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Supraspinal Fatigue Impedes Recovery From a Low-Intensity Sustained Contraction in Old Adults

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Supraspinal fatigue impedes recovery from a low-intensity sustained contraction in old adults

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Abstract

This study determined the contribution of supraspinal fatigue and contractile properties to the age difference in neuromuscular fatigue during and recovery from a low-intensity sustained contraction. Cortical stimulation was used to evoke measures of voluntary activation and muscle relaxation during

and after a contraction sustained at 20% of maximal voluntary contraction (MVC) until task failure with elbow flexor muscles in 14 young adults (20.9 ± 3.6 yr, 7 men) and 14 old adults (71.6 ± 5.4 yr, 7 men). Old adults exhibited a longer time to task failure than the young adults (23.8 ± 9.0 vs. 11.5 ± 3.9 min, respectively, $P < 0.001$). The time to failure was associated with initial peak rates of relaxation of muscle fibers and pressor response ($P < 0.05$). Increments in torque (superimposed twitch; SIT) generated by transcranial magnetic stimulation (TMS) during brief MVCs, increased during the fatiguing contraction ($P < 0.001$) and then decreased during recovery ($P = 0.02$). The increase in the SIT was greater for the old adults than the young adults during the fatiguing contraction and recovery ($P < 0.05$). Recovery of MVC torque was less for old than young adults at 10 min post-fatiguing contraction (75.1 ± 8.7 vs. $83.6 \pm 7.8\%$ of control MVC, respectively, $P = 0.01$) and was associated with the recovery of the SIT ($r = -0.59$, $r^2 = 0.35$, $P < 0.001$). Motor evoked potential (MEP) amplitude and the silent period elicited during the fatiguing contraction increased less for old adults than young adults ($P < 0.05$). The greater fatigue resistance with age during a low-intensity sustained contraction was attributable to mechanisms located within the muscle. Recovery of maximal strength after the low-intensity fatiguing contraction however, was impeded more for old adults than young because of greater supraspinal fatigue. Recovery of strength could be an important variable to consider in exercise prescription of old populations.

Neuromuscular fatigue is an exercise-induced reduction in the expected muscle force or power.⁷ It results from impairment in voluntary drive to the muscle (voluntary activation) and muscular factors that directly cause a loss of force in the fibers.^{8,9} Age-related alterations in the neuromuscular system can predispose old adults to a different magnitude and mechanism(s) of neuromuscular fatigue.^{2,14} Age-related loss of muscle fibers and a reduction in proportional area of type II (fast) fibers, for example, lead to a weaker but more oxidative and fatigue resistant muscle.^{1,22} In contrast, age-related changes in the structure and function of the central nervous system [for review see³⁵] such as loss of gray and white matter, reduced cortical excitability and connectivity, and motoneuron degradation [for example^{4,28,30,31}] may impair the ability of old adults to provide high levels of neural drive to the muscle during fatiguing contractions.^{19,42}

A reduction in neural drive to the muscle during voluntary activity (reduced voluntary activation) is known as central fatigue and is attributable to depression of activity from spinal and supraspinal sources.⁹ Voluntary activation can be quantified by evoking a brief contraction with stimulation along the nervous system during a maximal voluntary contraction (MVC). Any extra force that is elicited by the stimulus (i.e., a “superimposed twitch”) indicates the motor units were not all recruited voluntarily or they were discharging at rates that were not high enough to produce full fusion of force.¹¹ Stimulation of the motor cortex can evoke an increment in force from the muscle during a maximal effort, localizing the site of failure of voluntary drive at or above the level of the motor cortical output.^{10,40} This exercise-related fall in voluntary activation measured with cortical stimulation is called supraspinal fatigue and is attributable to suboptimal motor output from the motor cortex.⁹

A functionally important but largely unexplored aspect of fatigue with advanced age is the period of recovery after a fatiguing bout of exercise. Recently, it was shown that old adults have slower recovery of supraspinal and motoneuron output than young adults after high-intensity sustained contractions.^{6,19} Greater supraspinal fatigue remained more depressed for the older adults during a 10-min recovery period,¹⁹ although the age-related difference in fatigue during the sustained contractions was associated with slower contractile properties in older adults (muscular mechanisms).^{6,19} Whether recovery is

impaired by supraspinal mechanisms after a low-intensity sustained contraction, which is common to daily tasks, is not known.

Certainly, low-intensity sustained fatiguing contractions can elicit substantial fatigue within the central nervous system.^{36,43} We showed that central fatigue can be greater with age in upper limb muscles immediately after a sustained low-force contraction⁴² but the contribution from supraspinal sources is not known and prolonged recovery has not been investigated. The purpose of this study was to determine the contribution of supraspinal fatigue and contractile properties to the age difference in fatigue during and recovery from a low-intensity fatiguing contraction. We hypothesized that the age difference in time to task failure would be associated with muscular mechanisms, but older adults would exhibit greater impairment in recovery of maximal strength because of a reduced ability to activate supraspinal centers. To provide insight into age-related differences in supraspinal fatigue and contractile properties, we stimulated the motor cortex using transcranial magnetic stimulation (TMS) during brief maximal contractions before, during, and after a low-force fatiguing contraction performed with the elbow flexor muscles.

METHODS

Fourteen young adults (21.9 ± 3.6 yr, 19–30 yr, 7 men and 7 women) and 14 old adults (71.6 ± 5.4 yr, 65–82 yr, 7 men and 7 women) volunteered to participate in this study. All subjects were healthy with controlled blood pressure, no known neurological diseases, and were naive to the protocol. Prior to participation, each subject provided written informed consent and the protocol was approved by the Marquette University Institutional Review Board.

Subjects reported to the laboratory on two occasions, once for a familiarization session and once for an experimental session to perform a protocol that focused on a fatiguing contraction with the elbow flexor muscles of the left arm. The familiarization session involved a physical activity questionnaire,²⁴ habituation of the electrical stimulation to the brachial plexus and TMS to the motor cortex, and practice of brief submaximal contraction and MVCs. Hand dominance was estimated using the Edinburgh Handedness Inventory²⁷ with a score of 0.77 ± 0.16 for young and 0.61 ± 0.15 for old adults ($P = 0.26$) and a ratio of 1 indicated complete right handedness. The experimental session involved performance of an isometric fatiguing contraction for as long as possible at a force equivalent to 20% of each subjects MVC.

