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Voluntary Activation and Variability During Maximal Dynamic Contractions with Aging

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Abstract

Whether reduced supraspinal activation contributes to age-related reductions in maximal torque during dynamic contractions is not known. The purpose was to determine whether there are age differences in voluntary activation and its variability when assessed with stimulation at the motor cortex and the muscle during maximal isometric, concentric, and eccentric contractions. Thirty young (23.6 ± 4.1 years) and 31 old (69.0 ± 5.2 years) adults performed maximal isometric, shortening (concentric) and lengthening (eccentric) contractions with the elbow flexor muscles. Maximal isometric contractions were performed at 90° elbow flexion and dynamic contractions at a velocity of 60°/s. Voluntary activation was assessed by superimposing an evoked contraction with transcranial magnetic stimulation (TMS) or with electrical stimulation over the muscle during maximal voluntary contractions (MVCs). Old adults had lower MVC torque during isometric (− 17.9%), concentric (− 19.7%), and eccentric (− 9.9%) contractions than young adults, with less of an age difference for eccentric contractions. Voluntary activation was similar between the three contraction types when assessed with TMS and electrical stimulation, with no age group differences. Old adults, however, were more variable in voluntary activation than young (standard deviation 0.99 ± 0.47% vs. 0.73 ± 0.43%, respectively) to both the motor cortex and muscle, and had greater coactivation of the antagonist muscles during dynamic contractions. Thus, the average voluntary activation to the motor cortex and muscle did not differ with aging; however, supraspinal activation was more variable during maximal dynamic and isometric contractions in the old adults. Lower predictability of voluntary activation may indicate subclinical changes in the central nervous system with advanced aging.

Keywords

Sex differences, Electrical stimulation, Transcranial magnetic stimulation, Concentric, Eccentric, Elbow flexor muscles

Abbreviations

ANOVA Analysis of variance

EMG Electromyography

MEP Motor-evoked potential

MVC Maximal voluntary contraction

RMS Root mean square

SD Standard deviation

TMS Transcranial magnetic stimulation

Introduction

Old men and women are weaker and less powerful than young adults for most muscle groups primarily due to muscle atrophy (sarcopenia) (Hunter et al. 2000, 2016; Doherty 2003; Lanza et al. 2003), with evidence for some contribution from inadequate activation of the muscle (Stevens et al. 2003; Morse et al. 2004; Klass et al. 2007; Hunter et al. 2008). The age difference in maximal torque however, differs with the contraction type, contraction speed and the muscle group involved, indicating that the contributing mechanisms may also differ across tasks and muscle groups (Hunter et al. 2016). For example, age-related reductions in power during shortening contractions (concentric) are typically greater than for isometric contractions (Reid and Fielding 2012), particularly at fast contraction velocities (Hunter et al. 2016). Additionally, there is less of an age-related difference in maximal torque for eccentric (lengthening) than concentric contractions (Lindle et al. 1997; Pousson et al. 2001; Klass et al. 2005; Raj et al. 2010; Power et al. 2015, 2016). However, the mechanisms for the age-related reductions in maximal torque during both types of dynamic contractions, and the mechanism for the differences between these contraction types, are not well defined. Because muscle atrophy contributes to reduced maximal torque during all contraction types, the neural drive to the motor unit pool (voluntary activation) may explain the differences in the age-related loss of maximal torque between the contraction types (Hunter et al. 2016).

Voluntary activation is commonly assessed with the interpolated twitch technique (Merton 1954; Belanger and McComas 1981; Allen et al. 1995). Measurement of voluntary activation typically involves delivering a supramaximal stimulation (one or several pulses of electrical stimulation) to the nerve or the muscle during a maximal voluntary contraction (MVC), typically isometric, to quantify the volitional drive to the muscle (Taylor 2009). Any additional force elicited by the superimposed stimulus indicates submaximal activation of the muscle, due to an incomplete motor unit recruitment and/or suboptimal firing rates of the recruited motor units (Herbert and Gandevia 1999; Gandevia 2001). Further insight to the site of failure in voluntary drive to the muscle can be gained by stimulating the motor cortex with transcranial magnetic stimulation (TMS) and quantifying the resultant superimposed twitch force during the maximal contraction efforts to determine drive originating from the motor cortex (Todd et al. 2016). TMS has not been used to quantify supraspinal activation in old adults during maximal dynamic contractions, nor to determine differences between contractions types. Thus, it is not known if there are age differences in activation of the motor cortex that may contribute to age differences in maximal torque during dynamic contractions.

During maximal *isometric* contractions with minimal practice, old adults exhibited lower and more variable voluntary activation than young adults when assessed with stimulation of the muscle and also the motor cortex (Jakobi and Rice 2002; Yoon et al. 2008; Hunter et al. 2008). After practice, the findings vary as to whether age differences in voluntary activation exist, with some studies reporting a greater deficit in activation of old adults compared with young adults (Yue et al. 1999; Jakobi and Rice 2002; Stevens et al. 2003; Morse et al. 2004), and others reporting no age-related difference (Vandervoort and McComas 1986; Roos et al. 1999; Klass et al. 2005; Simoneau et al. 2005; Molenaar et al. 2012; for review, see Klass et al., 2007). The reason for the difference between studies is not clear but may involve variation in the number of stimulations used to evoke the superimposed twitch affecting the sensitivity of the measure (Shield and Zhou 2004) and the muscle group assessed because each muscle group varies in suitability to assess activation (Taylor 2009; Todd et al. 2016).

Whether there are age-related differences in activation of supraspinal centers during dynamic contractions is unknown. Several studies demonstrated minimal age-related differences in voluntary activation when assessed with stimulation at the motor nerve using either a single twitch or doublet stimulation (e.g. Klass et al. 2005; Wilder and Cannon 2009). Superimposing TMS during volitional dynamic contractions can reveal whether any age-related differences in maximal torque are due to neural drive to the motor cortex. Old adults are more variable in voluntary activation during maximal voluntary isometric contractions from both supraspinal and spinal sources (Jakobi and Rice 2002; Yoon et al. 2008; Hunter et al. 2008), but it is unknown whether old adults are more variable in voluntary activation during dynamic contractions. Larger variability in voluntary activation potentially exacerbates the age-related declines in strength, power and predictability of performance with aging (Hunter et al. 2016). In this study, the source of age-related variability in activation during dynamic contractions was determined by stimulating at the motor cortex and muscle.

Thus, the primary purpose of this study was to determine whether there are age differences in supraspinal voluntary drive during maximal concentric and eccentric contractions in men and women when assessed with transcranial magnetic stimulation over the motor cortex. We also determined whether there were age differences in the *variability* of voluntary activation assessed with stimulation of the motor cortex and at the muscle during maximal concentric and eccentric contractions. The elbow flexor muscles were assessed because the methods of stimulation to determine voluntary drive to the motor cortex and the muscle during maximal isometric contractions in this muscle group in young and old adults are well established (Todd et al. 2003, 2004, 2016; Hunter et al. 2008; Molenaar et al. 2012). Thus, we compared activation during the dynamic contractions (concentric and eccentric) to that during the maximal isometric contractions. Furthermore, upper limb muscles are less likely to be confounded by age-related differences in physical activity (Hunter et al. 2016). Because in many real-world circumstances only one attempt at a task is possible, we limited familiarization prior to the measurements of strength and activation.

