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SYMPOSIUM: SEX DIFFERENCES IN MUSCULOSKELETAL DISEASE AND SCIENCE

Sex Differences in Arm Muscle Fatigability With Cognitive Demand in Older Adults

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Abstract

Background Muscle fatigability can increase when a stressful, cognitively demanding task is imposed during a low-force fatiguing contraction with the arm muscles, especially in women. Whether this occurs among older adults (> 60 years) is currently unknown.

Questions/purposes We aimed to determine if higher cognitive demands, stratified by sex, increased fatigability in older adults (> 60 years). Secondarily, we assessed if varying cognitive demand resulted in decreased steadiness and was explained by anxiety or cortisol levels.

Methods Seventeen older women (70 ± 6 years) and 13 older men (71 ± 5 years) performed a sustained, isometric, fatiguing contraction at 20% of maximal voluntary contraction until task failure during three sessions: high cognitive demand (high CD = mental subtraction by 13); low cognitive demand (low CD = mental subtraction by 1); and control (no subtraction).

Results Fatigability was greater when high and low CD were performed during the fatiguing contraction for the women but not for the men. In women, time to failure with high CD was 16 ± 8 minutes and with low CD was 17 ± 4 minutes, both of which were shorter than time to failure in control contractions (21 ± 7 minutes; high CD mean difference: 5 minutes [95% confidence interval {CI}, 0.78–9.89], $p = 0.02$; low CD mean difference: 4 minutes [95% CI, 0.57–7.31], $p = 0.03$). However, in men, no differences were detected in time to failure with cognitive demand (control: 13 ± 5 minutes; high CD mean difference: −0.09 minutes [95% CI, −2.8 to 2.7], $p = 1.00$; low CD mean difference: 0.75 minutes [95% CI, −1.1 to 2.6], $p = 0.85$). Steadiness decreased (force fluctuations increased) more during high CD than control. Elevated anxiety, mean arterial pressure, and salivary cortisol levels in both men and women did not explain the greater fatigability during high CD.

Conclusions Older women but not men showed marked increases in fatigability when low or high CD was imposed

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
This study was conducted at Marquette University, Milwaukee, WI, USA.

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during sustained static contractions with the elbow flexor muscles and contrasts with previous findings for the lower limb. Steadiness decreased in both sexes when high CD was imposed.

Clinical Relevance Older women are susceptible to greater fatigability of the upper limb with heightened mental activity during sustained postural contractions, which are the foundation of many work-related tasks.

Introduction

Fatigability is quantified as a reduction in maximal strength or the time to failure of a submaximal fatiguing contraction [6, 10]. There are sex differences in fatigability because women are frequently less fatigable than men, although the specific demands of a task may change this difference [10]. For example, when a high-cognitive demand task, which increased stress, was performed while sustaining a contraction with the elbow flexor muscles, young women (18–30 years) had greater reductions in the time-to-task failure than young men [38], suggesting increased fatigability. Initial strength was predictive such that weaker participants (mostly women) exhibited the greatest increases in fatigability when a stressful cognitive demand was imposed [16, 38]. The young women also exhibited larger cardiovascular responses (increased blood pressure, heart rate, and rate pressure product) to the heightened cognitive demand at rest and during the fatiguing contraction. The findings potentially have significant clinical and scientific implications because heightened cardiovascular responses to stress long term during daily and work-related tasks will increase cardiac stress. Certainly, physiologic responses to stress are an important determinant of health [13].

Age-related reductions in strength [21] and subclinical reductions in cognitive function [29] may predispose older men and women (> 60 years) to increased fatigability of the upper limb when exposed to increased cognitive demand. Imposing a cognitive task that increases arousal and stress can reduce walking velocity, impair balance, and decrease steadiness in older men and women [1, 5, 20, 35, 36]. For the lower limb, imposing cognitive demand increased the between- and within-subject variability in motor performance among older adults much more than for the young, but fatigability of the ankle dorsiflexor muscles was not increased in either age group [35]. For older adults, however, fatigability of the upper extremity may respond differently to the lower limb as it does in younger persons [16, 38]. The upper limb has a greater number of corticospinal connections than lower limb muscles [3], which are more likely to receive interference from the prefrontal cortical areas when a cognitive task is imposed during a motor task [19]. Age-related reductions in corticospinal connections and prefrontal atrophy [27] could increase fatigability of the upper limb when cognitive demand is heightened. It is not known if the sex difference in fatigability and reduced steadiness seen for the upper limb of young adults [38] persist into older age. Describing population differences will be helpful in understanding susceptibility to fatigability during sustained upper limb muscle activity that is common to many postural daily and work-related tasks when cognitive demand is required.