Mechanical Recordings

Each subject was seated upright in an adjustable chair with their left arm slightly abducted. Their elbow was resting comfortably on a padded support, and the elbow joint was flexed to 90° so that the forearm was horizontal to the ground. The shoulders were restrained by two nylon straps to minimize shoulder movement. The hand and forearm were placed in a modified rigid wrist-hand-thumb orthosis (Orthomerica, Newport Beach, CA) midway between pronation and supination, and the force was directed upward when the elbow flexor muscles were activated. The forces exerted by the wrist in the vertical and horizontal directions were measured with a force transducer (Force-Moment Sensor, JR-3, Woodland, CA) that was mounted on a custom-designed adjustable support. The orthosis was fixed to the force transducer. The forces detected by the transducer were recorded online by using a Power 1401 A-D converter and Spike 2 software [Cambridge Electronics Design (CED), Cambridge, UK]. The

force exerted in the vertical direction was displayed on a 19-in. monitor located 1.5 m in front of the subject. The force signal was digitized at 500 samples/s.

Electrical Recordings

Electromyography (EMG) signals were recorded with a bipolar configuration using surface electrodes (Ag-AgCl, 8-mm diameter; 16 mm between electrodes) that were placed over the biceps brachii, brachioradialis, and triceps brachii muscles according to recommended placements.¹² Reference electrodes were placed on the lateral epicondyle of the elbow. The EMG signals were amplified (100×) and band-pass filtered (13–1,000 Hz) with Coulbourn modules (Coulbourn Instruments, Allentown, PA). The signal was displayed on an oscilloscope and recorded online via a Power 1401 A-D converter (CED). The EMG signals were digitized at 2000 samples/s.

Blood Pressure

As an index of the metaboreflex during the fatiguing contraction,²⁰ blood pressure was monitored with an automated beat-by-beat, blood pressure monitor (Finapres 2300, Ohmeda, Madison, WI). The blood pressure cuff was placed around the middle finger of the relaxed, right hand with the arm placed on a table adjacent to the subject at heart level. Initial blood pressure readings were taken manually at rest using a sphygmomanometer to calibrate the readings from the Finapres 2300. The blood pressure signal was recorded online at 500 samples/s.

Stimulation

Subjects were stimulated at the brachial plexus with electrical stimulation and at the motor cortex with TMS.

Brachial plexus stimulation.

The brachial plexus was electrically stimulated to produce a maximal compound muscle action potential (maximum M-wave: M_{max}) of the biceps brachii, brachioradialis, and triceps brachii muscles. A constant-current stimulator (model DS7AH, Digitimer, Welwyn Garden City, Hertfordshire, UK) was used to deliver single stimuli (100 μ s duration) to the brachial plexus. A cathode was placed in the supraclavicular fossa and an anode on the acromion. The stimulation intensity was determined by increasing the current until the peak-to-peak M-wave amplitude plateaued. The stimulation intensity ranged between 120 and 300 mA, and once this intensity was determined for each subject this level of stimulation was used for the remainder of the protocol.

Motor cortex stimulation.

TMS stimulation was delivered via a round coil (13.5-cm outside diameter) over the vertex of the motor cortex (Magstim 200, Magstim, Whitland, UK) to evoke motor-evoked potentials (MEPs) that were recorded from the biceps, brachioradialis, and triceps muscles. The vertex of the motor cortex was identified, and the scalp was marked to ensure repeatability of coil placement throughout the protocol. The right cerebral hemisphere was stimulated so the direction of the current flow in the coil preferentially activated the left limb. A single pulse was delivered over the motor cortex at an intensity that produced a large MEP in the agonist biceps muscle (minimum amplitude of 50% of M_{max} during a brief MVC of the elbow flexor muscles) and small MEP of the triceps (<20% M_{max}).⁴¹ TMS was delivered during voluntary contractions only.

Experimental Protocol

Optimal levels of stimulation intensities to the motor cortex and brachial plexus were determined, and these levels remained constant throughout the rest of the protocol. All procedures thereafter were as follows and are summarized in [Fig. 1](#).

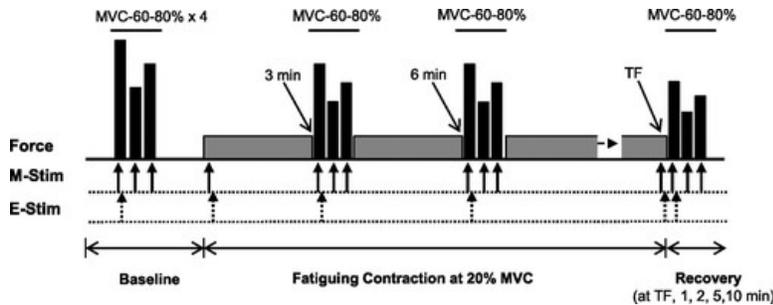


Fig. 1. Experimental protocol. *Top* order of force tasks performed by each subject with the elbow flexor muscles. Maximal voluntary contractions (MVC), followed by contractions at 60% and 80% of MVC (MVC-60–80%), were performed at the start, during the fatiguing contraction (at 3 and 6 min) and recovery [task failure (TF), and at 1, 2, 5, and 10 min after the fatiguing contraction]. The fatiguing contraction (20% of MVC) is symbolized with the shaded rectangle, and was performed by each subject until task failure. The second and third panel shows with the arrows, when the magnetic stimulation (M-Stim) and electrical stimulation (E-Stim) were applied during each contraction. Please note the figure is not to scale.

Maximal voluntary contractions.

Two MVCs of the elbow extensor muscles were performed so that peak EMG values could be obtained to normalize the triceps EMG activity during the fatiguing contraction. No stimulation was delivered during the elbow extensor contractions for either session. Four sets of brief contractions (2–3 s) with the elbow flexor muscles were performed and separated by 2 min of rest to minimize fatigue. Each set involved performance of a MVC followed by contractions at 60 and 80% MVC. Within each set, the start of each contraction was separated by 3–4 s. If peak forces from two of the four MVC trials were not within 5% of each other, additional trials were performed until this was accomplished. TMS was delivered during each contraction, and brachial plexus stimulation was delivered during the MVCs only within the set of contractions. Sets of contractions (MVC, 60, and 80% of MVC) along with the above described stimulation were also performed during the fatiguing contraction at 3 and 6 min and then several times during 10 min of recovery (see *Recovery measures*).

Fatiguing contraction.