The two primary *hypotheses* were that (1) old adults would demonstrate deficits in voluntary activation when assessed with cortical stimulation compared with young adults during isometric and concentric contractions, which are those contractions that exhibit larger age-related differences in strength than eccentric contractions, and (2) variability in voluntary activation assessed with both cortical and muscle stimulation would be larger for the old adults than the young for all three contraction types. We also determined whether there were age-related differences across the different contraction types in the electromyography (EMG) activity and EMG responses to stimulation at the motor nerve (muscle compound action potential, M-wave) and motor cortex including the motor evoked potential (MEP) and the silent period. Lastly, we assessed both men and women, although we did not expect a difference between the sexes in voluntary activation and its variability (Hunter 2016).

Methods

Subjects

Sixty-two adults, 31 young adults (18–35 years, 23.6 ± 4.1 years, 15 men and 16 women) and 31 old adults (60–80 years, 69.0 ± 5.2 years, 15 men and 16 women) volunteered to participate in this study. One young woman was removed from analyses because her MVC torque value was greater than 3 standard deviations below the group mean. All participants were healthy with no known neurological or cardiovascular disorders and were naive to the protocol. Informed consent was obtained from all individual participants included in the study. The protocol was approved by the Marquette University Institutional Review Board and the experiment was conducted according to the Declaration of Helsinki.

Mechanical Recordings

Each subject was seated upright in an adjustable chair (Biodex Medical System 4, Shirley, NY). The left shoulder was flexed at 50° in the sagittal plane (with 0° considered to be in line with the torso) and the elbow rested comfortably on a padded support. The forearm was placed in a fully-supinated position within a modified orthosis (Orthomerica, Newport Beach, CA) which was attached to the lever arm of the dynamometer. The axis of rotation of the dynamometer was aligned with the anatomical axis of the elbow. To limit extraneous movements, a shoulder harness was fixed across each shoulder and an additional strap was fixed across the hips. For the isometric contractions, the elbow joint was flexed at 90° (0° = full extension). Concentric and eccentric contractions were performed over a 60° range of motion between 60° and 120° elbow flexion and at a velocity of 60°/s in isokinetic mode. Torque, velocity and position were recorded from the dynamometer, exported and digitized at 1000 Hz using a Power 1401 A–D converter and Spike 2 software (Cambridge Electronics Design, Cambridge, UK).

Electromyography (EMG)

EMG signals were recorded with pairs of bipolar silver chloride circular (8 mm diameter) surface electrodes that were placed over the biceps brachii and triceps brachii muscles according to recommended placements (Hermens et al. 2000). For the biceps brachii, the electrodes were placed between the medial acromion and the fossa cubit at 1/3 from the fossa cubit. For the triceps brachii, the electrodes were placed on the long head midway between the posterior crista of the acromion and the olecranon. Reference electrodes were placed on the acromion. The EMG signals were amplified (×100) and band-pass filtered (13–1,000 Hz; Coulbourn Instruments, Allentown, PA), and recorded online at 2,000 Hz using a Power 1401 A–D converter and Spike 2 software (Cambridge Electronics Design, Cambridge, UK).

Stimulations

Subjects were stimulated at the brachial plexus and over the biceps brachii muscle with electrical stimulation and at the motor cortex with TMS. During concentric and eccentric contractions, stimulations were digitally triggered when the arm was at a joint angle of 90°, which was at the midpoint of the range of motion and at the same position of stimulation for the isometric contractions.

Brachial plexus stimulation

The brachial plexus was electrically stimulated at rest to produce a maximal M-wave (M_{max}) of both the biceps and triceps brachii muscles. Single stimuli (400 V and 100 µs duration) were delivered to the brachial plexus using a constant-current stimulator (DS7AH, Digitimer, Hertfordshire, UK). 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 of both biceps and triceps brachii muscles plateaued, and was then increased by 20% to ensure a maximal electrical response (supramaximal stimulation; range of 120–480 mA) and obtain M_{max}.

Muscle stimulation

The biceps brachii muscle was directly stimulated to produce a maximal twitch of the elbow flexor muscles. Paired (doublet) stimuli (100 Hz, i.e. 10 ms between stimuli) were delivered to intramuscular nerve fibers by a constant-current stimulator at 400 V and each pulse for 100 µs duration (DS7AH, Digitimer, Hertfordshire, UK) with custom-made electrodes (2.0 × 4.5 cm) adhered to the skin overlying the biceps brachii muscle. The cathode was placed directly over the muscle belly, midway between the anterior edge of the deltoid and the elbow crease, and the anode was placed over the distal biceps tendon. To establish maximal force of paired stimulations, the intensity of stimulation was increased until there was no further increase in the evoked force with at least two additional increases in the stimulation intensity (50 mA increase). The intensity of stimulation was not further increased to avoid activation of the triceps brachii muscle and was used for the remainder of the experiment (range of 100–550 mA), to evoke contractions at rest and during contractions to assess voluntary activation.

Cortical stimulation

TMS were delivered via a round coil (13.5 cm outside diameter; Magstim 200, Magstim, Whitland, UK) over the vertex to evoke motor-evoked potentials (MEPs) in the biceps and triceps brachii muscles during isometric elbow flexion contractions. The direction of current flow in the coil preferentially activated the motor cortex in the right hemisphere to innervate the left arm. The stimulation location was marked on an electroencephalography cap secured on the participant's head to ensure repeatability of coil placement throughout the experiment. Single stimuli were delivered over the motor cortex at an intensity that produced a large MEP in the agonist biceps brachii muscle (≥50% M_{max}) but only a small MEP in the antagonist triceps brachii muscle (≤15% M_{max}) during a brief isometric contraction of the elbow flexor muscle at 50% MVC (Todd et al. 2004). The TMS intensities for the young and old groups were 65 ± 8% and 71 ± 11% of stimulator output, respectively ($P < 0.05$).

Experimental Protocol

Each subject visited the laboratory for one experimental session to assess voluntary activation during maximal isometric, concentric and eccentric contractions of the elbow flexor muscles using TMS and muscle stimulation. The procedures occurred in the following order. *Maximal M-wave (M_{max})*. The M_{max} of the biceps and triceps brachii muscles was recorded in response to three *single* stimulations of the brachial plexus during three separate conditions (resting isometric, passive shortening and passive lengthening) with 10 seconds of rest between each stimulation.

MVCs without stimulation

Subjects performed two maximal voluntary isometric, concentric and eccentric elbow flexions followed by two maximal isometric elbow extensions. For the dynamic contractions, subjects were instructed to first produce a brief (~1 s) maximal isometric contraction before the dynamometer initiated the movement, and then sustain the maximal effort throughout the entire range of motion (Klass et al. 2005). Strong verbal encouragement and visual feedback on their performance with a screen in front of the subjects (~ 1m) were provided during each maximal effort (Gandevia 2001).

