidence for a sex difference in the reduction in voluntary activation (i.e. central fatigue). Thus, these findings indicate that the sex difference in muscle fatigue of dynamic contractions is task specific. These data also challenge the assumption that men and women respond in a similar manner to training and rehabilitation that involve fatiguing contractions to overload the neuromuscular system. There is, however, a tremendous opportunity for conducting high-impact studies to gain insight into those factors that define the sex-based differences in muscle fatigue during dynamic tasks. Such studies can define the boundaries to human performance in both men and women during athletic endeavours, ergonomic tasks and rehabilitation.

Introduction

Muscle fatigue can define the limits of human performance during athletic endeavours, ergonomic tasks and rehabilitation in both men and women. It is also the basis of neuromuscular overload and adaptation that is necessary for improvement in training and rehabilitation of skeletal muscle. Muscle fatigue is an acute activity-induced reduction in the force or power of a muscle; it is typically quantified as the reduction in maximal strength or power, or the time to failure of a submaximal task (Enoka & Duchateau, 2008; Fig. 1). Multiple mechanisms contribute to muscle fatigue, ranging from inadequate activation of the motor cortex and motoneurone pool to altered cross-bridge dynamics within the activated muscle fibres (Kent-Braun *et al*. 2012). The details of the task will determine which site(s) along the neuromuscular system is stressed most, resulting in a reduction in the required force or power during the task (Enoka & Duchateau, 2008). Thus, muscle fatigue and the contributory mechanisms are specific not only to the demands of the task but also to the physical characteristics of the population being assessed, including the sex of the individual.

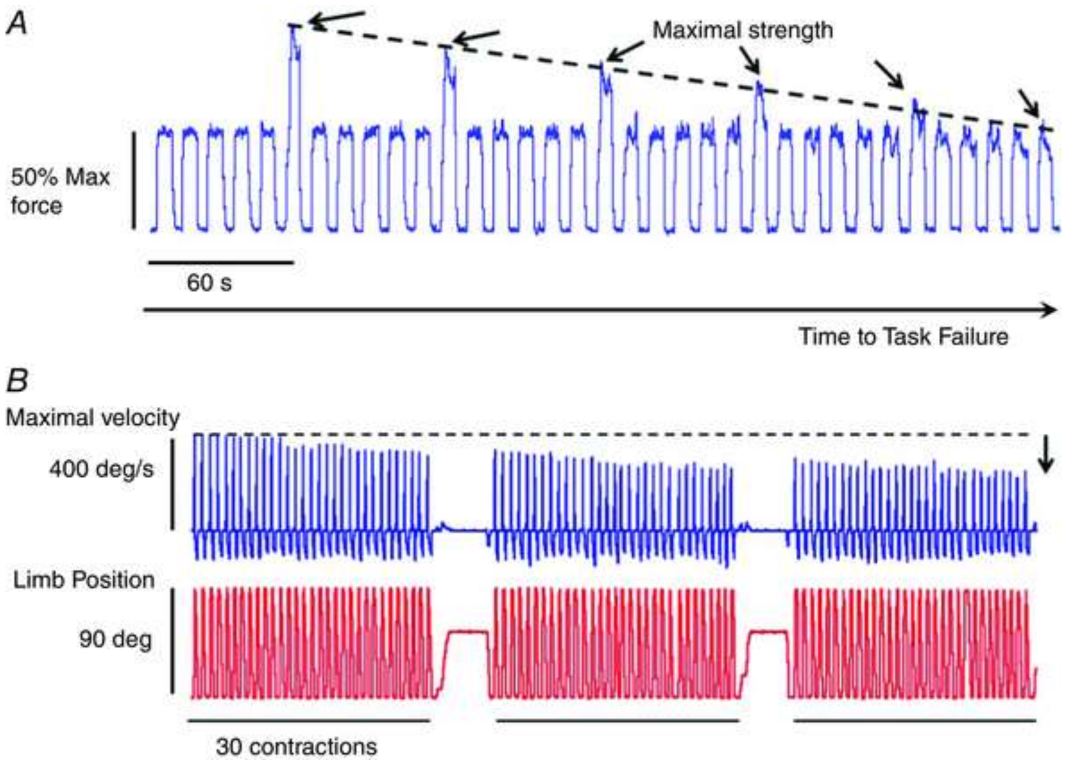

Figure 1. Individual data records showing fatiguing contractions for an intermittent isometric task (*A*) and a dynamic task (*B*) performed with the elbow-flexor muscles