We aimed to determine if higher cognitive demand, stratified by sex : (1) increased fatigability; (2) decreased steadiness; and (3) could be explained by increased arousal and stress (mean arterial pressure, anxiety, and salivary cortisol levels) in older adults during submaximal isometric fatiguing contractions with the upper extremity. We hypothesized that compared with the older men, older women would exhibit greater reductions in the time-to-task failure when a cognitive demand was imposed as previously reported in young adults [38]. Steadiness was quantified as an index of motor output variability/control of force and electromyographic activity was used to estimate neuromuscular adjustments.

Patients and Methods

Our study participants included 17 women (70 ± 6 years) and 13 men (71 ± 5 years). All were naive to the protocol, healthy, without any neurologic, orthopaedic, or cardiovascular condition, and with no reported history of anxiety or depressive disorder. Each participant provided informed consent and all study procedures were approved by the institutional review board at Marquette University.

Participants reported to the laboratory for an initial familiarization session followed by three experimental sessions (> 7 days apart). During the familiarization session, handedness [24], physical activity [17], and cognitive function were assessed with questionnaires (Table 1). During each experimental session, participants performed fatiguing contractions with elbow flexor muscles in high or low cognitive demand sessions and without cognitive demand (control session). All sessions were performed in the afternoon because of the circadian rhythm of cortisol [26, 30].

Cognitive Function Assessment

Neuropsychologic tests were administered to assure intact memory and executive functioning and to examine possible sources of sex differences on study variables. Dementia screening was conducted with the Mini-Mental State

Table 1. Physical characteristics and cognitive function of men and women participants

Physical characteristic and cognitive function	Men (n = 13)	Women (n = 17)	p value
Age (years)	70.5 ± 5.6	70.2 ± 6.2	0.91
Height (m)	1.73 ± 8.1	1.62 ± 5.1	< 0.001
Body mass (kg)	88.7 ± 9.3	64.4 ± 8.2	< 0.001
PAQ (MET-hour/week)	40.1 ± 36.0	33.7 ± 27.9	0.59
Handedness (0–1)	0.8 ± 0.1	0.7 ± 0.4	0.22
Years of education	15.6 ± 2.4	15.6 ± 2.2	0.99
Geriatric Depression Scale (0–15)	0.6 ± 0.8	1.0 ± 1.9	0.45
Mini-Mental State Examination (0–30)	28.2 ± 1.95	28.7 ± 1.84	0.41
Trail-Making Tests-A (seconds)	24.3 ± 6.4	26.1 ± 6.8	0.47
Trail-Making Tests-B (seconds)	61.6 ± 38.5	59.1 ± 25.3	0.85
Symbol Digit Modalities Test (correct)–oral	51.3 ± 7.5	56.1 ± 8.9	0.12
Symbol Digit Modalities Test (correct)–written	46.9 ± 7.7	50.5 ± 8.1	0.21
Letter Number Sequencing Test (total raw score)	9.4 ± 2.4	9.8 ± 2.4	0.65
RVLT (immediate recall)	7.4 ± 3.3	9.2 ± 2.3	0.09
RVLT (delayed recall)	7.1 ± 3.4	9.4 ± 2.9	0.06

Values are mean ± SD; handedness was assessed with the Edinburg Handedness Inventory with a ratio of 1 indicating complete right handedness. The short form of Geriatric Depression Scale (0–15) was used with values < 5 indicating little to no evidence of depression; PAQ = Physical Activity Questionnaire; MET = metabolic equivalent; RVLT = Rey Auditory Verbal Learning Test.

Examination (all > 24) [7]. Depression was screened for with the Geriatric Depression Scale (all < 5) [31]. Episodic memory was assessed using the Rey Auditory Verbal Learning Test [28, 34], and tests assessing executive functions (processing speed, attention, working memory) included the Trail-Making Tests A and B [33], Letter-Number Sequencing [37], and the Symbol-Digit Modalities Test [14]. All these tests were administered by a trained investigator (BS-D).

Each participant attended three sessions: control, low cognitive demand (low CD), and high cognitive demand (high CD). The order of the sessions was counterbalanced among the women and the men separately. Sessions were separated by at least 1 week and each session included the following procedures (Fig. 1): (1) maximal strength: measurements of three to four maximum voluntary isometric contractions (MVCs) of the elbow flexor muscles and the elbow extensor muscles with a 60-second rest between contractions. The greatest torque achieved with the elbow flexor muscles was used to calculate the 20% MVC target for the fatiguing contraction; (2) cognitive demand at rest: participants performed 4 minutes divided in 2-minute bouts (detailed as 2 minutes × 2 minutes in Fig. 1) of low CD, high CD, or quiet sitting (control) followed by approximately 20 minutes of quiet rest, which allowed salivary cortisol to peak in response to the stimulus [38]; (3) fatiguing contraction with the elbow flexor muscles at 20% MVC. Each participant matched the vertical target force that was displayed on the monitor and was encouraged to sustain the force for as long as possible. Task failure was detected automatically using a custom-designed program (Spike 2; Cambridge Electronic Design [CED], Cambridge, UK). To minimize the influence of transient fluctuations in motor output on the criteria of task failure, the fatiguing contraction was terminated only when force fell below 10% of the target force for 2.5 seconds of a 5-second interval. Mental math was performed during the contraction in the high and low CD sessions with no mental math during the control fatiguing contraction; and (4) recovery: MVCs were assessed immediately at task failure and then at 3, 6, 10, and 20 minutes after the fatiguing contraction (Fig. 1).