A fatiguing contraction was performed with the elbow flexor muscles at a target value of 20% MVC force (calculated from the peak MVC force). Each subject was required to match the vertical target force that was displayed on the monitor and encouraged to sustain the force for as long as possible. At 3 min and 6 min into the fatiguing contraction (prior to the set of brief contractions, i.e., MVC, 60, and 80%), TMS was delivered to elicit a MEP followed by electrical stimulation of the brachial plexus to elicit an M-wave while the subject was performing the 20% sustained contraction. The fatiguing contraction was terminated when an automated computer program (Spike 2, CED) indicated that the force had declined by 10% of the target value for 2.5 out of 5 consecutive seconds. This time was recorded as the time to task failure.

As an index of perceived effort, each subject verbally indicated their rating of perceived exertion (RPE) using the modified Borg 10-point scale³ at the start of the fatiguing contraction, every minute thereafter, and at task failure. The scale was anchored so that 0 represented the resting state and 10 corresponded to the strongest effort that the arm muscles could perform.

Recovery measures.

Sets of MVC force and submaximal contractions (60 and 80% MVC) were performed during recovery at the following times: immediately upon task failure and at 1 min, 2 min, 5 min, and 10 min after termination of the fatiguing contraction.

Data Analysis

The MVC force was quantified as the average value over a 0.5-s interval that was centered about the peak of the MVC. 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. The maximal EMG activity for each muscle was determined as the root mean square (RMS) value over a 0.5-s interval about the same interval of the MVC torque measurement. The maximal EMG value for the biceps brachii, brachioradialis, and triceps brachii was used to normalize the RMS EMG values recorded during the fatiguing contraction for each respective muscle. The RMS of the EMG signal of the elbow flexor muscles and triceps brachii muscles were quantified during the fatiguing contraction at the following time intervals: the first and last 15 s of task duration and 7.5 s either side of 25, 50, and 75% of time to failure.

The amplitude of the SIT elicited by TMS is reported as a percent of the voluntary torque measured immediately prior to TMS.¹⁰ The superimposed twitch amplitude was also used to calculate voluntary activation.⁴⁰ Voluntary activation was quantified by expressing the amplitude of the superimposed twitch (elicited by TMS) as a fraction of the estimated amplitude of the response evoked by the same stimulus at rest (estimated resting twitch). Because motor cortical and spinal cord excitability increase with activity¹³ the amplitude of the resting twitch was estimated (eRT) rather than measured directly.⁴⁰ During four brief maximal and submaximal contractions (60% MVC and 80% MVC) TMS was elicited, and the resting twitch was estimated by extrapolation of the linear relation between the amplitude of the SIT and voluntary torque. One regression analysis was performed for each set of brief contractions. The y-intercept was taken as the estimated amplitude of the resting twitch evoked by TMS. The amplitude of the estimated resting twitch can be accurately determined from three data points in fresh or fatigued muscle when the contractions are greater than 50% MVC.⁴⁰ Voluntary activation (%) was calculated as a percentage measured by cortical stimulation $[(1 - \text{SIT}/\text{eRT}) \times 100]$.⁴⁰ Data points were excluded when the regression of the estimated twitch was $r < 0.9$.¹⁹

Contractile properties of the elbow flexor muscle were also assessed. The amplitude of the estimated resting twitch was used as an index of the force generating capacity of the elbow flexor muscles. Peak relaxation rates were determined during each MVC by calculating the steepest falling of the torque during the EMG silence immediately following TMS.³⁹ This was determined as the highest negative derivative of the torque for an interval of 10 ms between two cursors placed either side of the fall in torque during the silent period. The steepest rate of torque decline was normalized to the total torque (MVC plus superimposed twitch) prior to the silent period.³⁹

The peak-to-peak amplitude and area of MEPs and M-wave were measured between two cursors placed at the start and end of the waveform for the biceps brachii muscles. Because MEP amplitude and area showed similar changes, only MEP amplitude is reported. M-waves were elicited after each MEP, so the MEP could be normalized to the ongoing M-wave amplitude. Voluntary torque was quantified by calculation of the mean torque over a 100-ms period immediately prior to TMS at the start and end of each sustained fatiguing contraction, during control and recovery MVCs, and during the submaximal contractions at 60 and 80% MVC. The silent period was measured as the interval from the stimulus to the resumption of continuous EMG. Silent period duration was assessed by two investigators independently. The coefficients of reliability were high when values from the two investigators were correlated (Cronbach's α above 0.98 for each of the time points compared), so the average value generated from the two investigators was analyzed and reported as the result.

Blood pressure was recorded during the fatiguing contraction and analyzed by comparing ~15-s averages at 25% intervals of the time to task failure (i.e., 15-s intervals at 0, 25, 50, 75, and 100% of time to failure). For each 15-s interval, the blood pressure signal was analyzed for the mean peaks [systolic blood pressure (SBP)] and mean troughs [diastolic blood pressure (DBP)]. Mean arterial pressure (MAP) was calculated for each epoch with the following equation: $MAP = DBP + 1/3(SBP - DBP)$. Two older adults were excluded from the analysis of MAP because they were on medication that controlled for blood pressure.

Statistical Analysis

Data are reported as means \pm SD within the text and displayed as means \pm SE in the figures. Analysis of variances (ANOVA, with age and sex as fixed factors) were used to compare physical characteristics, physical activity levels, time to task failure, baseline control variables including MVC, SIT, voluntary activation, estimated resting twitch amplitude, peak relaxation rate of muscle fibers, MEP amplitude, and the silent period duration in young and old adults. Repeated-measure ANOVAs with age and sex as fixed factors were used to compare the young and old adults across time for the following variables: MVC torque, SIT, estimated resting twitch amplitude, MEP amplitude, silent period duration, peak relaxation rate of muscle fibers. Separate ANOVAs were used to compare the change in these dependent variables across time 1) within a fatiguing contraction (control, 3 min, 6 min, and task failure) and 2) during recovery (task failure and 1 min, 2 min, 5 min, and 10 min recovery). Univariate ANOVAs with age as a factor were performed to compare rates of change in a dependent variable with time. Post hoc analysis (independent *t*-tests) was used to test for differences within the ANOVAs when appropriate. The strength of an association is reported as the squared Pearson product-moment correlation coefficient (r^2). A significance level of $P < 0.05$ was used to identify statistical significance.

RESULTS

Young and old adults were similar in height, handedness, levels of physical activity, and strength but different in body mass (see [Table 1](#)). Baseline data for young and old men and women for physical characteristics and other dependent variables are displayed in [Table 1](#).

