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Mechanisms Of Fatigue Differ After Low- And High-Force Fatiguing Contractions in Men and Women

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Abstract

The magnitude of failure in voluntary drive after fatiguing contractions of different intensities in men and women is not known. The purpose of this study was to compare the time to task failure and voluntary activation of men and women for a sustained isometric contraction performed at a low and high intensity with the elbow flexor muscles. Nine men and nine women sustained an isometric contraction at 20% and 80% of maximal voluntary contraction (MVC) force until task failure during separate sessions. The men had a shorter time to failure than women for the 20% but not the 80% MVC task. Voluntary activation was reduced to similar levels for the men and women at the end of the fatiguing contractions but was reduced less after the 80% MVC task than the 20% MVC contraction. Twitch amplitude was reduced similarly at task failure for both sexes and to similar levels at termination of the 20% and 80% MVC tasks. The rate of change in mean arterial pressure was the main predictor of time to failure for the low-force sustained contraction. These results suggest that women experienced greater muscle perfusion, less peripheral fatigue, and a longer time to task failure than men during the low-force fatiguing contraction. However, the low-force task induced greater central fatigue than the high-force contraction for both men and women. Thus, low-force, long-duration fatiguing contractions can be used in rehabilitation to induce significant fatigue within the central nervous system and potentially greater neural adaptations in men and women. *Muscle Nerve*, 2007

When an individual maintains a submaximal fatiguing contraction, failure of the task occurs due to a reduced force capacity of the muscle that involves both neural and muscular mechanisms.^{14, 44} The processes that contribute to task failure depend on the details of the task performed including the type and intensity of contraction and the sex of the individual.^{8, 14, 18, 24} For example, low-force contractions can be sustained longer than high-intensity contractions with greater contributions of neural mechanisms for the low-force tasks.^{3, 30} Neural mechanisms and the magnitude of central fatigue can be quantified as a reduction in voluntary activation. However, few studies have directly compared the magnitude of change in voluntary activation for a high- and low-intensity contraction when sustained to failure. Voluntary activation is often quantified as the extra force evoked when the motor nerve is stimulated during maximal contractions. This extra force implies a failure of voluntary drive at one or more sites proximal to the motor nerve and therefore within the central nervous system. A failure in voluntary activation during maximal efforts indicates that the level of neural drive to the muscle is suboptimal¹⁴ because either the motor units are not all recruited voluntarily or they are discharging at an insufficient rate to produce full fusion of force.¹⁷

Women can maintain steady low-force fatiguing contractions longer than men.^{5, 20, 26, 48} However, the sex difference in time to failure and muscle fatigability is task-dependent, such that the magnitude and mechanism for sex differences varies according to the muscle being assessed and the contraction type and its intensity.^{5, 22, 23, 37} For the elbow flexor muscles, reduction in voluntary activation was similar for men and women during maximal contractions when assessed by stimulating the motor cortex despite less fatigue experienced by the women.²⁵ The site of failure of voluntary drive therefore was at or above the level of motor cortical output^{41, 44, 45} and was similar for men and women.²⁵ It is unknown, however, whether there are sex differences in voluntary activation that originate between the motor cortex and neuromuscular junction and contribute to the sex differences in muscle fatigue.

One purpose of this study, therefore, was to compare the time to task failure and voluntary activation assessed at the peripheral motor nerve and muscle for men and women after a fatiguing contraction performed with the elbow flexor muscles. We examined these effects for both a low-force and high-force fatiguing contraction because the relative contribution of failure in voluntary drive for the different tasks is not known for men and women. We hypothesized that the time to task failure would be greater for women than men for the low-force

contraction but similar for the sexes for the high-force contraction and that the reduction in voluntary drive would be similar at task failure for both sexes and contraction intensities. Additional measures including torque fluctuations, electromyographic activity (EMG), mean arterial pressure (MAP), heart rate, and rating of perceived exertion (RPE) were recorded to determine the physiological adjustments and provide evidence for any difference in rate of change in central and peripheral mechanisms during the fatiguing tasks.

MATERIALS AND METHODS

Eighteen young adults (nine women, nine men; 21–33 years of age) were recruited for this study. All subjects were healthy, with no known neurological or cardiovascular diseases, and were naive to the protocol. Prior to participation in the study each subject provided informed consent and the protocol was approved by Institutional Review Board.

The physical activity level for each subject was assessed with a questionnaire that estimated the relative kilocalorie expenditure of energy per week.²⁸ All subjects were right-handed (0.71 ± 0.1 vs. 0.72 ± 0.2 for men and women, respectively, with a ratio of 1 indicating complete right-handedness) as estimated with the Edinburgh Handedness Inventory.