A, intermittent isometric fatiguing contraction performed at 50% of maximal voluntary isometric contraction (MVIC). The task involved repeated contractions for 6 s followed by a 4 s rest until failure, with an MVIC performed every minute. Muscle fatigue is quantified as the reduction in MVIC and also as the time to task failure. *B*, the dynamic fatiguing task (three sets of 30 contractions) with a load equivalent to 20% of MVIC. Shortening contractions were performed once every 3 s as fast as possible through a 90 deg range of motion with the elbow-flexor muscles. The participant's limb was returned passively to the starting position before each shortening contraction. Muscle fatigue was seen as the reduction in maximal velocity (starting at ~410 deg s^{-1} in this example) and declined by 35% by the end of the 90th contraction.

There are sex differences in muscle fatigue involving isometric contractions performed with single-limb muscle groups in that women are usually less fatigable than men (Hunter, 2014). Sex-based differences within the neuromuscular system can alter the rates at which a site is stressed for men and women for a given fatiguing contraction, resulting in a difference in muscle fatigue between men and women. However, when there is an alteration in the details of the fatiguing task, such as the intensity of isometric contraction or whether it is sustained or intermittent, the sex-based differences in muscle fatigue can also change. There is a limited understanding of whether there are sex differences in muscle fatigue for dynamic tasks, primarily because of an inadequate number of published studies. This symposium review highlights the emerging hypothesis from recent studies that the sex difference in muscle fatigue of dynamic tasks can depend on the velocity of the contraction and the muscle group involved. It is important first to summarize what is known about the sex differences of isometric fatiguing contractions and the contributory mechanisms, which have been studied more extensively than dynamic fatiguing tasks.

Isometric fatiguing contractions

Women are usually less fatigable than men for both sustained and intermittent isometric fatiguing contractions for many upper and lower limb muscle groups when the task is performed at the same relative intensity (e.g. Fulco *et al*. 1999; Hunter & Enoka, 2001; Russ & Kent-Braun, 2003; Clark *et al*. 2005; Hunter *et al*. 2006*a*,*b*; Wust *et al*. 2008), although not for the elbow extensor muscles (Dearth *et al*. 2010). The sex difference for isometric fatiguing contractions appears to be due primarily to contractile mechanisms that are associated with contractile properties that reflect a slower and more fatigue-resistant muscle in women compared with men (Hunter *et al*. 2006*a*; Wust *et al*. 2008). Women usually have a greater proportional area of type I fibres than men across several muscle groups (e.g. Miller *et al*. 1993) because they typically have a smaller type II fibre area (Carter *et al*. 2001; Roepstorff *et al*. 2006; also see Figure 5 of Hunter, 2014). Type I and II fibres differ in their calcium kinetics (Lamboley *et al*. 2014), which is consistent with a slower sarcoplasmic reticulum Ca^{2+}-ATPase activity (measured from muscle homogenate; Harmer *et al*. 2014) and slower rate of muscle relaxation in women compared with men (Hunter *et al*. 2006*a*; Wust *et al*. 2008). Thus, a difference in fibre-type proportional area between men and women may contribute to the sex difference in muscle fatigue during isometric contractions. In addition, women can also exhibit greater muscle perfusion than men because women have a greater vasodilatory response during exercise (e.g. Parker *et al*. 2007; Kellawan *et al*. 2015) and appear to be less occluded at the start of submaximal isometric sustained contractions for some muscle groups (Hunter *et al*. 2004, 2006*b*). Collectively, these studies suggest that sex differences in muscle metabolism (Russ *et al*. 2005) lead to larger increases in metabolite build-up in the muscle of men compared with women that interfere with contractile function and contribute to a clear sex difference in muscle fatigue during isometric fatiguing contractions.