Table 1. Subject characteristics and baseline values of young and old men and women

Variables	Unit	Young (n = 14)		Old (n = 14)		Age (P Value)	Sex (P Value)	Age × Sex (P Value)
		Men	Women	Men	Women			
Age	yrs	21.3 ± 3.9	20.5 ± 3.6	72.4 ± 5.6	70.8 ± 5.4	< 0.001	0.53	0.81
Height	cm	177 ± 10	164 ± 8	176 ± 13	164 ± 5	0.68	0.00	0.91
Body mass	kg	79.8 ± 10.5	57.9 ± 11.2	90.6 ± 11.7	69.2 ± 10.3	0.01	< 0.001	0.95
Handedness	a.u. (0-1)	0.7 ± 0.2	0.8 ± 0.2	0.7 ± 0.2	0.5 ± 0.7	0.27	0.49	0.37
Physical activity	METs·hr/wk	59.2 ± 36.3	30.9 ± 40.6	36.3 ± 40.6	35.0 ± 24.6	0.47	0.26	0.31
MVC torque	Nm	75.0 ± 27.2	34.6 ± 7.4	61.7 ± 8.8	31.4 ± 6.7	0.16	< 0.001	0.39
Time to task Failure	min	10.6 ± 4.1	12.4 ± 3.9	19.2 ± 6.7	28.3 ± 9.0	< 0.001	0.03	0.14
Voluntary activation	%	93.3 ± 4.5	91.1 ± 3.8	90.4 ± 3.1	85.4 ± 7.8	0.04	0.08	0.51
Resting twitch amplitude	Nm	27.9 ± 8.3	13.4 ± 3.7	26.4 ± 6.7	10.5 ± 3.1	0.33	0.001	0.76
Peak relaxation rate	s ⁻¹	12.7 ± 1.8	9.3 ± 1.0	11.0 ± 1.5	7.0 ± 1.4	< 0.001	< 0.001	0.57
Silent period	ms	199 ± 88.0	217 ± 61.1	226 ± 46.3	174 ± 50.3	0.72	0.49	0.16

Time to Task Failure and MVC Torque

Young adults had a briefer time to task failure than old adults for the 20% MVC fatiguing contraction (11.5 ± 3.9 vs. 23.8 ± 9.0 min, respectively, age effect, $F_{1,24} = 26.7$, $P < 0.001$). Women had a longer time to failure than the men (sex effect, 20.4 ± 10.6 vs. 14.9 ± 6.9 min, $F_{1,24} = 5.3$, $P = 0.03$). The age difference in time to failure was similar across the sexes (age × sex interaction, $F_{1,24} = 2.4$, $P = 0.14$).

MVC torque before the fatiguing contraction (control MVC) did not differ between the young and old adults (54.8 ± 28.4 vs. 46.5 ± 17.4 Nm, age effect, $F_{1,24} = 2.1$, $P = 0.16$). However, men had twice the strength of women (sex effect, 68.4 ± 20.6 vs. 33.0 ± 7.0 Nm, $F_{1,24} = 38.0$, $P < 0.001$) for both age groups (age × sex interaction, $F_{1,24} = 0.77$, $P = 0.39$); see [Table 1](#). MVC torque was reduced during and after the fatiguing contraction from control values for both age groups and sexes (time effect, $F_{3,22} = 54.5$, $P < 0.001$, [Fig. 2](#)). At the 6th min of the contraction, the relative decline in MVC (%change from control) was greater for the young adults than the old adults (time × age interaction, $F_{3,22} = 4.8$, $P = 0.01$). The 6th min

represented 52% of the time to failure of the young adults and 25% for the old adults. Immediately after termination of the fatiguing task, the relative decline in MVC torque from control was similar for the young and old adults (38.7 ± 10.0 vs. $38.4 \pm 11.9\%$, respectively, age effect, $F_{1,24} = 0.08$, $P = 0.78$). MVC torque gradually increased during the recovery period (time effect, $F_{4,21} = 9.8$, $P < 0.001$), but by 10 min of recovery, young adults had recovered relatively more MVC force than the old adults (83.6 ± 7.8 vs. $75.1 \pm 8.7\%$ of control MVC, respectively, age effect, $F_{1,24} = 7.0$, $P = 0.01$).

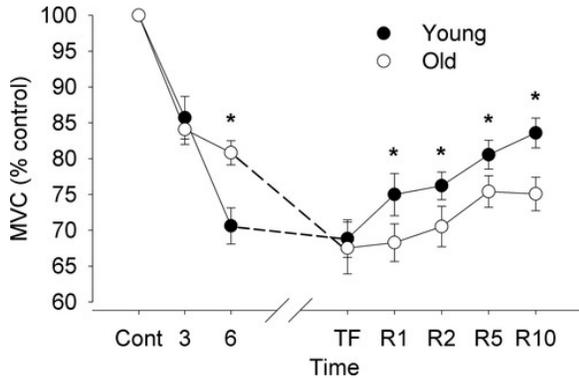


Fig. 2. MVC before, during and after the fatiguing contraction for the young and old adults. MVC force is expressed as a percent of the control MVC. The x-axis shows the mean MVC of control trials before the fatiguing contraction (Cont), at 3 min,³ 6 min,⁶ immediately after the fatiguing contraction (TF), and at 1 min (R1), 2 min (R2), 5 min (R5), and 10 min recovery (R10). The 6th min⁶ represented 52% of the time to failure of the young adults and 25% for the old adults. The dashed lines indicate the different durations to task failure for the young and old adults. Values are expressed as means \pm SE. *Age difference at $P < 0.05$.

SIT and Voluntary Activation

During the control MVCs, the SIT (relative to MVC) did not statistically differ between the young and old adults (2.9 ± 1.9 vs. $4.2 \pm 1.8\%$, respectively, age effect, $F_{1,24} = 3.7$, $P = 0.07$). Voluntary activation (calculated from the SIT) however, was greater for young adults ($92.1 \pm 4.1\%$, $n = 13$) compared with the old adults ($87.9 \pm 6.3\%$, $n = 14$, age effect, $F_{1,23} = 4.7$, $P = 0.04$) for the control MVCs.

SIT increased from initial control values during the fatiguing contraction and at task failure (time effect, $F_{3,21} = 13.9$, $P < 0.001$, Fig. 3A) and then decreased for both young and old adults during recovery (time effect, $F_{4,20} = 3.4$, $P = 0.03$). SIT, however, was greater for the old adults than young adults during the fatiguing contraction (age effect, $F_{1,24} = 6.5$, $P = 0.02$) and recovery (age effect, $F_{1,24} = 5.3$, $P = 0.03$). The age difference remained consistent during the fatiguing contraction and recovery (time \times age interaction, $F_{7,17} = 0.08$, $P = 0.61$).