Doublet Stimuli at Rest

Torque of the elbow flexor muscles was recorded in response to three separate doublet muscle stimulations performed during resting isometric conditions with the elbow at 90° flexion.

Voluntary activation

Voluntary activation was assessed during maximal voluntary isometric, concentric and eccentric elbow flexions with TMS or doublet muscle stimulations, resulting in six different MVC conditions. Each MVC condition was performed twice so there was a total of 12 MVCs performed. The 12 MVCs however, were performed across two subsets so that each MVC condition (e.g. isometric with TMS, concentric with muscle stimulation, etc.) was performed once in each subset of six MVCs. Each MVC was followed by three minutes of rest to avoid the effects of fatigue. The 12 MVCs always started and ended with an isometric MVC (randomized for TMS and muscle stimulation) to determine if fatigue had developed between the 1st and last MVC. All the other MVCs were randomized for each subject.

TMS and muscle stimulation were delivered at the torque plateau (isometric contractions) and at 90° of elbow flexion for the dynamic contractions (concentric and eccentric contractions). For MVCs with muscle stimulation, a resting doublet stimulation was delivered 3 s after the end of the contraction for the isometric contractions and at 90° during a passive shortening (concentric contractions) or lengthening (eccentric contractions) movement performed immediately after the contraction.

Data Analysis

The maximal voluntary torque and the associated RMS EMG of the biceps and triceps brachii muscles were measured during the MVCs without stimulation. For the isometric contractions, both measurements were assessed for a 100-ms period during the plateau of the MVC. For the concentric and eccentric contractions, the torque and the RMS EMG of the biceps and triceps brachii muscles were average for a 100-ms period around 90° (50 ms either side). Antagonist coactivation during the three contraction types was evaluated using the following formula: [(RMS EMG of the antagonist during agonist contraction/RMS EMG of the antagonist when acting as agonist) × 100] (Macaluso et al. 2002). The biceps brachii RMS EMG was normalized to the M_{max} to calculate the RMS/M_{max} ratio (Sale et al. 1982; Klass et al. 2005).

Voluntary activation was assessed using the twitch interpolation technique with muscle stimulation (Merton 1954; Allen et al. 1995; Gandevia 2001) and TMS (Todd et al. 2003). For muscle stimulation, any increment in elbow flexion torque evoked by a doublet stimulation during the MVC ("superimposed twitch") was expressed as a fraction of the amplitude of the response evoked by the same stimulus in the relaxed muscle ("potentiated twitch"). For TMS during isometric contractions, the potentiated twitch was estimated for each subject by extrapolation of the linear regression between the amplitude of the superimposed twitch and voluntary torque during brief maximal and submaximal contractions (MVC, 60% MVC and 80% MVC) (Todd et al. 2003, 2016). The level of voluntary activation was then quantified as a percentage using the formula: [(1 − superimposed twitch/potentiated twitch) × 100] (Allen et al. 1995; Gandevia 2001; Todd et al. 2003). It was not possible to estimate a resting twitch with TMS from submaximal dynamic contraction. Hence, to assess voluntary activation using TMS during dynamic contractions, the superimposed twitch was expressed as a fraction of the sum of the torque before the stimulation and the superimposed twitch using the formula: [Superimposed twitch torque/(MVC torque + Superimposed twitch torque) × 100] (Gandevia et al. 1996; Hunter et al. 2008). To compare the level of voluntary activation assessed with both stimulation methods (i.e. TMS and muscle stimulation), the superimposed twitch was also expressed using the latter formula when assessed with muscle stimulation. Because the mean and maximal values were similar for both voluntary activation and superimposed twitch, only the mean is reported. To determine the variability in voluntary activation and the superimposed twitch across trials, the standard deviations (SD) were calculated across the 4 trials for each contraction type (2 trials with muscle stimulation and 2 with TMS).

During concentric and eccentric contractions, the MVC torque changed throughout the range of motion, as expected (Hasan and Enoka, 1985). Therefore, the MVC torque at the time of the stimulus was determined by a linear extrapolation of the torque signal from 50 ms before the stimulus beyond the point at which the superimposed twitch torque was measured (Gandevia et al. 1998; Klass et al. 2005; Wilder and Cannon 2009). The superimposed twitch torque was subsequently determined as the difference between torque at the peak of the twitch and the torque of the extrapolated MVC (i.e. estimated MVC at the time of the peak twitch).

For isometric MVC contractions, fluctuations in torque were calculated for 0.5 s and 1.0 s intervals immediately prior to the time of stimulation (TMS or electrical stimulation). Torque fluctuations were calculated as the standard deviation (SD) of the torque during the time interval and coefficient of variation (CV) of the torque (SD/mean torque × 100). Each contraction was repeated twice, therefore, the mean torque fluctuations (SD or CV of torque) of the two contractions was compared between groups. Because the results did not differ between those for the 0.5 s and 1.0 s intervals, nor between the results for the SD and CV, only the CV that was calculated for a 1.0s interval is presented.

Contractile properties of the elbow flexor muscles were assessed during doublet muscle stimulations at rest and included the following variables: peak torque, contraction time, half-relaxation time and peak rates of torque development and relaxation.

During MVCs, the amplitude and area of MEPs and the duration of the silent periods were measured from biceps brachii EMG responses to TMS. Because amplitude and area showed similar findings, only the MEP amplitude is reported. The amplitude of each MEP was normalized to the amplitude of M_{max} that was elicited at rest at the start of the experiment. The duration of the silent period was determined as the interval from the stimulus to the return of continuous EMG (Taylor et al. 1996).

Statistical Analysis

Data are reported as means ± SD in the text and displayed as mean ± SE in the figures and table. The superimposed twitch amplitude was analyzed using a two-way repeated measures analysis of variance (ANOVA) with age and sex as between-subjects factors, and contraction type and stimulation method as within-subjects factors. Repeated measures ANOVAs with age and sex as between-subjects factors and contraction type as within-subjects factor were used to compare variables between young and old (age) and between men and women (sex) across eccentric, isometric and concentric contractions (contraction type). The variables include MVC torque, normalized MVC torque, voluntary activation assessed with muscle stimulation, SD of the superimposed twitch, EMG RMS/M_{max} ratio, coactivation, M_{max} amplitude, MEP amplitude, MEP/M_{max} ratio and silent period duration. Univariate ANOVAs were performed to compare voluntary activation assessed with TMS during isometric contractions, SD of voluntary activation, torque response to doublet stimulations at rest (amplitude, contraction time, half-relaxation time, rate of torque development and rate of torque relaxation) and the CV of torque for the isometric MVCs across age and sex. Independent samples t-test was used to compare the CV of torque between the two stimulation methods. Significant main or interaction effects were followed up by post hoc analysis (Bonferroni's test), when appropriate. A significance level of $P < 0.05$ was used for all analyses and all the analyses were performed with IBM Statistical Package for Social Sciences (SPSS).