Mental math is an established technique to induce stress and it was used to vary the levels of cognitive demand [13, 23]. The high CD task involved serial subtraction from a four-digit number by 13 with one count required every 3 seconds. When the participant made an error or was not able to provide the correct answer within 3 seconds, the participant was required to begin with a new four-digit number [35, 38]. The low CD task involved continuous subtraction by 1, starting from 100, with one count every 3 seconds (Fig. 1).

The experimental setup has been previously described [16, 38]. In brief, the elbow flexor muscle forces were assessed with participants seated upright with the nondominant arm abducted slightly and the elbow flexed to 90°. The nondominant arm was chosen to minimize variability between

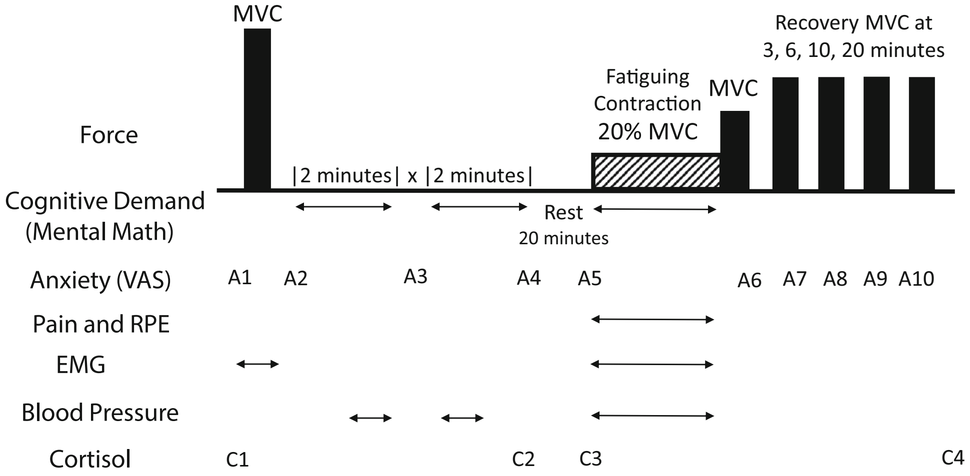

Fig. 1 The experimental protocol design is shown. Order of isometric force tasks performed by each participant with the elbow flexor muscles is shown in the top panel. Maximum voluntary contraction (MVC) (solid bars) were performed at the start and during recovery (immediately after the fatiguing contraction and at 3, 6, 10, and 20 minutes of recovery). The fatiguing contraction (20% MVC) is shown with the hatched rectangle and was performed until task failure. Bottom panels show horizontal arrows indicating when the mental math (cognitive demand) was performed: (1) at rest for two 2-minute bouts each before the fatiguing contraction; and (2) continuously during the fatiguing contraction. In the control session, each participant sat quietly for 4 minutes (divided in 2 minutes [represented by 2 × 2 minutes]) and performed the fatiguing contraction with no cognitive demand. Horizontal arrows also indicate when electromyography (EMG), blood pressure, visual analog scale (VAS) for rating of perceived exertion (RPE), and pain were recorded during each test session. Time points to record salivary cortisol (C1-C4) and anxiety (A1-A10) are indicated throughout the protocol. Note that the schematic is not to scale for time or force.

subjects that may occur as a result of differences in activities performed with the dominant arm. The forearm was placed midway between pronation and supination. Force was recorded online at 500 samples/second using a Power 1401 A-D converter (CED) and Spike 2 software (CED).

Electromyography (EMG) was recorded with bipolar surface electrodes placed over biceps brachii, brachioradialis, and triceps brachii muscles according to international standards [8]. Reference electrodes were placed on a bony prominence at the elbow. EMG was bandpass-filtered (13–1000 Hz) and amplified (× 1000) (Coulbourn Instruments, Allentown, PA, USA) before being recorded online at 2000 samples/second.

Heart rate and blood pressure were monitored during the period of cognitive demand at rest (2 minutes × 2 minutes with no contraction) and during the fatiguing contractions (Fig. 1). Heart rate and blood pressure were measured with an automated beat-by-beat blood pressure monitor (NIBP-100D noninvasive blood pressure system coupled with a MP150 data acquisition system; Biopac, Goleta, CA, USA). The blood pressure cuffs were placed around the index and middle fingers 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 a computer with the Power 1401 A-D converter and Spike 2 software (CED) at 500 samples/s.

Anxiety was assessed at baseline and during the protocol (Fig. 1) using a 10-point visual analog scale (VAS) anchored at the far left by "not at all anxious" and at the far right by "very anxious" as described before [38].