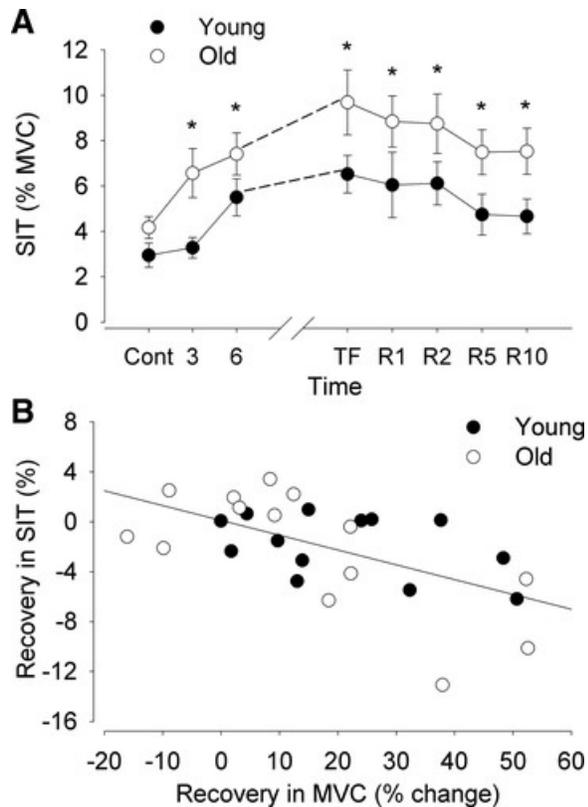


Fig. 3. Superimposed twitch (SIT) and associations with strength. *A*: SIT of young and old adults for control trials (averaged) before the fatiguing contraction (Cont), at 3 min,³ 6 min,⁶ immediately after the fatiguing contraction (TF), and at 1 min (R1), 2 min (R2), 5 min (R5), and 10 min recovery (R10). The 6th min⁶ represented 52% of the time to failure of the young adults and 25% for the old adults. The dashed lines indicate there were different durations to task failure for the young and old adults. Values are expressed as means \pm SE. *B*: association between the percent change in MVC torque from task failure to 10 min recovery and percent change in SIT (expressed as %MVC) between the same time points for young and old adults. Those individuals who had the greatest recovery of MVC torque (%increase) had the greatest recovery of SIT (absolute decrease in SIT when expressed as %MVC). A linear relation is shown ($r = 0.59$, $r^2 = 0.35$, $P = 0.01$).

Recovery of the MVC torque between task failure and 10 min of recovery was associated with the decrease in the SIT (absolute decrease in SIT when expressed as %MVC) ($r = -0.59$, $r^2 = 0.35$, $P < 0.001$, Fig. 3B). Thus those individuals who had the greater recovery in MVC torque also had the greater recovery of the SIT.

Estimated Resting Muscle Twitch

Estimated resting muscle twitch amplitude was similar for young (20.1 ± 9.6 Nm, $n = 13$) and old adults (18.5 ± 9.6 Nm, $n = 14$, age effect, $F_{1,23} = 1.0$, $P = 0.33$). Estimated twitch amplitude decreased during the fatiguing contractions (time effect, $F_{3,16} = 5.4$, $P = 0.01$) similarly for the young and old adults (time \times age interaction, $F_{3,16} = 2.3$, $P = 0.12$). Twitch amplitude decreased at task failure to 16.0 ± 7.7 Nm (20.5%) for the young adults and to 14.7 ± 7.6 Nm (20.6%) for the old adults. By 10 min recovery the twitch amplitude recovered to 90% of control values for both young and old adults.

Peak Rate of Relaxation of Muscle Fibers

The peak rate of relaxation during the control MVC was faster for young adults than the old adults (-10.9 ± 2.2 vs. -9.0 ± 2.5 s^{-1} , age effect, $F_{1,23} = 13.5$, $P = 0.001$). The absolute value of peak rate of relaxation increased by task failure (time effect, $F_{3,21} = 4.6$, $P = 0.01$, Fig. 4A), but the age difference remained consistent during the fatiguing contraction (time \times age interaction, $F_{3,21} = 1.5$, $P = 0.25$). Peak rate of relaxation increased during recovery (time effect, $F_{4,20} = 7.6$, $P < 0.001$), and the increase was greater for young adults than the old adults (time \times age interaction, $F_{4,20} = 4.2$, $P = 0.01$).

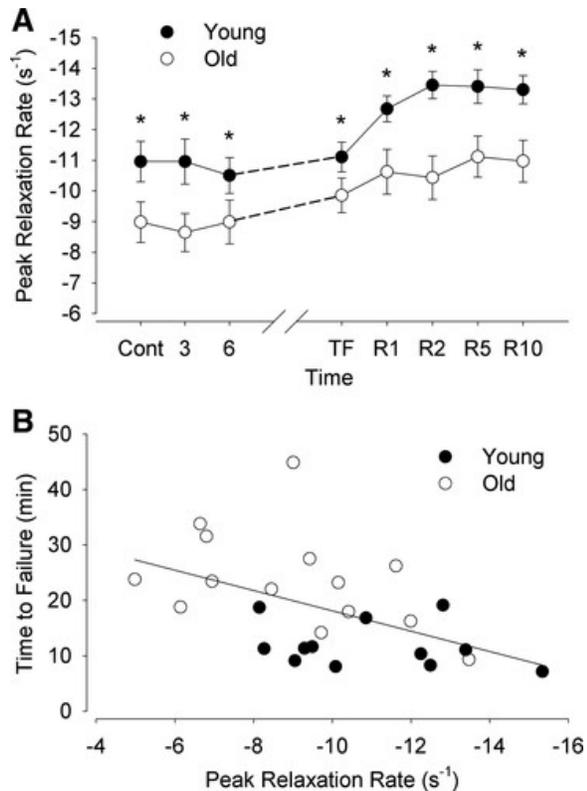


Fig. 4. Peak relaxation rate of muscle fibers in the young and old adults during MVCs. **A:** peak relaxation rate of young and old adults for the mean of control MVCs before the fatiguing contraction (Cont), at 3 min,³ 6 min,⁶ immediately after the fatiguing contraction (TF), and at 1 min (R1), 2 min (R2), 5 min (R5), and 10 min recovery (R10). The 6th min⁶ represented 52% of the time to failure of the young adults and 25% for the old adults. The dashed lines indicate there were different durations to task failure for the young and old adults. Values are expressed as means \pm SE. The peak relaxation rate of muscle fibers was faster for young than the old adults during the brief control MVCs before fatigue, during the fatiguing task and recovery. Note that the y-axis is inverted. Larger negative numbers indicate more rapid relaxation. *Age difference at $P < 0.05$. **B:** association between time to failure and peak relaxation rate in young and old adults. Those who had briefer time to task failure for the 20% MVC fatiguing contraction had greater absolute value in peak relaxation rate. A linear relation is shown ($r = 0.50$, $r^2 = 0.25$, $P = 0.01$). Individuals with a slower initial peak relaxation rate of muscle fibers exhibited a longer time to task failure.