Results

MVC Torque

The maximal torque during the MVCs performed at the start and end of sessions were not different (time effect, $P = 0.37$), and there were no interactions (contraction type × age, $P = 0.48$; contraction type × sex, $P = 0.68$) indicating that the participants did not fatigue across the 12 MVCs. MVC torque was less in the old adults compared with the young adults for the eccentric (−9.9%), isometric (−17.9%) and concentric contractions (−19.7%, age effect, $P < 0.01$, Figure 1A–B) for both men and women (sex × age, $P = 0.22$).

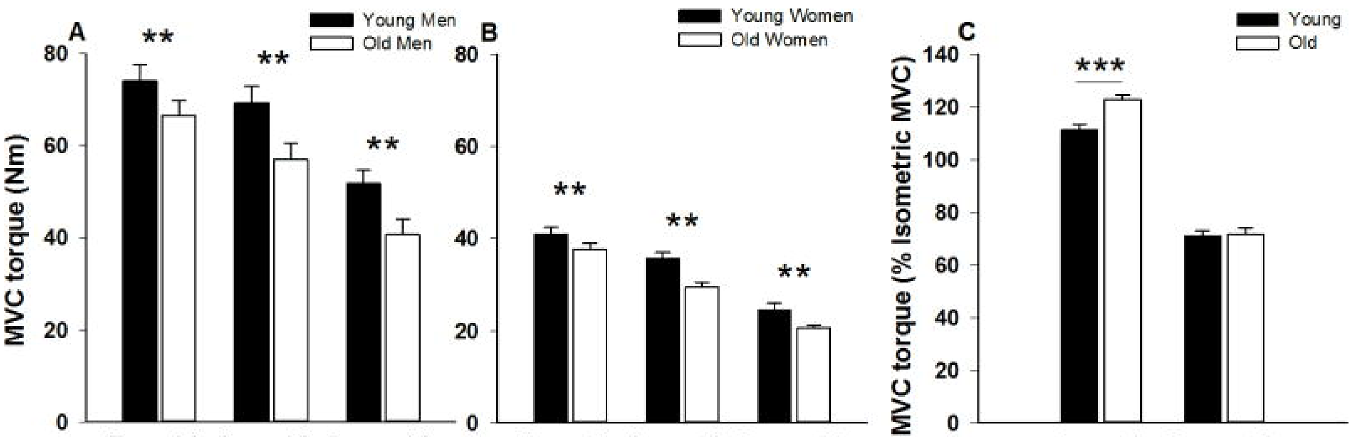

Fig. 1 Maximal eccentric, isometric and concentric voluntary torque of young and old men (A) and women (B) and normalized to the isometric MVC torque (C). For both absolute and normalized values, MVC torque was greater during eccentric contractions than for isometric contractions, and both were greater than the MVC of the concentric contractions ($P < 0.01$). Men were stronger than women for every contraction type ($P < 0.001$). MVC: maximal voluntary contraction. Significant age difference: **$P < 0.01$, ***$P < 0.001$

Men were stronger than women regardless of contraction type in both the young and old groups (sex effect, $P < 0.001$). There were also differences in maximal torque between contractions. For all groups, maximal eccentric torque (54.5 ± 18.7 Nm) was greater than that for the isometric contractions (47.6 ± 19.0 Nm), and both were greater than for the maximal concentric torque (34.2 ± 15.5 Nm; contraction type effect, $P < 0.001$; post hoc, all $P < 0.001$). When the maximal concentric and eccentric torques were normalized to the isometric torque (Figure 1C), the old adults had higher relative eccentric values compared with young adults (122.8 ± 10.0% of isometric MVC vs. 111.5 ± 11.3% of isometric MVC, respectively; age effect, $P < 0.001$). In contrast, the relative concentric torque was similar in young and old adults (71.3 ± 9.0% of isometric MVC vs. 71.9 ± 14.5% of isometric MVC, respectively; age effect, $P = 0.93$). Despite the age- and sex-related differences in maximal torque, there were no differences in variability in MVC torque across the repeated contractions (age effect, $P = 0.61$; sex effect, $P = 0.09$).

Voluntary Activation

Muscle stimulation

Voluntary activation assessed with electrical stimulation of the muscle, was similar in young and old adults (Figure 2; age effect, $P = 0.85$) during the maximal eccentric (95.5 ± 3.9% vs. 94.9 ± 4.9%), isometric (94.9 ± 4.1% vs. 95.7 ± 3.2%) and concentric contractions (95.8 ± 5.3% vs. 95.5 ± 3.4%). There was no difference in voluntary activation assessed with muscle stimulation between the three types of contraction (contraction type effect, $P = 0.86$) for both men and women (contraction type × sex, $P = 0.24$).

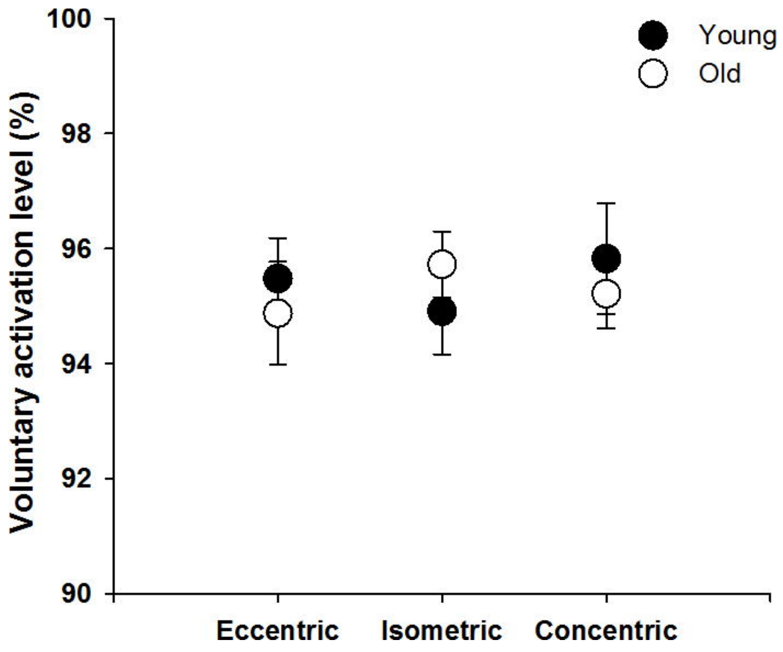

Fig. 2 Voluntary activation assessed with electrical stimulation of the muscle in young and old adults during maximal eccentric, isometric and concentric contractions. Voluntary activation was assessed with the twitch interpolation technique using doublet stimulations, and calculated using the following formula: [(1 − superimposed twitch/resting twitch) × 100]. There was no age, sex nor contraction difference in voluntary activation level ($P > 0.05$)

TMS

Voluntary activation assessed with TMS during isometric contractions was also similar in young and old adults (94.9 ± 3.5% vs. 95.4 ± 3.5%; age effect, $P = 0.57$), regardless of sex (age × sex, $P = 0.97$). Voluntary activation was not calculated during concentric and eccentric contractions with TMS because of the technical limitations in estimating a resting twitch during dynamic contractions using this technique.