A modified Borg 10-point scale was used to assess perception of effort of the arm during the fatiguing contraction [2]. The scale was anchored so that "1" was complete rest and "10" corresponded to the hardest effort to perform a muscle contraction with the arm. Rating of perceived exertion (RPE) was recorded every minute until task failure occurred during the fatiguing contraction [38].

A VAS was used to access pain in the elbow flexor muscles. The scale was anchored so that "0" represented no pain and "10" corresponded to the worst pain imaginable [4].

Salivary cortisol was assessed during each experimental session as previously described [26, 38]. Four saliva samples were collected using oral swabs (Salimetrics LLC, State College, PA, USA) during each session at the following time points: before MVC, immediately after the mental math at rest (no muscle contraction), 20 minutes after the 2 × 2-minute intervals, and 20 minutes after the fatiguing contraction (Fig. 1, C1–4). The samples were stored at −30° C for later analysis. Enzymatic immunoassay (Salimetrics LLC) was used to determine levels of free cortisol. One baseline sample at night (approximately 10 PM) was also collected on a typically less stressful day.

MVC torque was quantified as the average force over a 0.5-second interval centered about the peak. The maximal

EMG for each muscle was determined during the same 0.5-second peak force as the root mean square (RMS) and used to normalize EMG during the fatiguing contractions. Steadiness (force fluctuations) during the fatiguing contractions was quantified using the coefficient of variation (CV) of the force (CV = SD/mean × 100). RMS EMG, blood pressure, and CV of force were quantified during the fatiguing contraction at five 30-second intervals during each fatiguing contraction (ie, the first and last 30 seconds of task duration and 15 seconds either side of 25%, 50%, and 75% of time to task failure) (Fig. 1).

For each cognitive demand period (2 minutes × 2 minutes at rest) and fatiguing contractions, 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). Mean arterial pressure (MAP) was calculated for each epoch with the following equation: $MAP = DBP + 1/3\ (SBP - DBP)$.

Data were reported as mean ± SD. Each dependent variable (time-to-task failure, CV of force, anxiety and pain levels, EMG [%MVC], MVC force, MAP, heart rate, and RPE) was analyzed with repeated-measures analysis of variance with sex (men, women) as a between-subject factor. Repeated measures included session (control, low CD, and high CD), time (before, middle, and after the 2 × 2-minute cognitive demand), time during the fatiguing contraction (0%, 25%, 50%, 75%, and 100% of fatiguing contraction), and recovery (up to 20 minutes).

Physical characteristics, activity levels, and cognitive function data were compared between sexes with independent t-tests. Spearman correlation analysis was used to determine associations between variables. Level of significance was $p < 0.05$ and the analyses were performed in SPSS (Version 21; IBM, Armonk, NY, USA).

Results

Older men were taller and heavier than the older women, but otherwise the sexes did not differ in age, physical activity levels, handedness, or cognitive function involving executive function and working memory (Table 1). Men were stronger than the women at baseline (66 ± 7 versus 32 ± 8 Nm; sex effect: $p < 0.001$) and the MVC was similar across sessions (session: $p = 0.11$) for both sexes (session × sex: $p = 0.17$) (Fig. 2A). There was no difference in the error rate of mental math during high CD between men (2 ± 1 errors/min^{-1}) and women (3 ± 1 errors/min^{-1}; $p = 0.27$). Time to task failure was less (ie, greater fatigability) when high and low CD were imposed during the fatiguing contraction for the older women but not for the older men (session × sex: $p = 0.04$) (Fig. 2B). In older women, time to failure with high CD was 16 ± 8 minutes and with low CD was 17 ± 4 minutes, both of which were less than time to failure during the control session (21 ± 7 minutes; high CD mean difference: 5 minutes [95% confidence interval {CI}, 0.78–9.89], $p = 0.02$; low CD mean difference: 4 minutes [95% CI, 0.57–7.31], $p = 0.03$). However, in older men, there were no differences in time to failure with the differing cognitive demands (control: 13 ± 5 minutes; high CD mean difference: −0.09 minutes [95% CI, −2.8 to 2.7], $p = 1.00$; low CD mean difference: 0.75 minutes [95% CI, −1.1 to 2.6], $p = 0.85$).

At task failure, MVC force was reduced similarly across sessions (session: $p = 0.61$) for both older men and women (session × sex: $p = 0.20$). MVC force recovered similarly across sessions (session $p = 0.53$) for older men and (session × time: $p = 0.14$) (Fig. 2A).

Force fluctuations increased with fatigue (time effect: $p < 0.001$) (Fig. 2C) and there were greater force fluctuations during the high CD than control session (session effect: $p = 0.03$) (Fig. 2C). Consequently, when the five time points are pooled, analysis by cognitive demand revealed that the control session had lower CV (4 ± 1.1%) compared with high CD (5 ± 2.1%, mean difference: −1.1% [95% CI, −2.1 to −0.1], $p = 0.03$) but not compared with low CD (4 ± 0.7%, mean difference: 0.001% [95% CI, −0.49 to 0.50], $p = 0.20$). There was no influence of sex on the CV of force (sex effect: $p = 0.52$; session × sex: $p = 0.24$).