Torque reduction can be exacerbated via activation of metoboreceptors in the muscle (group III and IV afferents) that can inhibit the motoneurone pool. This inhibitory feedback may explain the greater reductions in voluntary activation (i.e. greater central fatigue) of men compared with women (Russ & Kent-Braun, 2003; Martin & Rattey, 2007), particularly in extensor muscles (Martin *et al*. 2006). The sex difference in the reduction of voluntary activation appears mainly to occur in lower-limb extensor muscles. For the elbow-flexor muscles, the reduction in voluntary activation (central fatigue) can be substantial (accounting for up to 25% of fatigability), but there are minimal sex differences during or after an isometric fatiguing contraction (Hunter *et al*. 2006*a*; Yoon *et al*. 2007; Keller *et al*. 2011). Thus, a sex difference in muscle fatigue of an isometric task is driven primarily by mechanisms originating within the muscle. Some of these sex differences in muscle physiology and function are also relevant to dynamic fatiguing tasks, which are more metabolically demanding than sustained isometric contractions (Newham *et al*. 1995).

Dynamic fatiguing tasks

Less is known about the sex differences in fatigability of dynamic contractions and the responsible mechanisms. This is in part because there are fewer studies and also a large number of dynamic variables, including the velocity of the contraction (see Figure 1b of Hunter, 2014). Recent studies, however, demonstrate that there is a sex difference in fatigability for repeated slow-velocity contractions (Yoon *et al*. 2015) that is diminished when the repeated contractions are relatively high in velocity (Senefeld *et al*. 2013).

Women were less fatigable than men for a low-load and relatively slow-velocity dynamic fatiguing task with the elbow-flexor muscles (Yoon *et al*. 2015). Men and women performed repeated dynamic contractions until task failure at an average velocity of ~60 deg s^{-1} with a load equivalent to 20% of maximal voluntary isometric contraction (MVIC). Each contraction cycle of lifting and lowering of the load over a 90 deg range of motion was completed over 3 s. Women were able to sustain the dynamic task for 41% longer than the men (9.7 ± 5.5 *versus* 6.1± 2.1 min, respectively). Transcranial magnetic stimulation was used to assess supraspinal fatigue (an increase in the evoked force, i.e. the superimposed twitch amplitude during an MVIC) and the peak rate of muscle relaxation. The time to task failure was best predicted by the peak rates of muscle relaxation and explained 55% of the variability between participants (Yoon *et al*. 2015). Women had a slower peak rate of relaxation at the start of the contraction and slowed less than the men by the end of the dynamic fatiguing task (Fig. 2*A*). Supraspinal fatigue increased but did so in a similar manner for the men and women (Fig. 2*B*) and did not explain the longer time to task failure for the women. Ideally, voluntary activation would be measured during dynamic contractions but is technically challenging in these experiments with submaximal loads. Regardless, evidence indicates that rate-limiting contractile mechanisms associated with relaxation rates were responsible for the increased fatigability of the elbow flexors of men compared with women for a dynamic fatiguing task performed at a slow angular velocity.