The initial peak rate of relaxation (during control MVC) correlated with the time to task failure. Those individuals who had faster peak rates of relaxation had a briefer time to failure ($r = 0.50$, $r^2 = 0.25$, $P =$

0.01, Fig. 4B). There was no correlation, however, between the initial peak rate of relaxation and recovery of MVCs or between the change in peak rate of relaxation and recovery of MVCs ($r = 0.25$, $r^2 = 0.06$, $P = 0.2$).

Motor Evoked Potential

MEPs and M-waves elicited during the fatiguing contraction.

M_{\max} of biceps brachii elicited at the end of the fatiguing contraction did not change compared with that elicited at the start for young or old adults (time effect, $F_{1,24} = 2.2$, $P = 0.16$). MEP amplitude, however, increased between the start and the end of the fatiguing contraction (time effect, $F_{1,24} = 13.5$, $P < 0.001$) more for the young adults (46.6% increase from the start of contraction) than the old adults (27.3% increase, time \times age interaction, $F_{1,24} = 6.12$, $P = 0.02$).

MEPs and M waves elicited during MVCs.

M_{\max} was used to normalize MEP amplitude of biceps brachii elicited during MVC. M_{\max} did not change for young or old adults between control compared with those elicited at 3 min and 6 min into the fatiguing contraction and at task failure or during recovery (time effect, $F_{7,17} = 1.0$, $P = 0.48$). Thus any change in the MEP was not attributable to changes at the neuromuscular junction.

MEP amplitude of biceps brachii elicited during control MVCs was similar for the young and old adults (67.6 ± 19.7 vs. $78.6 \pm 35.7\%$ of ongoing M_{\max} amplitude, respectively, age effect, $F_{1,24} = 0.1$, $P = 0.40$). MEP amplitude of biceps brachii during MVCs did not change during or by the end of the fatiguing contraction for young or old adults (time effect, $F_{3,21} = 2.4$, $P = 0.08$). Thus the MEP amplitude at 3 and 6 min and at task failure was similar to control values. There was also no change in MEP amplitude during recovery (time effect, $F_{4,20} = 1.4$, $P = 0.28$).

Silent Period

Silent period elicited during the fatiguing contraction.

Silent period duration increased from the start of the contraction to just prior to task failure (time effect, $F_{3,22} = 4.2$, $P = 0.02$). The silent period for the young adults changed from 210 ± 18 to 228 ± 22 ms and for the old adults from 207 ± 10 to 208 ± 15 ms (time \times age interaction, $F_{3,22} = 2.8$, $P = 0.06$).

Silent period elicited during the MVC.

Silent periods during control MVCs were similar for young and old adults (209 ± 73 vs. 200 ± 54 ms, respectively, age effect, $F_{1,24} = 0.1$, $P = 0.72$). There was a time by age interaction ($F_{3,22} = 5.0$, $P = 0.01$) during the fatiguing contraction because the young adults showed an increase in the silent period at the 6th min of the fatiguing contraction (to 231 ± 91 ms), but the old adults showed no change (195 ± 58 ms). At task failure the silent period during the MVC was 216 ± 82 ms for the young and 200 ± 65 ms for the old adults. During recovery there was no age-related difference in silent period duration (age effect, $F_{1,24} = 0.6$, $P = 0.47$) and no change in silent period for either age group (time effect, $F_{4,21} = 1.4$, $P = 0.28$).

EMG Activity During the Fatiguing Contraction

The amplitude of the RMS EMG (%MVC) of biceps brachii and brachioradialis muscles increased during the fatiguing contraction (time effect, $F_{4,21} = 52.0$, $P < 0.001$). Old adults showed greater RMS EMG of biceps brachii during the fatiguing contraction (age effect, $F_{1,24} = 6.6$, $P = 0.02$). The age effect for the brachioradialis was $F_{1,24} = 3.9$, $P = 0.06$. [Figure 5](#) shows the EMG activity of the biceps brachii and

brachioradialis averaged. The rate of change in RMS EMG [rate of change = $100 \times (\text{initial} - \text{final})/\text{initial}$ EMG] was greater for the young adults than the old adults (age effect, $P = 0.01$): by task failure the young had a greater increase from the start of the contraction compared with the old adults (Fig. 5B). Triceps brachii RMS EMG (%MVC) activity increased during the fatiguing contractions with no age difference (age effect, $F_{1,24} = 0.79$, $P = 0.36$).

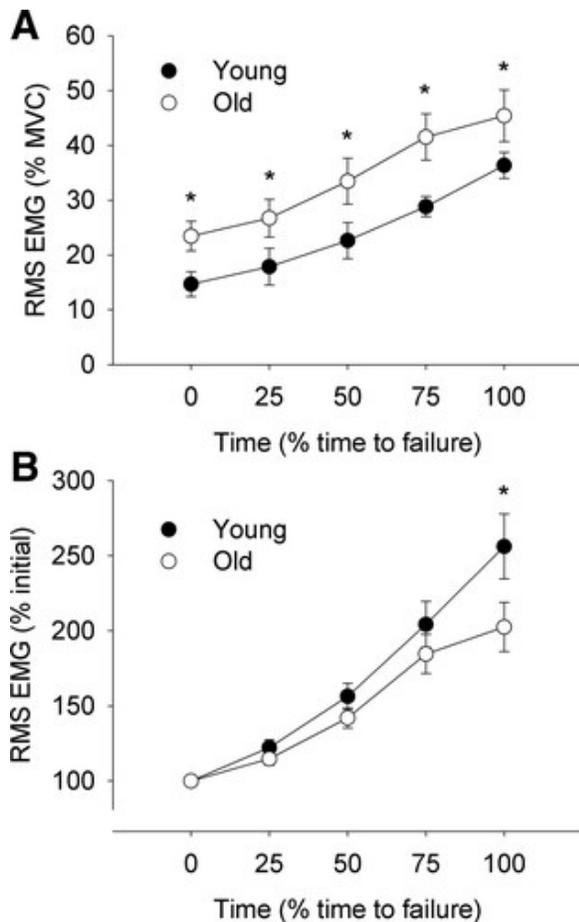


Fig. 5. Root mean squared (RMS) EMG activity for the biceps brachii and brachioradialis pooled during the fatiguing contraction in young and old adults. **A:** RMS EMG normalized to the MVC values (%MVC) during the fatiguing contraction. Shown is the mean \pm SE of 15-s intervals in 25% increments of the time to task failure. Old adults had greater EMG activity than young for the biceps brachii and brachioradialis (pooled). *Age difference at $P < 0.05$; $P < 0.05$. **B:** EMG is normalized to EMG at the start of the contraction. The young adults increased at a greater rate than the old adults (* $P < 0.05$).