EMG activity of the biceps brachii was less for older men (23 ± 9% of MVC) than women (33 ± 9% MVC; mean difference: 10% of MVC [95% CI, 3.4–17] of MVC when data during fatiguing contraction are pooled over the five time points; sex effect: $p < 0.001$, Fig. 3A). For biceps brachii, the EMG activity increased during all fatiguing contractions (time effect: $p < 0.001$) for both the older men and women (time × sex: $p = 0.11$) with no session effect ($p = 0.31$) so that EMG ended at similar amplitudes for each session despite the briefer time to failure for the women. Moreover, there was also no sex difference in biceps brachii EMG activity at task failure. EMG activity of the brachioradialis and triceps brachii both increased during the fatiguing contractions (time effect: $p < 0.001$) with no differences between the older men and women or no difference between sessions (session effect and session × sex: $p > 0.56$; Fig. 3B).

Elevated anxiety and salivary cortisol levels in both older men and women did not explain the greater fatigability during high CD. The VAS for anxiety was similar at baseline across all sessions for older men and women (session effect: $p = 0.71$; session × sex: $p = 0.88$; Fig. 4A, A1–2). When high CD was imposed at rest, anxiety tended to increase more for older women than men (session × sex: $p = 0.05$).

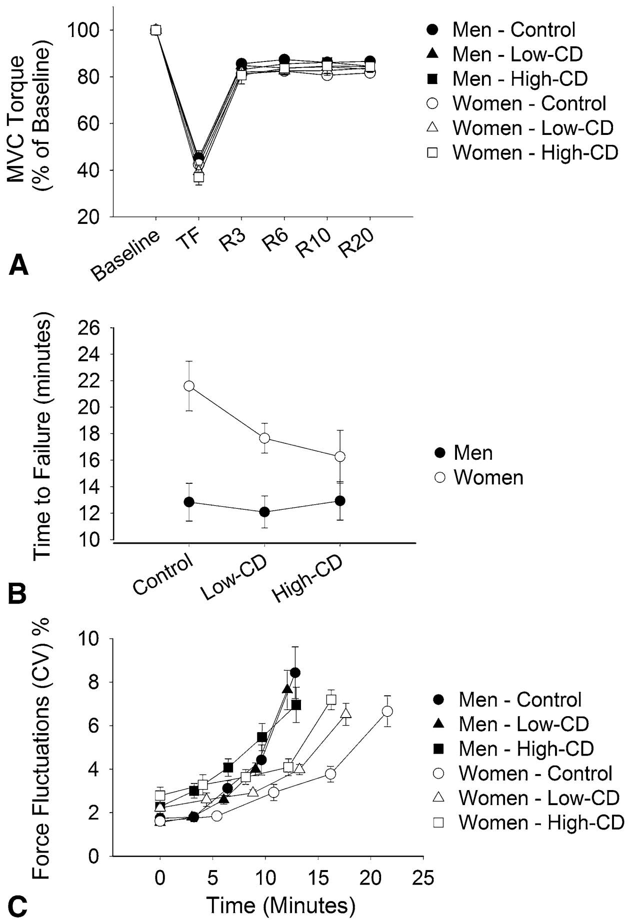

Fig. 2A–C (**A**) Percent maximum voluntary contraction (MVC) torque for older men and women before fatigue (baseline) and immediately at the end of the fatiguing contraction (task failure [TF]) is shown. Recovery time points are indicated by R3, R6, R10, and R20 (representing 3, 6, 10, and 20 minutes from task failure, respectively). Both older men and women had similar reductions in MVC force at task failure for all test sessions ($p > 0.05$). (**B**) Time-to-task failure for control, low cognitive demand (Low-CD) and high cognitive demand (High-CD) sessions. (**C**) Force fluctuations quantified as the CV of force (%) during the fatiguing contraction. CV values during the fatiguing contraction are shown at 25% increments of time-to-task failure for 30-second intervals. For all panels, each data point shown as mean ± SE. Control = control session; Low-CD = low cognitive demand session; High-CD = high cognitive demand session.