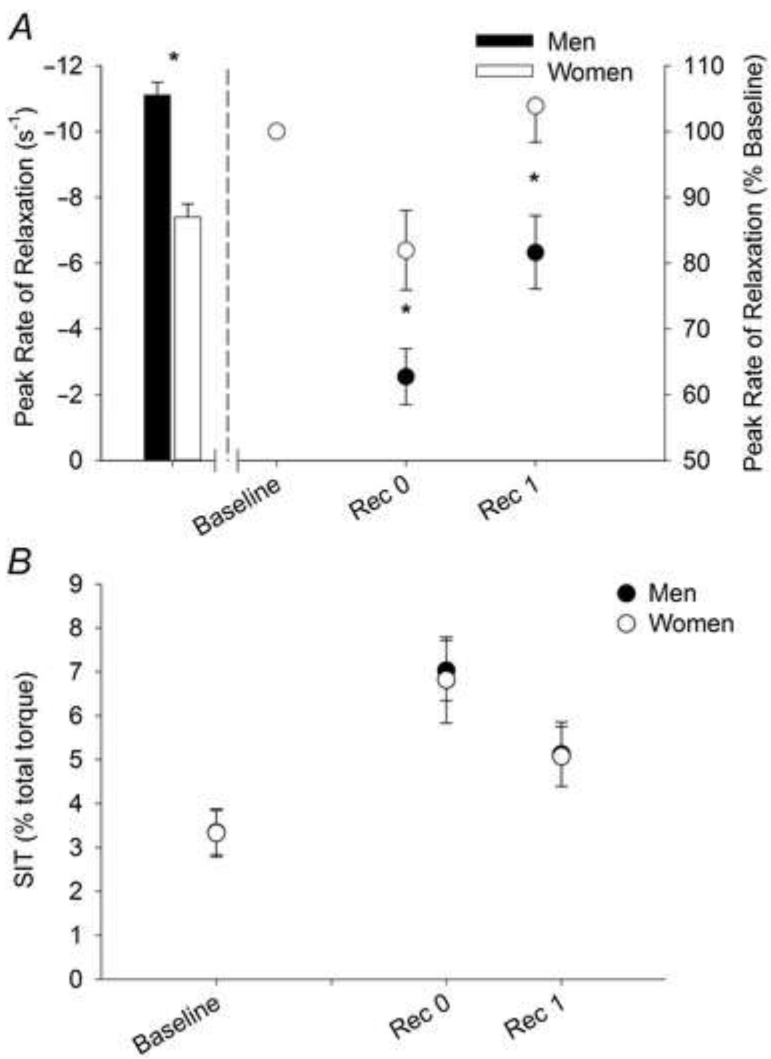

Figure 2. Peak relaxation rate of muscle fibres (*A*) and superimposed twitch (SIT) amplitude (*B*) elicited from cortical stimulation during MVICs before and after a slow-velocity dynamic fatiguing task performed with the elbow-flexor muscles

The fatiguing task was performed by 25 men and 29 women and involved lifting and lowering a weight equivalent to 20% MVIC at 60 deg s^{-1} until task failure. *A*, the peak relaxation rates of muscle fibres of men and women (means ± SEM) are shown at baseline (left *y*-axis) and then as the percentage of baseline (right *y*-axis) immediately after the dynamic fatiguing task (Rec 0) and at 1 min of recovery (Rec 1). *Sex difference at $P < 0.05$. *B*, SIT is expressed relative to the MVIC torque (%; mean ± SEM) and shown at baseline, immediately after the dynamic fatiguing task (Rec 0) and at 1 min of recovery (Rec 1). Data are adapted from Yoon *et al*. (2015), with permission.

In contrast to slow-velocity contractions, when men and women contracted with the elbow-flexor muscles as quickly as possible through the 90 deg range of motion, the decline in maximal velocity was similar for men and women (Senefeld *et al*. 2013). The dynamic task involved 90 dynamic contractions (one contraction every 3 s) performed as fast as possible with a load equivalent to 20% MVIC torque (see Fig. 1*B*). Before the fatiguing task, the elbow-flexor muscles of men were more powerful than those of women; men had 63% greater MVIC torque and were able to contract more quickly than the women by 23% (400 *versus* 310 deg s^{-1}, respectively). Muscle fatigue, however, was similar for the men and women observed as a reduction in maximal velocity (29% for both) and also as a reduction in the MVIC torque (15 *versus* 13%, respectively; Senefeld *et al*. 2013). Besides contraction velocity, the two dynamic fatiguing tasks differed in the work-to-rest ratio of the dynamic contractions. The larger work-to-rest ratio task performed at ~60 deg s^{-1} (Yoon *et al*. 2015) resulted in a greater sex difference in fatigability than when the work-to-rest ratio was less (Senefeld *et al*. 2013); this pattern is in contrast to that seen with maximal isometric contractions (Russ & Kent-Braun, 2003; Russ *et al*. 2008). Alternatively, a possible explanation for the diminished sex difference during the fast-velocity contractions may involve energy utilization of the different fibre types (which differs between men and women, as described earlier) during different contractions of varying velocity. Relative to isometric contractions, larger increases in energy utilization were seen for 'slow' muscles compared with 'fast' muscles during maximal-velocity shortening contractions of animal muscle (Barclay *et al*. 1993). If applicable to humans, it is reasonable to assume that the greater fatigue resistance of women compared with men during slow contractions would be diminished during fast-velocity contractions that involve a smaller work-to-rest ratio.