Superimposed Twitch (% MVC)

Voluntary activation was also expressed as the fraction of the superimposed twitch relative to the sum of the torque of the MVC before the stimulus and the superimposed twitch. Representative traces of eccentric, isometric and concentric MVCs with superimposed twitch with TMS are presented on Figure 3A.

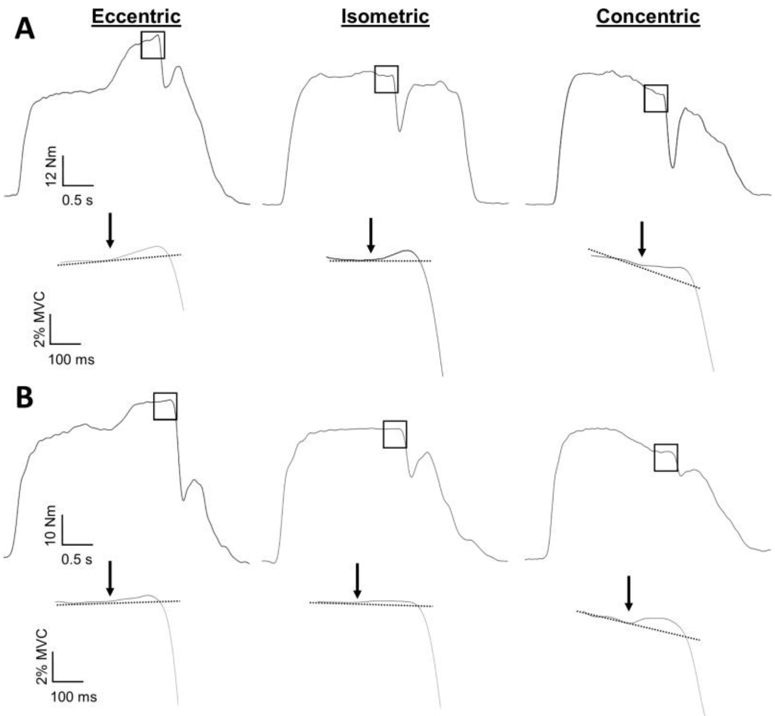

Fig. 3 Representative data showing the superimposed twitch elicited with TMS during maximal contractions by a young (A) and an old (B) male during eccentric, isometric and concentric contractions. The inset shows an amplification of the torque at the time of stimulation superimposed during the maximal torque contraction. The vertical arrow indicates the time at which the stimulation was delivered. The dotted line represents the linear extrapolation of the torque signal from before the stimulus to beyond the point at which the superimposed twitch torque was measured.

Muscle stimulation

When assessed with muscle stimulation, the amplitude of the superimposed twitch was similar between the three contraction types (contraction type effect, *P* = 0.53), and also similar between the young and old adults (average of the men and women and the three contraction types, 0.9 ± 0.9% vs. 1.0 ± 0.9%, respectively, age effect, *P* = 0.36; Figure 3B). There was no difference between the men and women (sex effect, *P* = 0.33) and no interactions between age and sex (*P* = 0.08). Within old adults, the amplitude of the superimposed twitch was not correlated with age during the maximal eccentric (r = 0.13, *P* = 0.48), isometric (r = −0.03, *P* = 0.87) or concentric (r = −0.17, *P* = 0.37) contractions.

TMS

When the superimposed twitch was elicited with TMS, the amplitude was similar in young and old adults (average of the men and women and the three contraction types, 1.0 ± 0.7% vs. 1.2 ± 0.7%, respectively, age effect, *P* = 0.24) in the three contraction types (contraction type effect, *P* = 0.59; Figure 3C). The superimposed twitch was also similar for men and women (sex effect, *P* = 0.66) with no interactions between age and sex (*P* = 0.90). Within the old adults, the amplitude of the superimposed twitch was not correlated with age during the maximal eccentric (r = −0.15, *P* = 0.94), isometric (r = −0.18, *P* = 0.34) or concentric (r = −0.14, *P* = 0.45) contractions.

Variability: Voluntary Activation and Superimposed Twitch

For the voluntary activation during the isometric contractions calculated as the superimposed twitch relative to the resting twitch, the assessment of voluntary activation did not differ with the two stimulation methods (*P* = 0.58). There was also no difference in the SD of voluntary activation when compared for site of stimulation (TMS vs. muscle, *P* = 0.11). Hence, we calculated the SD across the four trials (2 trials with muscle stimulation and 2 trials with TMS). Again, the SD was greater for old adults compared with young adults (3.0 ± 1.0% vs. 2.3 ± 1.2%, respectively; age effect, *P* < 0.01) with no difference between the sexes (sex effect, *P* = 0.79) and no interaction between sex and age (*P* = 0.20). Thus, there was greater variability in voluntary activation in the old adults across the 4 isometric trials.

Muscle stimulation and TMS evoked similar increases in torque [superimposed twitch (% MVC)] during isometric, concentric and eccentric contractions (stimulation method effect, *P* = 0.17). There was also no difference in the SD of voluntary activation when compared for site of stimulation (TMS vs. muscle, *P* = 0.80) so the SD was compared across the 4 trials for the three contraction types. The superimposed twitch amplitude was more variable among old adults compared with young adults, independent of the contraction type (age effect, *P* < 0.01; contraction type × age, *P* = 0.10, Figure 4A) and these results are consistent with the results when the superimposed twitch was normalized to the resting twitch (as above). Both young and old adults were more variable during concentric (*P* < 0.05) and eccentric (*P* < 0.01) contractions compared with isometric contractions, separately (contraction type effect, *P* < 0.01, Figure 4B), with no difference between the sexes (sex effect, *P* = 0.09).

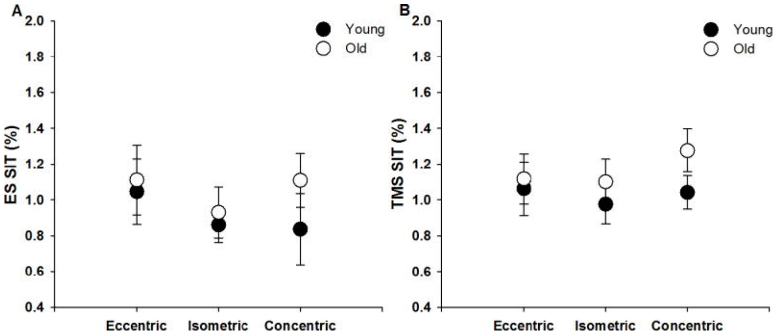

Fig. 4 Mean superimposed twitch amplitude assessed with electrical stimulation of the muscle (A) and transcranial magnetic stimulation (B) during maximal eccentric, isometric and concentric contractions. The superimposed twitch was assessed with the twitch interpolation technique using the following formula: [Superimposed twitch torque/(Maximal voluntary torque + Superimposed twitch torque) × 100]. There were no age, sex nor contraction difference for the superimposed twitch elicited by electrical stimulation of the muscle (B) or transcranial magnetic stimulation (C). SIT: superimposed twitch. ES: electrical stimulation. TMS: transcranial magnetic stimulation

Torque Fluctuations (Isometric Contractions)

Torque fluctuations were calculated to determine whether there were age differences that may have influenced the variability in voluntary activation. CV of torque did not differ between young and old adults during the MVC prior to TMS (age effect, *P* = 0.28, age × sex, *P* = 0.99), electrical stimulation (age effect, *P* = 0.39, age × sex, *P* = 0.88), nor when both stimulation methods were combined in the analysis (age effect, *P* = 0.13, age × sex, *P* = 0.61). Stimulation methods didn’t influence torque fluctuations (stimulation methods effect, *P* = 0.75).