Subjects reported to the laboratory on three occasions: once for a familiarization session and then for two experimental sessions that were 7–10 days apart to perform a protocol that focused on a fatiguing contraction with the elbow flexor muscles of the nondominant arm. In each experimental session the fatiguing contraction involved maintaining a force that was equivalent to 20% or 80% of the maximal voluntary contraction (MVC) force for as long as possible. The order of the experimental sessions was randomized for each subject. Five men and three women performed the 20% MVC task during their first experimental session.

Mechanical Recording.

Subjects were seated upright in an adjustable chair with the nondominant arm abducted slightly and the elbow resting on a padded support. The elbow joint was flexed to 90° so that the forearm was horizontal to the ground and the force at the wrist was directed upward when the elbow flexor muscles were activated during a voluntary contraction. Two nylon straps were placed vertically over each shoulder to restrain the subject and minimize shoulder movement. The hand and forearm were placed in a modified wrist-hand-thumb orthosis (Orthomerica, Newport Beach, California) and the forearm was placed midway between pronation and supination. The force exerted by the wrist in the vertical direction was measured with a transducer (JR-3 Force-Moment Sensor; JR-3 Inc., Woodland, California) that was mounted on a custom-designed, adjustable support. The orthosis was attached to the force transducer. The force detected by the transducer was recorded online using a Power 1401 A-D converter and Spike2 software (CED, Cambridge, UK). The force exerted was displayed on a 19-inch monitor with an oscilloscope display located at eye level and 1.5 m in front of the subject. The force was adjusted for each subject so a horizontal cursor that represented the required target force was displayed at ~60% the height of the screen. Each subject was asked to trace the horizontal cursor with the force signal for as long as possible. The force signal appeared on the screen from the right side of the monitor at 2.5 cm/s.

In addition, the force exerted under the elbow joint was measured with a load cell (YB6; Sentran, Ontario, California) placed under the padded elbow support. The force under the elbow joint was monitored to ensure that each subject placed and maintained the elbow on the padded support. The force was displayed on an oscilloscope and recorded online with Spike2 software (CED, Cambridge, UK) at 500 samples/s.

Electrical Recordings.

EMG signals were recorded with bipolar surface electrodes (Ag–AgCl, 8-mm diameter; 16 mm between electrodes) that were placed over biceps brachii, brachioradialis, and triceps brachii muscles. Reference

electrodes were placed on a bony prominence at the elbow. The EMG signal was amplified ($\times 100$) and bandpass-filtered (13–1000 Hz) with Coulbourn modules (Coulbourn Instruments, Allentown, Pennsylvania) prior to being recorded directly to computer with the Power 1401 A-D converter and Spike2 software (CED). The EMG signals were digitized at 2000 samples/s.

Cardiovascular Measurements.

Heart rate and blood pressure were monitored during the fatiguing contractions because these adjustments involve central and peripheral processes.^{32, 36} Both heart rate and blood pressure were monitored with an automated beat-by-beat blood pressure monitor (Finapres 2300; Ohmeda, Madison, Wisconsin). The blood pressure cuff was placed around the middle finger of the relaxed, dominant hand with the arm placed on a table adjacent to the subject at heart level. The blood pressure signal was recorded online to computer at 500 samples/s.

Electrical Stimulation.

Electrical stimulation of muscle was used to evoke force in the biceps brachii muscle to assess voluntary activation during an MVC. The stimulating cathode was placed over the biceps brachii (midway between the anterior edge of the deltoid and antecubital fossa) and an anode was placed over the bicipital tendon (2 cm proximal to the elbow).^{1, 46} Activation of the muscle was achieved by a constant-current stimulator (Digitimer DS7AH, Welwyn Garden City, UK) that delivered a rectangular pulse of 100- μ s duration and at a maximal amplitude of 400 V. The stimulation intensity (~ 200 mA to 500 mA) was set to 10% above the level required to produce a resting twitch of maximal amplitude so that the level of stimulation was supramaximal. This level of stimulation was used for the remainder of the protocol. Control twitches were evoked at rest and when the muscle was potentiated with an MVC task.¹⁴ To assess voluntary activation, a single twitch was interpolated during the plateau of the MVC by the constant-current stimulator as determined by the investigator. This occurred during the MVCs performed before and immediately after the fatiguing contraction.

Experimental Protocol.