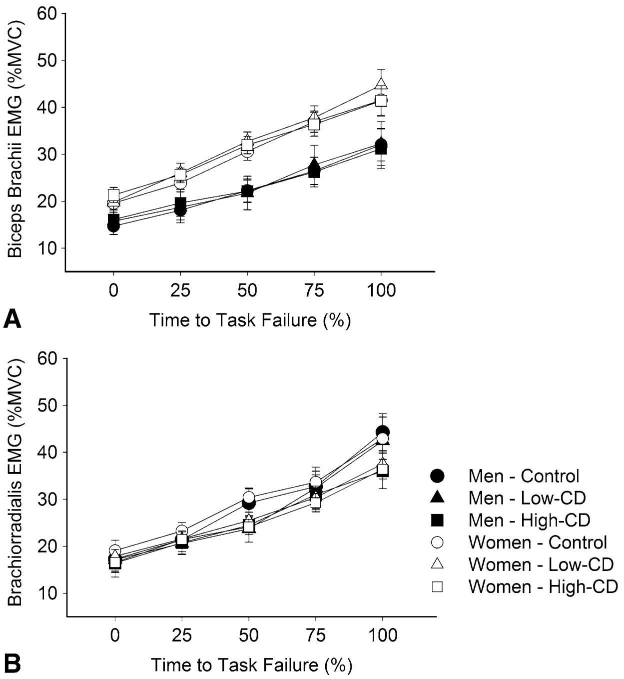

Fig. 3A–B Electromyographic activity (EMG) of (**A**) biceps brachii and (**B**) brachioradialis is represented as the root mean square (RMS) EMG (% of maximum voluntary contraction [MVC]). Each data point represents mean ± SE at 25% increments of the time-to-task failure for a 30-second interval. Control = control session; Low-CD = low cognitive demand session; High-CD = high cognitive demand session.

Post hoc analysis indicated that older women increased anxiety with high CD (5 ± 2 au [95% CI, −4.6 to −2.5]; mean difference: 3.6; $p < 0.001$) and low CD (2 ± 1 au [95% CI, −1.9 to 0.6] mean difference: 1.2; $p = 0.001$) compared with control (1.0 ± 1 au). Older men also had increased anxiety with high CD (3 ± 2 au [95% CI, 1.7–4.3]) compared with control (0.8 ± 1 au [95% CI, 0.01–1.6]; mean difference: 2; $p = 0.002$) but not with low CD (1.6 ± 1 au; mean difference: 0.8 [95% CI, −1.7 to 0.1]; $p = 0.07$) (Fig. 4A, A4). There was no correlation between the increase in anxiety and fatigability or steadiness with cognitive demand for both men or women (all analyses showed $r < 0.20$; $p > 0.27$) After the fatiguing contraction, anxiety was higher during the high CD than control and low CD sessions (session: $p < 0.001$, Fig. 4A, A6), but the increase was similar for the men and women (session × sex: $p = 0.49$).

Cortisol increased with high CD (session × time: $p < 0.001$, Fig. 4B, C3) and was similar for men and women (session × time × sex: $p = 0.86$). Analysis by cognitive demands revealed that when the four time points during the session are pooled, the control session had lower values (0.18 ± 0.05 $\mu g/dL^{-1}$ compared with high CD (0.22 ± 0.1 $\mu g/dL^{-1}$, mean difference: −0.04 [95% CI, −0.07 to 0.005], $p = 0.03$) but not compared with low CD (0.18 ± 0.1 $\mu g/dL^{-1}$, mean difference: −0.003 [95% CI, −0.03 to 0.02], $p = 0.82$). There was no association between cortisol and time to task failure with cognitive demand ($r < -0.5$; $p > 0.12$).

Other Findings

Heart rate and MAP increased across sessions and the sexes in a similar pattern so only MAP is reported (Fig. 4C).