Mean Arterial Blood Pressure and Perceived Exertion

MAP increased during the fatiguing contraction for the young adults (91.9 ± 9.3 to 127.2 ± 20.6 mmHg) and old adults (108.3 ± 16.6 to 133.0 ± 17.3 mmHg, time effect, $F_{4,19} = 33.7$, $P < 0.001$). There was no age difference in MAP between the young and old adults throughout the fatiguing contraction (age effect, $F_{1,22} = 2.6$, $P = 0.12$). The rate of increase in MAP, however, was greater for the young adults than old adults (3.37 ± 1.9 and 1.27 ± 0.8 mmHg/min, respectively, age effect, $F_{1,22} = 18.6$, $P < 0.001$) during fatiguing contraction. The rate of change in MAP correlated with the time to task failure ($r = -0.67$, $r^2 = 0.45$, $P < 0.001$) in that those with a briefer time to task failure had a greater rate of rise in MAP.

RPE increased during the fatiguing contraction ($F_{4,21} = 66.0, P < 0.001$). RPE for young and old adults was similar at the beginning (1.9 ± 0.8 vs. 2.2 ± 1.1 , respectively, age effect, $F_{1,24} = 0.7, P = 0.41$) and end (10.0 ± 0.4 vs. 9.8 ± 0.4 , respectively, age effect, $F_{1,24} = 3.2, P = 0.09$) of the fatiguing contraction. However, the rate of increase in the RPE was more gradual for old than young adults (0.4 ± 0.2 vs. $0.8 \pm 0.1 \text{ min}^{-1}$, age effect, $F_{1,24} = 31.9, P < 0.001$).

DISCUSSION

This study used cortical stimulation to examine age-related differences in supraspinal fatigue and contractile properties during and after a low-intensity fatiguing contraction with the elbow flexor muscles. The novel findings of this study were that for the elbow flexor muscles 1) old adults had increased SIT amplitude (supraspinal fatigue) relative to the young adults during a low-intensity fatiguing contraction and during recovery; 2) the longer time to task failure with age was associated with a slower peak rate of relaxation of the muscle, measured with cortical stimulation and a slower rate of increase in the pressor response (MAP); 3) recovery of maximal strength was less rapid in the old adults than young adults, and this was associated with a slower recovery of SIT (supraspinal fatigue); and 4) MEP amplitude and silent period duration elicited during the fatiguing contraction showed less increase for the old adults than the young adults. Thus the greater fatigue resistance of the older adults for a low-intensity sustained contraction was associated with a slower muscle and less modulation of corticomotor excitability and inhibition. Old adults, however, had impaired recovery of strength because of slower recovery of neural drive. The greater fatigue resistance of muscle of the old adults relative to the young, suggests that the lower neural drive to the motor cortex of the old adults was attributable to factors other than inhibitory feedback from small diameter muscle afferent fibers.

Time to Failure was Associated with Peripheral Fatigue

The old adults had a longer time to task failure for the sustained contraction than the young adults. These findings are consistent with previous studies indicating that old adults are more fatigue resistant than young adults for submaximal^{16,42} and maximal isometric contractions [for reviews see^{5,14,22}]. Because the initial strength was similar for both groups, the greater fatigue resistance was not attributable to age-related differences in strength or target force [as for sex differences¹⁵] and is consistent with results for young and old adults who were matched for strength.¹⁷ Time to failure was, however, associated with the initial peak rate of relaxation and the rate of increase in MAP (pressor response). The peak relaxation rates were faster in young adults than old adults before and after the fatiguing contraction, suggesting that old adults had a greater proportional area of type I fibers^{18,23} and slower calcium uptake into the sarcoplasmic reticulum.¹⁸ Accordingly, the reduced rate of increase in pressor response in older adults²⁵ was likely because of less metabolite buildup in more oxidative muscle²² and a lower metaboreflex (metabolic arm of the pressor response), which is regulated via metabolic feedback from group III and IV afferents.²⁰ Consequently the longer time to failure of the older adults than the young was predominantly explained by a more fatigue-resistant muscle with age.

In contrast to the slowing of relaxation during sustained maximal contractions,¹⁹ the peak rates of relaxation changed little during the submaximal contraction as seen before, and is probably related to increased muscle temperature.²¹ There was, however, a reduction in the estimated twitch amplitude at task failure that was similar with age ($\sim 20\%$ at task failure), indicating fatigue within the muscle contributed to the reduction in MVC force for both age groups. This 20% reduction twitch amplitude was less than the $\sim 38\%$ reduction in MVC force from control levels, indicating that a significant portion

of MVC fatigue was because of an inadequate neural drive to the muscle for both young and old adults. The twitch amplitude had recovered to 90% of initial amplitude by 10 min of recovery for the young and old adults, suggesting that the age differences in recovery of MVC torque were not attributable to peripheral fatigue within the muscle.

Supraspinal Fatigue Increased but Recovered More Slowly with Age

Supraspinal fatigue progressively increased during the submaximal fatiguing contraction for both young and old adults and then decreased during the 10-min recovery. This was shown by the increase in the SIT (indicating a fall in voluntary activation) during the contraction and at task failure followed by the decrease in SIT during recovery (indicating an increase in voluntary activation). Thus both young and old adults had less than optimal drive from the motor cortex during the submaximal fatiguing contraction and at task failure with the elbow flexor muscles.⁹ The reduction in MVC torque at the end of fatiguing contraction, therefore, was due in part to supraspinal fatigue in both young and old adults. The levels of supraspinal fatigue at task failure were similar to those when central fatigue was quantified at the motor nerve of the elbow flexor muscles for young and old adults.⁴² Taken together, the predominant portion of fatigue within the central nervous system during and after a low-intensity isometric contraction can be attributed to impairment upstream of the motor cortex.