The protocol for each experimental session comprised the following procedures: (1) determination of supramaximal levels of electrical stimulation, (2) assessment of MVC torque and voluntary activation for the elbow flexor muscles, (3) performance of an MVC of the elbow extensor muscles, (4) brief submaximal isometric contractions of the elbow flexor muscles to determine the EMG–force and voluntary activation–torque relations, (5) performance of a fatiguing contraction at either 20% or 80% MVC force, immediately followed by (6) a twitch contraction, a recovery MVC with the elbow flexor muscles, and another twitch contraction.

MVC Torque and Voluntary Activation.

Each subject performed four MVC trials with the elbow flexors, followed by two trials with the elbow extensor muscles. The MVC task involved a gradual increase in force from zero to maximum over ~ 2 s, with the maximal force held for 2–3 s. The force exerted by the wrist was displayed on a monitor and each subject was verbally encouraged to achieve maximal force. MVCs with the elbow extensor muscles were performed so that maximal EMG could be recorded and used to normalize the triceps EMG activity during the fatiguing contractions. For the elbow flexor muscles, a single electrical stimulus at the predetermined supramaximal level was delivered once the force was at a plateau and also 3 s after termination of the MVC while the muscle was at rest.¹ Pilot data on subjects indicated that there was no difference in voluntary activation levels when using a single or paired pulse (10 ms apart). These results are consistent with those previously reported.² There was a 60-s rest between MVC trials. When the peak forces from two of the three trials were not within 5% of each other, additional trials were performed until this was accomplished. The greatest torque achieved by the subject was taken as the MVC torque and used as the reference to calculate the target level for the constant-force and fatiguing contractions of the elbow flexor muscles.

Brief Submaximal Contractions.

The EMG activity of the involved muscles was recorded in standardized tasks so that the force–EMG relation could be compared across experimental days. These relations for the men and women were examined to ensure that changes in EMG during the fatiguing contractions and at task failure represented physiological adjustments and were not due to differences in recording conditions across the experimental days. The subjects performed a sustained constant-force contraction with the elbow flexor muscles for 6 s at target values of 20%, 40%, 60%, and 80% MVC force with 60-s rest between each contraction. A single electrical stimulus was delivered to the biceps brachii muscle during and after the brief contractions to assess voluntary activation levels during the submaximal tasks. The order of the contractions was randomized across subjects, but remained constant for each subject on the two experimental days.

Fatiguing Contraction.

A fatiguing contraction was performed with the elbow flexor muscles in each experimental session at a target value of either 20% or 80% MVC force. The subject was required to match the vertical target force as displayed on the monitor and was verbally encouraged to sustain the force for as long as possible. The fatiguing contraction was terminated when the force declined by 10% of the target value for 3 of 5 s despite strong verbal encouragement to maintain the force. This time was recorded as the time to task failure. Subjects were not informed of their time to task failure until completion of the second session. Neither the subject nor the investigator who terminated the task knew the time during the tasks.

An index of perceived effort, the rating of perceived exertion (RPE), was assessed with the modified Borg 10-point scale. Subjects were instructed to focus the assessment of effort on the arm muscles performing the fatiguing task. The scale was anchored so that 0 represented the resting state and 10 corresponded to the strongest contraction that the arm muscles could perform. The RPE was recorded at the beginning of the contraction and every minute thereafter until task failure for the 20% MVC fatiguing contraction. Because of the brevity of the 80% MVC task, subjects were asked their RPE at the beginning of the contraction and at task failure.

Data Analysis.

The torque for the MVC and submaximal contractions was calculated as the product of force and the distance between the elbow joint and the point at which the wrist was attached to the force transducer.

Voluntary activation was quantified by measurement of the force responses to stimulation of the muscle.^{1,14} Any increment in elbow flexion force evoked during a contraction (superimposed twitch) was expressed as a fraction of the amplitude of the control twitch evoked 3 s after the MVC. The level of voluntary activation was derived by the formula: Voluntary activation = $100 \times (1 - T_{\text{interpolated}}/T_{\text{control}})$, where $T_{\text{interpolated}}$ was the size of the interpolated twitch and T_{control} was the amplitude of the control twitch produced by stimulation of the peripheral nerve in a relaxed but potentiated muscle.¹⁴

The MVC torque was quantified as the average value over a 0.5-s interval that was centered about the peak. The maximal EMG for each muscle was determined as the root mean squared (RMS) value over a 0.5-s interval about the same interval of the MVC torque measurement. The RMS EMG value of the constant-force contractions for the elbow flexors performed at 20%, 40%, 60%, and 80% of MVC torque was averaged over the 2-s period prior to electrical stimulation during the 6-s contraction.