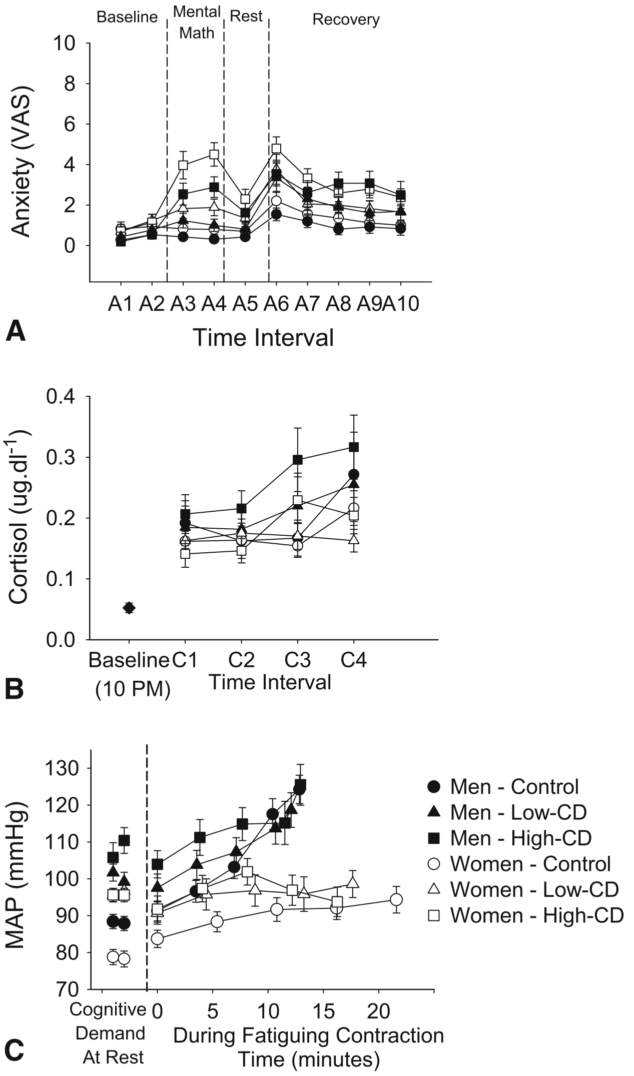

Fig. 4A–C (**A**) Visual analog scale (VAS) scores for anxiety throughout the protocol are shown. Time intervals were: baseline before and after maximum voluntary contraction (MVC) (A1, A2); after the first 2 minutes of cognitive demand at rest (A3); after the second bout of 2 minutes of cognitive demand at rest (A4); after 20 minutes of rest (A5); immediately after fatigue (A6); and during recovery at 3, 6, 10, and 20 minutes (A7-A10). (**B**) Free cortisol levels from saliva samples. Baseline level was assessed at approximately 10:00 PM on a minimally stressful day. Other data points represent: C1 = the beginning of each test session at rest; C2 = after the 4 minutes (2 × 2 minutes) of cognitive demand at rest; C3 = after approximately 20 minutes of the cognitive demand at rest; C4 = 20 minutes after the fatiguing contraction. (**C**) Mean arterial pressure (MAP) at rest (the 4 minutes divided in 2 × 2 minutes) and during fatiguing contraction for control, low- and high-cognitive demand sessions. During fatiguing contraction, the values are represented at 25% increments of the time to task failure. Each data point represents mean ± SE. Control = control session; Low-CD = low cognitive demand session; High-CD = high cognitive demand session.

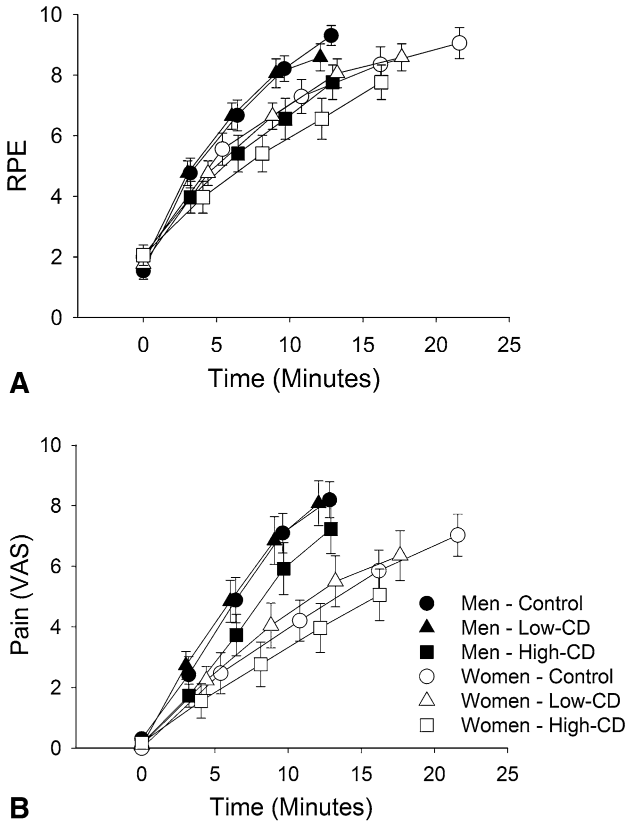

Fig. 5A–B (**A**) Rating of perceived exertion (RPE); and (**B**) pain rating from the visual analog scale (VAS) during the fatiguing contraction in all sessions for older men and women. Each data point represents the mean ± SE at 25% increments of the time-to-task failure. Control = control session; Low-CD = low cognitive demand session; High-CD = high cognitive demand session.

When low and high CD were imposed at rest (ie, Cognitive Demand at Rest in Fig. 4C), MAP increased compared with control session (session effects: $p < 0.001$) without sex differences (session × sex: $p > 0.05$). MAP increased during the fatiguing contractions across all sessions (time effect: $p < 0.001$). MAP, however, was greater during the low and high CD compared with control session (session effect: $p < 0.02$). Older men increased MAP at greater rates than the older women (time × sex: $p < 0.001$) as a result of greater baseline MVC of men ($r = 0.63$; $p < 0.001$), but the relative increase in MAP with high and low CD was similar between sexes (session × sex: $p > 0.52$; time × sex × session: $p > 0.85$). There was no association between MAP and time to task failure or steadiness ($r < 0.2$; $p > 0.26$).