The old adults, however, exhibited greater supraspinal fatigue than the young. By 3 and also 6 min into the sustained contraction, old adults exhibited a larger SIT than young adults and also at task failure. Small-diameter muscle afferents (group III and IV) likely play a large role in impairing voluntary drive during a sustained contraction and recovery in young adults, and their role may be even greater during sustained submaximal tasks than maximal tasks.³⁸ Our data suggest, however, that factors other than inhibitory influences of small diameter afferents acting upstream of the motor cortex, contributed to the age-related differences in supraspinal fatigue that we observed. At 6 min, the fall in MVC force was relatively less for the old adults than young, but the SIT was larger for the old than the young adults. Supraspinal fatigue therefore contributed relatively more to the fall in MVC at 6 min for the old adults than for the young, although 6 min represented only 25% of the time to task failure for the old adults and 52% for the young. At these time points, the buildup of metabolites and excitation of the group III and IV afferents was likely to be less for the old adults because of their more fatigue-resistant muscle, as reflected in the reduced pressor response. Accordingly, supraspinal fatigue was significant for both young and old adults, but its magnitude at task failure, which was larger in old adults, was not associated with the time to failure.

An age difference in supraspinal fatigue did, however, explain the slower recovery of MVC torque after the fatiguing contraction for the old compared with the young adults. Those individuals who had the least relative recovery in MVC torque also had less recovery of the SIT, and this explained 35% of the variance between subjects. Old adults also had slower recovery of the SIT than young adults after a sustained maximal contraction with the elbow flexor muscles¹⁹ and slower recovery of motor unit discharge rate than young adults, which could contribute to a diminished ability to drive the muscle⁶. Again, group III and IV afferents can impair voluntary drive to the motor cortex³⁸ and slow recovery of motor unit discharge rate after a sustained contraction. The role of these the small diameter muscle afferents in impairing recovery of voluntary activation in older adults is not clear but is not likely responsible for the slower recovery of maximal force in the older adults relative to the young. Certainly, there are numerous age-related cortical changes that can include loss of white and gray matter,^{31,34}

structural degradation of cortical neurons,⁴⁴ decreased levels of dopamine, acetylcholine, serotonin, and norepinephrine [see³⁵ for review], altered net motor cortical excitability,^{28,29} and a decline in effective connectivity between distant motor-related cortical areas.³³ Such age-related changes could compromise neural drive during a sustained contraction and also contribute to a slower recovery of maximal force production with aging.

Adjustments in EMG during the Fatiguing Contraction

As supraspinal fatigue increased during the fatiguing contraction, there was an increase in EMG activity representing a progressive increase in excitability of the motoneuron pool.³⁸ The increase in EMG activity during submaximal fatiguing contractions represents an increase in motor unit recruitment and changes in discharge rates as the already active motor units become progressively fatigued.³² Although EMG activity increased for both age groups, old adults had greater relative EMG activity (normalized to MVC) than young adults (Fig. 5A). The normalized activation may have been elevated in the old adults relative to the young because the old adults had slightly lower voluntary activation during the control MVC. When the EMG activity was normalized to the initial levels of EMG, however, the rate of EMG increase was greater for the young than old adults and less at task failure for the old adults (Fig. 5B). The slower age-related rate of increase in EMG activity during the sustained contraction could be attributable to a slower development of fatigue in the active fibers in the old adults.³⁸ At task failure, however, old adults had reduced EMG activity relative to young adults, suggesting that old adults may have less capacity than young adults to activate the available motoneuron pool at that time.

MEP and Silent Period

The EMG response to cortical stimulation, the MEP and silent period, increased less for the old adults than the young during the fatiguing contraction. The MEP represents the net output of all the excitatory and inhibitory influences to the corticospinal neurons, the response of the motoneuron pool to the descending volleys, and the muscle fiber action potentials.³⁷ Any change in MEP size in our study was not due to changes in propagation of the muscle fiber action potential because the M-wave amplitude (M_{max}) did not change for young or old adults during or after the sustained contraction. MEP size typically increases during a maximal sustained contraction,^{19,37} more slowly for submaximal sustained contractions when elicited during brief MVCs,^{21,36} and then quickly recovers. As we observed, the recovery of the MEP and silent period are more rapid than supraspinal fatigue³⁸ in both young and old adults.¹⁹ During a fatiguing contraction, the increase in MEP typically seen is probably attributable to increased cortical drive to progressively less responsive motoneurons.^{26,38} Similar to the lack of change in rate of relaxation elicited during the MVC after the fatiguing contraction in our study, MEP size did not change greatly in young or old adults. However, the MEP elicited during the submaximal contraction increased at failure of the task but more so for the young adults. At task failure, the loss of drive to the motor cortex (supraspinal fatigue), requires an increase in excitability of neural centers downstream of the motor cortex to continue to drive the muscle to develop the required force while the fibers fatigue. This age difference in the MEP at task failure is consistent with the RMS EMG activity and could reflect less net excitation of the old adults than the young or less responsive motoneurons of the old adults at task failure.

The silent period in EMG is thought to reflect the intracortical inhibition,⁹ although more recent data suggest an increase in the silent period with fatigue represents a profound loss of responsiveness of the motoneuron.²⁶ Old adults usually have a briefer duration in silent period during complex tasks²⁸ and

maximal fatiguing contractions,¹⁹ indicating less effective corticospinal activity.²⁹ Although there was no age difference before or during recovery from the fatiguing contraction when elicited during maximal contractions, silent periods lengthened for young adults by 6 min but did not demonstrate any modulation for old adults. This may be attributable to a less fatigued muscle in the old adults during the contraction despite the increase in supraspinal fatigue (increased SIT) that was greater than the young adults. This dampened responsiveness during the sustained submaximal contraction and at task failure for the old adults relative to young is consistent with the lower increase in MEP amplitude and global EMG activity. Together these results indicate that at task failure, old adults may have less capacity to modulate corticomotor excitability and inhibition compared with the young.

In summary, recovery of MVC torque was impaired with age because of supraspinal fatigue despite old adults performing a longer time to task failure than the young. Supraspinal fatigue contributed substantially to the loss of MVC force during the sustained contraction and at task failure but did not explain the age difference in time to task failure. Greater loss of neural drive to the motor cortex in the old adults during the fatiguing contraction and recovery was likely attributable to age-related factors that were not associated with inhibitory feedback from small diameter muscle afferent fibers. The age difference in time to failure was associated with slower peak rates of relaxation of the muscle and reflected in a slower pressor response and a more fatigue-resistant muscle. EMG measures, however, indicated that at task failure the old adults may have had less capacity to activate the available motoneuron pool. Recovery of strength after fatiguing exercise in old adults has received minimal attention to date but could prove to be an important variable to consider in exercise prescription of older populations.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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