The fluctuations in force and the RMS of the EMG signal of the elbow flexor muscles and triceps brachii muscles were quantified during the fatiguing contraction performed at 20% of MVC at the following time intervals: the first and last 60 s of task duration, and 30 s either side of 25%, 50%, and 75% of time to task failure. The fluctuations in force and RMS EMG during the high force (80% MVC) task were quantified at five continuous

intervals equivalent to 20% of the task duration. The EMG activity of the elbow flexor and extensor muscles during the fatiguing contraction was normalized to the RMS EMG value obtained during the MVC for each muscle. The amplitude of the force fluctuations was quantified as the coefficient of variation ($CV = SD/mean \times 100$).

Heart rate and MAP recorded during the fatiguing contraction were analyzed by comparing ~ 15 -s averages at 25% intervals throughout the low-force fatiguing contraction. For each interval the blood pressure signal was analyzed for the mean peaks [systolic blood pressure (SBP)], mean troughs [diastolic blood pressure (DBP)], and number of pulses per second (multiplied by 60 to determine heart rate). MAP was calculated for each epoch with the following equation: $MAP = DBP + \frac{1}{3}(SBP - DBP)$. Heart rate and blood pressure were only analyzed for the 20% MVC fatiguing contraction due to a poor signal during recording of many of the 80% MVC tasks.

Statistical Analysis.

Data are reported as means \pm SD within the text and displayed as means \pm SE in the figures. ANOVAs with repeated measures on a combination of variables including contraction intensity (20%, 80% MVC), time (0, 25%, 50%, 75%, 100% of time to failure), fatigue (precontraction, postcontraction), and force (20%, 40%, 60%, and 80% MVC) with sex (men, women) as a between-subject factor were used to compare the various dependent variables. Specifically, the statistical designs were as follows for the dependent variables: (1) contraction intensity \times sex for time to task failure, the relative change of MVC torque, relative change in voluntary activation and the relative change in control twitch amplitude; (2) contraction intensity \times time \times sex for comparison of torque fluctuations, RPE, and RMS EMG for each muscle during the fatiguing contractions; (3) contraction intensity \times fatigue \times sex for comparison of voluntary activation, MVC and twitch amplitude; (4) contraction intensity \times force \times sex for comparison of voluntary activation and RMS EMG during the brief constant force contractions performed prior to each of the fatiguing contractions; and (5) time \times sex for comparison of heart rate and MAP during the low-force sustained contraction. Multiple comparisons with Tukey post-hoc tests were used to determine differences among pairs of means. A significance level of $P < 0.05$ was used to identify statistical significance.

The contribution of several variables to the time to task failure were analyzed using multiple linear regressions and the associated partial correlations (r). These variables included the change in EMG activity of the biceps brachii and brachioradialis, MAP (20% MVC task only), voluntary activation, MVC force, twitch amplitudes, and physical activity levels. The associated partial correlation coefficients were used to identify the contribution of each independent variable to the time to task failure for each of the contraction intensities. The strength of an association is reported as the squared Pearson product-moment correlation coefficient (r^2).

RESULTS

The men and women were similar in age (22.4 ± 4.4 years vs. 22.2 ± 4.3 years, respectively) but differed in height (181.3 ± 5.2 cm vs. 168.5 ± 7.6 cm, $P < 0.05$) and mass (80.9 ± 11.4 kg vs. 63.1 ± 10.9 kg, $P < 0.05$). The estimated physical activity levels were similar for the men and women (51.9 ± 33.7 Met.hour/week vs. 59.5 ± 28.3 Met.hour/week, respectively).

Time to Task Failure and MVC Torque.

The men had a shorter time to task failure than the women for the 20% MVC fatiguing contraction (10.6 ± 2.0 min vs. 17.0 ± 8.7 min, respectively) but a similar time for the 80% MVC task (25.0 ± 6.5 s vs. 24.3 ± 6.6 s, contraction intensity \times sex, $P < 0.05$). The range in time to failure for the 20% MVC task was 11.3–38.8 min for the women and 6.5–13.0 min for the men. The range in time to failure for the 80% MVC task was 13–32 s for the women and 17–34 s for the men. Correlation analysis showed no association between the order of testing and

the time to task failure for men and women analyzed separately (women: $r = 0.38$, $P = 0.32$; men: $r = 0.16$, $P = 0.69$) or pooled ($r = 0.20$, $P = 0.42$).