EMG

RMS EMG relative to M_{max}

Biceps EMG RMS/M_{max} ratio during the MVC (across all contractions) did not differ between young and old adults (0.09 ± 0.03 vs. 0.08 ± 0.03; age effect, $P = 0.11$). Nor was there a difference between contraction types (isometric: 0.08 ± 0.03, concentric: 0.08 ± 0.02, eccentric: 0.08 ± 0.02; contraction type effect, $P = 0.27$). This ratio was greater for the men than the women (0.09 ± 0.03 vs. 0.07 ± 0.02; sex effect, $P < 0.01$).

Coactivation

Coactivation is commonly quantified as the ratio of antagonist EMG/agonist EMG, with both antagonist and agonist EMG normalized to EMG values during a MVC. Because this experiment used only MVCs, the agonist EMG relative to EMG during MVC is always equivalent to 1. Therefore, coactivation during the MVCs was quantified as the ratio between EMG activity of the antagonist muscle when acting as antagonist and the maximal EMG activity of the antagonist muscle. Old adults demonstrated greater coactivation than the young adults during concentric (35.6 ± 8.8% vs. 25.4 ± 10.3%, P < 0.01) and eccentric contractions (38.6 ± 12.6% vs. 26.6 ± 12.3%, P < 0.01) but not during isometric contractions (33.4 ± 10.9% vs. 28.0 ± 11.4%, P = 0.33). Similarly, women had a greater coactivation relative to men during the dynamic contractions (concentric, $P < 0.05$; eccentric, $P < 0.01$) but not during the isometric MVC (P = 0.07).

MEP (% M_{max})

There was no age difference ($P = 0.24$) nor sex difference ($P = 0.74$) in biceps MEP amplitude (% M_{max}). However, the MEPs were smaller during the eccentric contractions (47.3 ± 14.6 %) than during the isometric (57.6 ± 18.6 %) and concentric contractions (58.6 ± 21.6 %, contraction type effect, $P < 0.001$; Figure 5) with no interactions of age, sex and contraction type ($P = 0.22$).

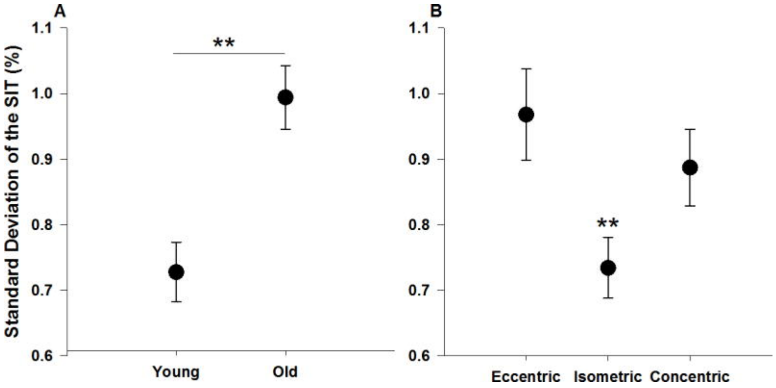

Fig. 5 Standard deviation (SD) of the superimposed twitches across trials in young and old adults (all contraction types merged, A), and during maximal eccentric, isometric and concentric contractions (young and old adults merged, B). The SD was calculated across four trials (2 with electrical stimulation and 2 with transcranial magnetic stimulation). Old adults had a greater SD compared with young adults (**$P < 0.01$). SD was greater during eccentric and concentric contractions compared with isometric contractions (** $P < 0.01$). SIT: superimposed twitch

Silent Period

The duration of the silent period in the biceps brachii EMG following cortical stimulation was similar for the young and old adults (146.7 ± 46.7 ms vs. 146.6 ± 38.5 ms, age effect, $P = 0.99$), and for men and women (145.5 ± 43.4 ms vs. 147.9 ± 42.0 ms, sex effect, $P = 0.79$). However, the silent period was longer during the concentric contractions (168.3 ± 47.8 ms) than during the isometric (134.3 ± 30.3 ms) and eccentric contractions (137.5 ± 39.6 ms, contraction type effect, $P < 0.001$; Figure 5) with no interactions of age, sex and contraction type ($P = 0.58$).

Muscle Properties

Muscle properties for all groups are shown in Table 1. The amplitude of M_{max} of the biceps brachii was larger in young adults compared with old adults (10.6 ± 4.2 mV vs. 6.9 ± 2.8 mV, respectively; age effect, $P < 0.001$), and also larger in men compared with women (10.8 ± 4.3 mV vs. 6.7 ± 2.5 mV; sex effect, $P < 0.001$). There were no differences in M_{max} amplitude elicited during resting isometric, passive shortening or passive lengthening movements (contraction type effect, $P = 0.09$).

Table 1 EMG response to electrical stimulation of the brachial plexus, and torque response to a doublet stimulation of the muscle in young and old men and women. M_{max} and doublet parameters are averaged from the three single and doublet stimulations at rest, respectively.

		Young (n = 30)		**Old (n = 31)**		**P value**		
Variables	**Unit**	**Men (n = 15)**	**Women (n = 15)**	**Men (n = 15)**	**Women (n = 16)**	**Age**	**Sex**	**Age × Sex**
Age	yrs	23.9 ± 1.0	23.3 ± 1.1	68.9 ± 1.0	69.1 ± 1.6	< 0.001	0.87	0.75
M-wave Amplitude (M_{max})								
Lengthening	mV	13.5 ± 1.1	8.2 ± 0.6	8.4 ± 0.8	5.5 ± 0.4	< 0.001	< 0.001	0.18
Isometric	mV	13.3 ± 1.1	8.1 ± 0.6	8.4 ± 0.7	5.4 ± 0.5	–	–	–
Shortening	mV	12.7 ± 1.0	8.0 ± 0.7	8.3 ± 0.8	5.4 ± 0.4	–	–	–
Doublet								
Amplitude	Nm	10.4 ± 0.7	6.6 ± 0.3	9.6 ± 0.7	6.8 ± 0.3	0.55	< 0.001	0.40
Contraction Time	ms	91.0 ± 2.6	95.2 ± 3.8	87.4 ± 2.5	89.1 ± 2.0	0.10	0.31	0.66
Rate of Torque Development	Nm.s^{-1}	118.1 ± 10.4	71.1 ± 3.9	111.5 ± 9.0	79.1 ± 5.1	0.93	< 0.001	0.35
Half-Relaxation Time	ms	79.2 ± 3.0	99.2 ± 4.7	100.7 ± 5.2	113.1 ± 3.1	< 0.001	< 0.001	0.37
Rate of Torque Relaxation	Nm.s^{-1}	66.8 ± 5.7	34.8 ± 2.2	50.3 ± 5.5	30.3 ± 1.5	0.02	< 0.001	0.17

ms, milliseconds; Nm, newton meters; mV, millivolts

The peak torque amplitude elicited at rest with doublet stimuli in the isometric condition was similar between young and old adults (age effect, $P = 0.55$, Table 1). However, half-relaxation time was ~20% longer in old adults than the young adults (age effect, $P < 0.001$, Table 1) and peak rate of torque relaxation was ~20% slower with age (age effect, $P < 0.05$, Table 1).