In the same study with the fast contractions, participants performed the same protocol with the knee-extensor muscles, i.e. three sets of 30 contractions with a load equivalent to 20% MVIC, performing the shortening contraction as fast as possible (Senefeld *et al*. 2013). As observed for the elbow-flexor muscles, the reduction in maximal velocity was similar in the men and women for the knee-extensor muscles. However, the reduction in MVIC torque of the knee-extensor muscles, which was measured immediately after the dynamic task, was greater for men than for women (18 *versus* 10% decline, respectively; Senefeld *et al*. 2013). To understand the potential mechanisms, our recent (J Senefeld, HM Pereira & SK Hunter, unpublished) data with the knee-extensor muscles indicate that the electrically evoked twitch amplitude declined more in the men (37%) than in the women (23%), and this paralleled the reduction in MVIC torque (J Senefeld, HM Pereira & SK Hunter, unpublished results). A reduction in the voluntary activation, assessed with the interpolated twitch technique during the MVIC, was similar for the men and women. These results suggest that the sex difference in the reduction in MVIC torque after the dynamic task was the result of a sex difference in the contractile mechanisms.

Implications for whole-body exercise

These findings with dynamic fatiguing tasks of the single-limb muscle groups provide insight into the mechanisms for the sex differences in fatigability often observed for exercise that involves multiple muscle groups (Billaut & Bishop, 2009). For example, women exhibit less muscle fatigue after multiple sprint exercise (Laurent *et al*. 2010; Billaut & Bishop, 2012) and also after very long-duration exercise (110 km run; Temesi *et al*. 2015). The greater reduction in maximal strength for the men compared with the women after the 110 km run was a result of contractile mechanisms (Temesi *et al*. 2015), although the contribution of muscle damage from the repeated lengthening contraction is not known. Collectively, these studies suggest that recovery of skeletal muscle can differ for men and women in response to single- and multiple-limb dynamic fatiguing exercise.

Final thoughts and conclusion

The boundaries of human performance differ for men and women because of distinct sex differences in physiology and anatomy. Men are stronger, more powerful and faster than women. Sex differences in fatigability of both dynamic and isometric tasks potentially shift these boundaries during a fatiguing task and in recovery because, in general, women are less fatigable than men for a task of the same relative intensity. Initial evidence shown here supports the hypothesis that the sex difference in muscle fatigue of repeated shortening dynamic contractions is specific to the requirements of the task, including the velocity of contraction and the muscle group involved. Women are less fatigable than men for the elbow-flexor muscles at slow- but not high-velocity contractions, and in the lower limb when fatigability and recovery are assessed with MVICs and isometric contractile function. For those dynamic tasks that demonstrate clear sex differences in muscle fatigue, contractile mechanisms are primarily responsible. While a reduction in voluntary activation (central fatigue) contributes to muscle fatigue after a dynamic fatiguing task, it does so in a similar manner for both men and women.

These data challenge the assumption that men and women respond in a similar manner to training and rehabilitation that involves fatiguing contractions to overload the neuromuscular system. Furthermore, the dearth of understanding the sex difference in the fatigability of dynamic fatiguing tasks highlights the tremendous opportunity for new and high-impact studies in this area.

Additional information

Competing interests

None declared.

Author contributions

The author has approved the final version of the manuscript and agrees to be accountable for all aspects of the work. The person designated as author qualifies for authorship, and all those who qualify for authorship are listed.

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Ancillary

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