The men were stronger than the women ($P < 0.05$) on both days of testing (88.0 ± 22.1 N.m vs. 45.3 ± 7.2 N.m; pre-fatigue values) before and after the fatiguing contractions. MVC torque was reduced from the initial MVC at the end of the fatiguing contractions (main effect of fatigue, $P < 0.05$). These reductions were greater ($P < 0.05$) for the 20% MVC task ($24.1 \pm 12.1\%$) than the 80% MVC task ($15.8 \pm 4.3\%$). The decline in MVC torque was greater for the women than men ($P < 0.05$) at the end of the 20% MVC fatiguing contraction: $31.6 \pm 11.1\%$ vs. $16.7 \pm 8.1\%$) but was similarly reduced at the end of the 80% MVC task ($15.4 \pm 5.3\%$ vs. $16.1 \pm 3.2\%$). The range in relative reduction in MVC torque after the 20% MVC task was 15%–51% for the women and 9%–35% for the men. The greater reduction in MVC force for the women was due to two subjects who had a large relative decrease in their MVC torque (44% and 51%). However, when these two data points were excluded the contraction intensity \times sex interaction for the relative reduction in MVC torque was not significant and the time to task failure remained significantly different between the sexes for the low-force task (17.9 ± 9.8 min for the women, $n = 7$).

Voluntary Activation.

The size of the twitch evoked during each of the brief submaximal constant-force tasks decreased and voluntary activation increased as the intensity of contraction increased between 20% and 80% of MVC force ($P < 0.05$) similarly for the men and women. The increase in voluntary activation was similar for each experimental day with no interactions.

Voluntary activation assessed during the MVC before the fatiguing contractions was similar for the men and women and there was no difference between experimental sessions. Voluntary activation was reduced ($P < 0.05$) at the end of the 20% MVC fatiguing contraction similarly for the men ($95.6 \pm 4.3\%$ to $85.2 \pm 10.3\%$) and women ($97.7 \pm 1.0\%$ to $80.6 \pm 10.0\%$). Voluntary activation also declined after the 80% MVC task ($P < 0.05$) similarly for the men ($97.6 \pm 2.2\%$ to $93.1 \pm 5.6\%$) and women ($98.2 \pm 1.1\%$ to $92.7 \pm 5.4\%$). However, the reduction in voluntary activation was greater after the 20% MVC task ($14.3 \pm 9.9\%$, men and women pooled) compared with the 80% MVC fatiguing task ($5.1 \pm 4.3\%$, contraction intensity \times fatigue, $P < 0.05$). There were no other significant interactions for contraction intensity, sex, and fatigue.

Twitch Amplitude.

The amplitude of the potentiated control twitch torque was greater for the men than women (8.2 ± 2.2 N.m vs. 5.9 ± 1.1 N.m, $P < 0.05$) before the fatiguing contractions and was similar for each of the experimental days. Twitch torque was reduced at the end of both fatiguing contractions ($P < 0.05$) for both men and women and there were no interactions. The relative decline of twitch amplitude evoked immediately after the 20% MVC fatiguing task was similar for the men ($23 \pm 24\%$) and women ($33 \pm 9\%$). Twitch torque was also reduced similarly after the 80% MVC fatiguing task for the men ($37 \pm 17\%$) and women ($29 \pm 13\%$), indicating a similar magnitude of peripheral fatigue at the termination of both tasks in both sexes.

Fluctuations in Torque during the Fatiguing Contractions.

The amplitude (CV) of the vertical fluctuations in force increased during the 20% and 80% MVC fatiguing contractions ($P < 0.05$, Fig. 1). The increase in fluctuations during the low-intensity fatiguing task was similar for men and women and represented over a 3-fold increase. At the start of the fatiguing task the range of torque fluctuations was 1.0%–2.6% for the women and 1.0%–3.9% for the men. At the end of the low-intensity task the ranges were similar for the women (4.1%–7.5%) and men (4.0%–8.6%). However, the rate of change in fluctuations for men was greater than women ($P < 0.05$) during the 20% MVC force fatiguing contraction. Furthermore, the increase in fluctuations during the 80% MVC fatiguing task was similar for men and women

with no interaction for sex \times time. At the start of the 80% MVC fatiguing task the range of torque fluctuations were 0.8%–3.2% for the women and 0.7%–4.1% for the men. At the end of the high-intensity task the ranges were 3.0%–9.9% and 2.5%–7.4%, respectively.