The peak torque amplitude was greater in men compared with women (sex effect, $P < 0.001$; Table 1). Women exhibited slower rates of torque development and relaxation compared with men (sex effect, $P < 0.001$), as well as longer half-relaxation time (sex effect, $P < 0.001$).

Discussion

The main finding of the present study was that with minimal practice, old adults were more *variable* in activation across maximal voluntary isometric, concentric and eccentric contractions (within a subject) than young with no age-related differences in the mean voluntary activation of the elbow flexor muscles (between the groups). The mean voluntary activation and its variability was similar across the two sites of stimulation (cortical and muscle) indicating the primary source of the age-related variability was supraspinal. Men and women did not differ in voluntary activation levels or its variability in the three contraction types regardless of age and site of stimulation (i.e. motor cortex or muscle). Thus, in healthy old adults the lower maximal force with advancing age during isometric and slow-to-moderate velocity contractions with the elbow flexor muscles was not attributed to the capacity to voluntarily activate the motor cortex or the muscle. There was however, less of an age difference in MVC torque during the eccentric contractions than isometric and concentric contractions, indicating muscular mechanisms likely contributed to this preservation of eccentric torque with aging. Accordingly, there were no age differences in MEP amplitude (normalized to Mmax) nor the silent period in this healthy cohort. However, the stimulated contractile properties of the skeletal muscle were slower in the old adults and women compared with the young adults and men.

Maximal Strength

The age-related reduction in maximal torque was specific to the contraction type, with a smaller age difference for eccentric contractions (~10%) than for isometric and concentric contractions (~20%). The ~20% age-related deficit in maximal isometric torque was similar to our previous findings with the elbow flexor muscles (Hunter et al. 2004; Yoon et al. 2013; Pereira et al. 2015). The smaller age difference in maximal torque during eccentric contractions has been observed in the elbow flexor muscles (Pousson et al. 2001), knee extensors (Hortobágyi et al. 1995; Lindle et al. 1997) and ankle dorsiflexor muscles (Porter et al. 1997; Klass et al. 2005). Thus, our findings confirm that maximal force capacity is more preserved with advanced age in healthy adults during maximal eccentric contractions than during isometric and concentric contractions at a relatively slow-to-moderate velocity of 60°/s in the upper limb. This velocity corresponds to ~15–20% of maximal elbow flexion velocity for the young adults (~380°/s with a 20% MVIC load) and old adults (~320°/s with a 20% MVIC load) (Yoon et al. 2013; Senefeld et al. 2017). Furthermore, and as discussed below, because voluntary activation did not differ between contraction types, the relative preservation of the torque during eccentric contractions compared with the other contraction types with aging is likely due to muscular mechanisms.

Voluntary activation

The age-related reduction in maximal strength of the elbow flexors was not due to a deficit in voluntary activation among old adults during isometric, concentric or eccentric contractions despite minimal practice. Both young and old adults demonstrated voluntary activation of ~95%, which has been observed in the elbow flexors (Klein et al. 2001; Hunter et al. 2006; Yoon et al. 2007, 2015; Keller et al. 2011), knee extensor (Babault et al. 2001; Wilder and Cannon 2009) and index finger abductor muscles (Eichelberger and Bilodeau 2007), although, the ankle dorsiflexor muscles are reported to have larger levels of activation even among old adults (Vandervoort and McComas 1986; Kent-Braun et al. 2002; Klass et al. 2005). Thus, the age-related reduction in maximal torque production during dynamic contractions was not explained by an age-related difference in the capacity to activate the muscles. The similar voluntary activation levels between young and old, and between men and women is supported in our study by the similar RMS EMG/M_{max} ratios observed between young and old adults across the three contraction types.

The dynamic contractions were relatively slow-to-moderate in velocity at 60°/s and extensive piloting in our laboratory showed the interpolated twitch technique is technically challenging to accurately achieve at high velocities of contraction. Age-related differences in maximal torque and power are larger for high velocity contractions in the lower limb muscles (Lanza et al. 2003; Callahan and Kent-Braun 2011) and so activation deficits may limit torque and power for old adults at these higher velocities. It would be useful to assess voluntary activation during isotonic contractions where the velocity is not constrained but the load is constant and are likely similar to contractions performed during many daily tasks. However, it is technically challenging to perform the interpolated twitch technique under these conditions. We performed extensive piloting and found 60°/s was at the up range in velocity to achieve reliable measures. Other techniques may need to be used in future studies to achieve estimates of activation and, also, in much older adults. Given that larger numbers of old adults are living to >80 years [e.g. (https://www.census.gov/population/projections/data/national/2014.html)], a greater understanding of potential deficits in neural drive in adults >80 years, which is the age that large decrements in motor function occurs (Hunter et al. 2016), is needed.

The level of voluntary activation was similar when assessed with electrical stimulation at the muscle and TMS during isometric, concentric and eccentric contractions for both young and old adults. Our findings in the upper limb muscles extend the findings in the lower limb that observed no age-related difference in voluntary activation using electrical stimulation during dynamic contractions of the ankle dorsiflexor (Klass et al. 2005) and knee extensor muscles (Wilder and Cannon 2009). TMS however, provided additional information about the effectiveness of the motor cortical output (Gandevia 2001). Voluntary activation assessed with both muscle stimulation and TMS were similar demonstrating that the capacity to send optimal motor cortical output is preserved in these healthy men and women aged 60 to 80 years, at least in the upper limb where age-related reductions in strength are less than for lower limb muscles such as the knee extensor muscles (Hunter et al. 2000; Raj et al. 2010; Venturelli et al. 2015).

There were no differences in voluntary activation between eccentric, concentric and isometric contractions. In young adults, deficits in activation have been shown during eccentric contraction compared with concentric and isometric contractions for muscle groups where activation is not so easily attainable such as the knee extensor muscles (Beltman et al. 2004) [for review see (Duchateau and Enoka 2016)]. Our findings of minimal differences between contraction types are similar to that reported for the ankle dorsiflexor muscles in both young and old adults (Klass et al. 2005). Thus, there is a growing body of evidence that it is possible to activate muscle eccentrically, at least at slow-to-moderate velocities to a similar magnitude as concentric and isometric contractions, and in young and healthy old adults. Thus, our results indicate that age differences in strength across the contraction types in the upper limb are due to muscular mechanisms.