The rate of increase in pain was greater in older men (0.83 ± 0.3 pain/min^{-1}) compared with women (0.43 ± 0.04 pain/min^{-1}; mean difference: 0.40 pain/min^{-1} [95% CI. 0.11–0.69]; sex effect: $p = 0.01$). For the rate of increase in RPE, older men (0.79 ± 0.3 number/min^{-1}) also presented greater increases than women (0.49 ± 0.4 number/min^{-1}; mean difference: 0.30 number/min^{-1} [95% CI, 0.05–0.55]; sex effect: $p = 0.02$]. Despite the sex differences in the rate of increase in pain and RPE during fatiguing contraction, cognitive demand reduced the pain and RPE (session effect: $p < 0.001$) similarly in men and women (session × sex: $p > 0.84$; Fig. 5).

Discussion

We previously showed that young women (18–30 years) and not men had greater fatigability and decreased steadiness during a sustained isometric contraction with the elbow flexor muscles when high CD was imposed but not low CD [16, 38]. The current study was designed to identify whether older men and women increased fatigability and decreased steadiness during submaximal isometric fatiguing contractions with the elbow flexor muscles. We also determined if altered motor performance could be explained by increased arousal (indicated by MAP, anxiety, and salivary cortisol levels) in older adults.

The greater fatigability when high CD was imposed during the isometric sustained contractions in young adults was associated with baseline strength [16] such that weaker individuals were more susceptible to increased fatigability, possibly as a result of altered muscle perfusion [11, 12, 16]. This was achieved because we were able to match some of the male and female cohort for strength [16]. A limitation of the current study was the differences in strength between the older men and women were large and did not overlap between groups. Thus, although we were able to establish that older women had greater changes in fatigability with imposed cognitive demand and that they were weaker than the older men, we were not able to identify any relationship with strength because of the large between group strength differences in older adults. Our study did, however, examine the role of various indices of arousal and different levels of cognitive demand imposed in this older cohort.

The novel findings are that older women exhibited greater fatigability of the arm muscles when both low and high CD were imposed during sustained static contractions, whereas older men showed no change in fatigability. Both younger and older men and women, however, did not have altered fatigability of a lower limb muscle group (ankle dorsiflexors) when performed at 30% MVC [35]. A larger number of corticospinal connections on the upper than lower limb muscles [3] and greater potential interference from the prefrontal cortical areas when increased cognitive demand is required may decrease motor performance [25] and fatigability more for the upper limb muscles [19]. Alternatively, the stressor-induced fatigability may only be relevant during low-force contractions. Accordingly, cognitive demand influenced the fatigability of the shoulder abductors during a moderate intensity but not in a high-intensity, intermittent contraction in young adults [18]. Furthermore, low-force contractions, which were sustained for longer durations than high-force tasks, involve greater fatigue originating from the central nervous system and upstream of the motor cortex, particularly in older adults [32, 39, 40].

Steadiness decreased with heightened levels of cognitive demand. A possible explanation for the loss of steadiness is related to changes in the common synaptic input [22] with cognitive demand. The lack of sex differences in steadiness with cognitive demand indicates that the disruption in the common synaptic input with cognitive demand was likely similar in older men and women. There are two potential mechanisms leading to altered common synaptic input to motor units as cognitive demand increased. First, heightened cognitive demand could directly influence the common synaptic input [22, 25]. Second, sympathetic activation induced by cognitive demand may be responsible. Accordingly, MAP and cortisol levels were not different between sexes, which is consistent with the lack of sex differences in steadiness. However, we did not find any association between indices of sympathetic activity (such as MAP) and steadiness, which is consistent with another study [5]. Thus, direct influence of cognitive demand on common synaptic input may be involved.

Our study established that the increase in fatigability of the women was not associated with baseline cognitive function (executive function, including working memory), anxiety levels, cortisol levels in response to the different cognitive demands and contractions, error rates in mental math during the contractions, or physical activity levels because none of these factors differed between the older men and women. Although women reported a tendency for higher anxiety than the men during the high CD session when the mental math was performed at rest, there was no association between anxiety and fatigability. Anxiety levels were also similar at task failure between the sexes. Cortisol, which increases in response to stress [13], was greater during the high CD task than control but did not differ between men and women. MAP also increased with low and high CD similarly in older men and women and consequently did not explain the sex differences in fatigability with cognitive demand. Interestingly, pain and perceived effort were less during the high CD session than control and low CD for both older men and women, possibly as a result of stress-induced analgesia [9]. EMG was greater in women than men at the start and end of the fatiguing contraction representing differences in muscle activation, but EMG did not alter with cognitive demand during the sessions. Reductions in the MVC were also similar at task failure across all sessions and between men and women (Fig. 2A), indicating the sustained contractions did not end prematurely in older women. Collectively these findings suggest that other factors must explain the greater fatigability with cognitive demand such as changes upstream of the motor cortex or even possibly strength-related mechanisms as we have noted for the young [16].

In summary, older women, who are generally weaker than similar-aged men, were vulnerable to increased fatigability and loss of steadiness during upper limb sustained contractions when cognitive demand was increased. These data have significant implications for sustained work-related motor tasks that require high and low mental activity in an aging workforce. The mechanisms for greater fatigability with increased cognitive demand among older women warrant further investigation to inform strategies to offset potential motor deficits.

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