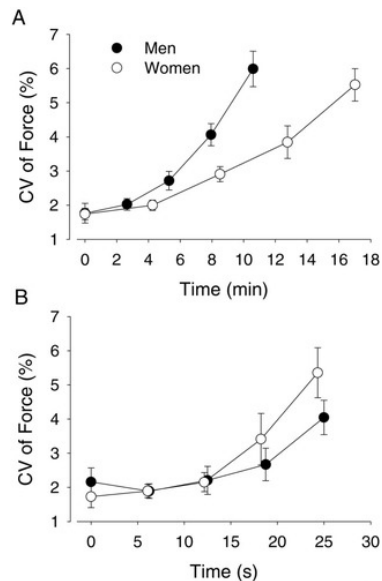


Figure 1 Force fluctuations for men and women during 20% **(A)** and 80% MVC fatiguing contractions **(B)**. The amplitude of the vertical fluctuations in force increased for men and women during both sessions. Shown are the means and SEM for intervals at the start and end of the contraction and at the 25%, 50% and 75% of time to failure. **(A)** The rate of change in fluctuations during 20% MVC fatiguing contraction for men was greater compared with the women. **(B)** The rate of change in fluctuations during 80% MVC task was similar for the men and women.

EMG Activity.

EMG–Force Relation.

EMG activity increased ($P < 0.05$) with contraction intensity on both days similarly for the men and women during the brief submaximal contractions of the biceps brachii and brachioradialis muscles. There were no differences in the EMG activity across experimental days, nor any interactions of sex \times contraction intensity.

RMS EMG during the Fatiguing Contraction.

The amplitude of the RMS EMG (% MVC) for each of the elbow flexor muscles increased ($P < 0.05$) during the 20% and 80% MVC force fatiguing contractions (Fig. 2). RMS EMG of biceps brachii for the women was greater than the men at the end of the 20% MVC fatiguing contraction but not for the 80% (contraction intensity \times time \times sex, $P < 0.05$). The amplitude of RMS EMG for brachioradialis was less for the women compared with the men for the 20% MVC fatiguing contraction but similar for the sexes for the 80% MVC fatiguing contraction (contraction intensity \times sex, $P < 0.05$). Furthermore, RMS EMG for triceps brachii of the women was greater compared with the men ($P < 0.05$) for the 80% MVC fatiguing contraction throughout the task.

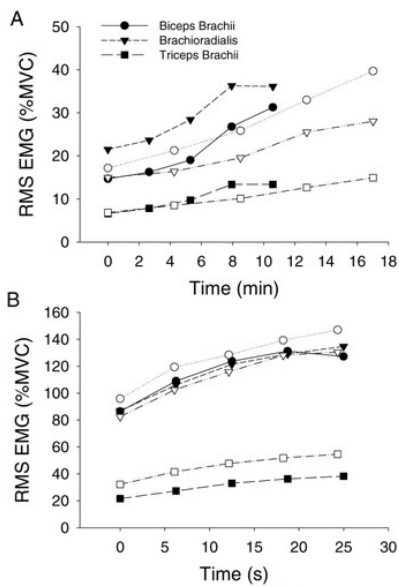


Figure 2 RMS EMG normalized to the MVC values (% MVC) for men (filled symbols) and women (open symbols) during 20% MVC fatiguing contraction **(A)** and 80% MVC fatiguing contraction **(B)**. The pattern of change in RMS EMG for each flexor muscles was different between sessions. **(A)** The amplitude of RMS EMG (% MVC) for biceps brachii in women was greater than in men at the end of the 20% MVC fatiguing contraction ($P < 0.05$), but the EMG activity of the brachioradialis in women was less than men throughout the fatiguing contraction ($P < 0.05$). **(B)** The amplitude of RMS EMG for the biceps brachii and brachioradialis muscles were similar for the men and women during the 80% MVC task ($P > 0.05$), but the women showed greater triceps brachii EMG activity compared with the men ($P < 0.05$).

Mean Arterial Blood Pressure (MAP) and Heart Rate.

MAP increased during the low-force fatiguing contraction for the men and women (main effect of time, $P < 0.05$) (Fig. 3A). MAP increased more for the men than the women during the 20% MVC task (interaction of time \times sex, $P = 0.05$) so that at task failure the men had a greater MAP than the women. Consequently, the rate of increase was greater for the men compared with the women (6.37 ± 1.52 and 3.15 ± 1.42 mmHg/min, respectively, $P < 0.05$). MAP and heart rate was not able to be analyzed for the 80% MVC task due to poor signal recordings.

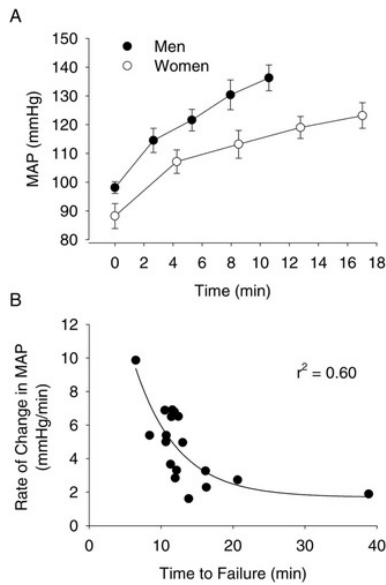


Figure 3 (A) Mean arterial pressure (MAP) for men and women during the 20% MVC fatiguing contraction. Shown are the means and SEM for intervals at the start and end of the contraction and at the 25%, 50%, and 75% of time to failure. Men had greater MAP at task failure than the women and a greater rate of increase in MAP throughout the fatiguing contraction ($P < 0.05$). **(B)** The association between the rate of change in MAP and the time to task failure was best described as by an exponential decay ($r = 0.77$, $r^2 = 0.60$). The exponential relation was $y = 1.7 + 22.8e^{-0.168x}$.

Heart rate also increased during the low-force fatiguing contraction ($P < 0.05$) and was similar for the men and women. The men and women had similar heart rate values at the start (70 ± 8 beats/min and 74 ± 12 beats/min, respectively) and end (99 ± 18 beats/min and 104 ± 19 beats/min, respectively) of the 20% MVC task. There was no interaction of time \times sex and no difference in the rate of increase in the heart rate between men and women (2.87 ± 1.98 beats/min and 2.00 ± 1.13 beats/min).

Perceived Exertion during the Fatiguing Contractions.

RPE increased during both fatiguing contractions ($P < 0.05$). RPE was similar for the men and women at the beginning (2.2 ± 1.2 vs. 1.8 ± 1.0) and end (9.7 ± 0.7 vs. 10.0 ± 0.0) of the fatiguing contraction for the 20% MVC task. However, the rate of increase in the RPE was more gradual for the women than the men (0.95 ± 0.2 /min vs. 0.68 ± 0.2 /min, $P < 0.05$) for the 20% MVC task. All subjects reported an RPE of 10 at task failure of the 80% MVC contraction.

Factors that Contributed to Time to Failure: Regression Analysis.

Regression analysis showed the rate of change in MAP ($r^2 = 0.39$, $P < 0.05$) was the single significant predictor of time to failure for the 20% MVC task. For the 80% MVC task there were no significant predictors of time to task failure. Further analysis indicated that the relation between rate of change in MAP and the time to task failure was best described as an exponential decay ($r = 0.77$, $r^2 = 0.60$, $P < 0.05$, Fig. 3B). Those individuals who had the greatest rate of change in MAP had the shortest time to failure.

DISCUSSION

The main findings of this study were that (1) men had a shorter time to task failure than women for the 20% MVC force fatiguing contraction but a similar time for the 80% MVC task; (2) voluntary activation was reduced to a greater magnitude after the 20% MVC task compared with the 80% MVC task for both men and women; (3) voluntary activation was reduced similarly for both sexes after the fatiguing contractions; (4) the reduction in

the amplitude of the potentiated control twitch was similar for men and women after the 20% and 80% MVC fatiguing tasks; and (5) the rate of change in MAP was the single predictor of time to failure for the 20% MVC fatiguing contraction.

Sex Difference in Time to Task Failure Was Intensity-Dependent.

The women were weaker than the men, but they had a longer time to task failure for the low-intensity fatiguing contraction, which is consistent with other studies.^{5, 20, 26, 37, 48} In contrast, the time to failure was similar between men and women for the 80% MVC task. Muscle perfusion may explain the sex difference in time to failure for the sustained contractions at low forces. First, there was no sex difference in time to task failure for the sustained 80% MVC task, when blood flow is usually occluded,^{4, 35} and this has been shown for other muscle groups including the finger flexors and quadriceps.^{31, 48} The difference in muscle fatigue between men and women was also eliminated when the sexes were matched for strength for a low-force sustained contraction^{16, 22, 26} and when perfusion was occluded with a cuff and the muscle made ischemic.^{6, 37} Furthermore, the sex difference persists for moderate-to-high intensity intermittent contractions when blood flow is periodically restored and is therefore not a limitation to task duration.^{6, 12, 23, 37}

Second, the rate of increase in MAP was the main predictor of time to failure for the 20% MVC sustained contraction. The rate of increase in MAP was less for the women than men during the low-force task. The increase in MAP (pressor response) during an isometric contraction is due to peripheral reflexes, mainly the metaboreflex, which is driven by an increase in metabolites in a progressively occluded muscle.^{32, 36} The pressor response is also influenced by central command. However, the peripheral reflex appeared to have more influence during these low-force contractions because the increase in heart rate, which is due to central command,^{32, 36} did not differ between the men and women. Consequently, mechanically altered muscle perfusion was likely less for women than men during the 20% MVC task and is consistent with sex differences in forearm blood flow after isometric contractions of the handgrip muscles.²⁶ Other sex-related mechanisms that influence perfusion, however, may also mediate the task-dependent difference in muscle fatigue between men and women including differences in: (1) fiber type composition^{34, 40, 47}; (2) rates of glycolytic metabolism^{38, 42}; (3) metabolic vasodilators of the muscle⁷ mediated by chronic exposure to sex hormones^{19, 33}; and (4) sympathetic activation, such that vasoconstriction is less for women than men during static exercise.⁹

Voluntary activation was reduced to similar magnitudes for men and women after the fatiguing contractions, indicating similar magnitudes of impairment to optimally drive the muscle during a maximal effort at termination of both tasks. Either the motor units were not all recruited voluntarily or they were discharging at rates that were insufficient to produce full fusion of force¹⁷ after the fatiguing contractions. However, the change in voluntary activation was not a predictor of the time to failure for the 20% MVC contractions, and therefore secondary to fatigue within the muscle. An increased accumulation of metabolites in the muscle of men compared with women likely increased afferent feedback to spinal and supraspinal centers¹⁴ influencing voluntary activation after the low-force task. Supraspinal fatigue contributes significantly to the reduction in voluntary activation and muscle fatigue during low-force and high-force fatiguing tasks and is attributable to suboptimal output from the motor cortex.^{13, 25, 41, 43} Supraspinal fatigue was similar for men and women during repeated sustained maximal contractions of the elbow flexor muscles but the men fatigued more than the women because the women experienced less peripheral fatigue.²⁵ The present study, therefore, confirms previous findings for the elbow flexor muscles.

Men and women utilized different activation patterns and strategies among the elbow flexor muscles during the low-force sustained contraction. The men showed greater activation of the brachioradialis and the women utilized the biceps brachii to greater magnitudes than the men toward task failure of the low-force task. These differences in EMG activity were not due to any sex differences in the recording conditions because the EMG

activity was similar across experimental days and the sexes during brief submaximal contractions at varying intensities that were recorded before the fatiguing contractions. The increase in EMG activity during a low-force submaximal sustained contraction is largely due to the recruitment of larger motor units as the muscle becomes progressively fatigued.^{10, 15} Differences in activation patterns and recruitment patterns within a muscle and among agonist muscles will alter time to task failure for a low-force contraction.^{21, 27, 39} However, there was no association between changes in EMG activity for either of the elbow flexor muscles and time to failure. Although activation patterns differed between men and women, the influence on the sex differences in time to failure was small.

In contrast, the elbow flexor muscles of the men and women were similar in their activation patterns during the 80% MVC task, which is an intensity at which the majority of motor units are recruited.²⁹ The women had greater activation of the triceps brachii during the high-force task than the men, but the magnitude of this difference was small and therefore unlikely to contribute to differences in time to failure.

Mechanisms of Fatigue Vary with Contraction Intensity.

The magnitude of reduction in voluntary activation was greater after the low-intensity task (14%) than the high-force, short-duration task (5%). The reduction in voluntary drive was in part due to fatigue at or processes that occur prior to the motor cortex for the low-force task.⁴¹ Consistent with these results, the EMG activity increased during both tasks but was less than maximal after the 20% MVC task but maximal at task failure for the 80% MVC contraction. The differences in EMG activity between high- and low-force contractions at task failure was also shown for a small muscle of the hand.^{11, 30} These differences in EMG activity and voluntary activation likely originated from a decrease in descending drive and reduced excitability of the motor neuron pool at spinal sources for the low-force task with some contribution from feedback via afferents.¹⁴

The similar reduction in twitch amplitude after the two fatiguing contractions suggests the average rate of peripheral fatigue was much greater during the 80% MVC task than the 20% MVC contraction. Taken together with the observation of the small reduction in voluntary activation after the high-intensity task, failure of the 80% MVC task can be attributed primarily to fatigue within the muscle.

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Abbreviations

CV, coefficient of variation; DBP, diastolic blood pressure; EMG, electromyography; MAP, mean arterial pressure; MVC, maximal voluntary contraction; RPE, rating of perceived exertion; RMS, root mean squared; SBP, systolic blood pressure

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