Variability in Voluntary Activation

A key finding of this study was that young adults had lower variability in voluntary activation than the old adults and this age difference was independent of the contraction type. Voluntary activation to the motor cortex and muscle was more variable in old adults during isometric contractions especially during the first attempts with no previous practice (Jakobi and Rice 2002; Hunter et al. 2008). We extend these findings and show that variability is also greater in the old men and women than the young for concentric and eccentric contractions when the velocity of contraction was controlled. The greater variability in the old adults was not due to differences in the amplitude of torque fluctuations because these were similar for the young and old adults. Both young and old adults had greater variability of activation during concentric and eccentric contractions compared with isometric contractions. This greater variability of activation reflects the difficulty to generate a well-controlled motor output during dynamic contractions (Heckman and Enoka 2004) even in young adults when velocity is controlled. The lack of difference however, in the variability of activation between the two sites of stimulation (cortical vs muscle), indicates that the source of this variability across all contractions is likely to be supraspinal.

Men and women had similar variability in activation among the old adults, as we observed in the young men and women in our cohort, and also in the elbow flexor muscles with activation from supraspinal sources before and after an isometric exercise (Hunter et al. 2006). Our study extends these findings to show similar variability between the sexes with aging during slow-to-moderate dynamic contractions in the upper limb. For both men and women, however, the age-difference in variability during the three contraction types was not related to the lower maximal torque in old adults. Certainly, the lower consistency in activation between trials with aging may have larger effects during submaximal tasks that require greater force control than a brief MVC (Enoka et al. 2003) or when velocity is not controlled.

The significance of these findings of the greater age-related variability is that activation may be inadequate in older adults during tasks that allow only one attempt as routinely observed in real-world situations. Despite the small age difference in variability of activation, the differences could be functionally important. Recently, we demonstrated that increased variability of maximal velocity contractions (with a load of 20% of MVC) during repeated and fatiguing dynamic contractions with the knee extensor muscles was associated with worse functional performance (six-minute walk test) (Senefeld et al. 2017). Similarly, force variability of arm and hand muscles was associated with functional tests (e.g. pegboard test of dexterity) (Marmon et al. 2011; Almuklass et al. 2016), demonstrating the impact of upper extremity variability. Thus, even small increases in variability in activation from supraspinal and spinal sources as we showed in this study, may have biological and even functional consequences. Importantly, these findings also show that only comparing the mean results of old and young adults for a physiological variable potentially masks subtle age-related changes in physiology (Hunter et al. 2016).

Coactivation

A possible explanation for the lower strength with age is simultaneous activation of the agonist and antagonist muscles (i.e. coactivation) during maximal contractions. During contractions with the elbow flexors muscles, old adults had greater levels of coactivation than younger adults during both concentric and eccentric contractions, but not during isometric contractions. Increased coactivation during dynamic but not during isometric contractions with aging was observed in muscles of the hand (Burnett et al. 2000). A higher level of coactivation limits the potential torque at the joint and may contribute to an age-related difference in strength of agonist muscles (Macaluso et al. 2002). Increased coactivation can also increase joint stiffness and thus reduce the impact of perturbations during joint movement (Gribble et al. 2003; Dideriksen et al. 2015) and this is consistent with old adults increasing the activation of antagonist muscles during dynamic contractions to stabilize the joint during movement.

MEP amplitude and silent period

The MEP amplitude was smaller for eccentric contractions compared with isometric and concentric contractions, with no differences between sexes or age groups. The differences in MEP amplitude during eccentric contractions are due to pre- and postsynaptic inhibitory mechanisms acting at the spinal level, specifically, enhanced Ia afferents activity or lower spinal efficacy (Duclay et al. 2011, 2014). Because the MEP amplitude reflects the balance between excitatory and inhibitory input to the corticospinal volley (Devanne et al. 1997), the absence of age differences in the average values demonstrates that corticospinal excitability is relatively preserved with aging in this current-study cohort of old men and women.

The duration of the silent period was longer during concentric contractions than the isometric and eccentric contractions for all groups. The initial part of the silent period (50–100 ms) is influenced by both spinal and cortical mechanisms, but the latter part represents activity in intracortical inhibitory circuits (Inghilleri et al. 1993). Although the silent period largely represents intracortical and spinal mechanisms, the longer silent period during the concentric than the isometric and eccentric contractions could be due to the presence of low-level EMG that lengthens the duration of the silent period (Taylor et al. 1996). The immediate fall in force following cortical stimulation is associated with muscle lengthening caused by the relaxation of the muscle. The lengthening of the muscle is thought to increase the firing of muscles spindles, which facilitates spinal motoneurones and induces very low level EMG activity during the silent period (Butler et al. 2012). During concentric contractions, the muscle continues to shorten for the duration of the silent period so the relaxation occurs at a lower absolute force compared with the isometric and eccentric contractions. This is believed to result in a lower muscle spindle discharge during concentric contractions and an absence or a lower level of EMG and a longer silent period (Butler et al. 2012).

Contractile Properties

Despite the minimal age differences in voluntary activation and indices of corticospinal excitability, old adults exhibited lower contractile speed of the torque response to the doublet stimulation (longer relaxation time and lower rate of torque relaxation) than the young adults. A lower rate of muscle relaxation is generally attributed to slower cross-bridge mechanics (Dux 1993) and slower rate of Ca^{2+} reuptake into the sarcoplasmic reticulum (Hunter et al. 1999, 2016). This slowing of the muscle with aging is accompanied by a reduction in the proportional area of type II muscle fibers (Hunter et al. 1999) and lower shortening velocity of both type I and type II muscle fibers (Larsson et al., 1997; Krivickas et al., 2001; for review see Hunter et al., 2016). In our study, there were however, no age differences in the electrically evoked doublet amplitude at rest, nor in the rate of torque development. Some studies have shown a decrease in amplitude of the evoked force with aging (De Serres and Enoka 1998; Yue et al. 1999; Wilder and Cannon 2009), and others have not (Klass et al. 2005). The lack of age difference in the evoked force amplitude may reflect the relatively small age differences in strength in the healthy cohort of old men and women in this study.

There were however, large sex differences in contractile properties for both age groups. The men had a larger amplitude of the doublet, and greater rates of torque development and relaxation, and shorter half-relaxation time than the women. This is consistent with previous findings showing that elbow flexor muscle mass is larger in men with a greater proportional area of type II muscle fibers compared with women (Simoneau and Bouchard 1989; Hunter 2014, 2016). Thus, the differences in muscle properties between men and women were greater than the differences between the young and old adults.

Conclusion

We demonstrated that in healthy community-dwelling old men and women up to 80 years, the variability in supraspinal activation was larger than in young adults when performing maximal effort slow-to-moderate velocity dynamic and isometric contractions with the upper limb with minimal practice. We also showed that the similarities in the variability of activation between sites of stimulation (cortical vs muscle) indicate that the primary source of age-related variability and the greater variability during maximal eccentric and concentric contractions than the isometric contractions is likely supraspinal.

The mean voluntary activation (neural drive to the motor cortex and to the muscle) of old adults during maximal dynamic contractions of the upper limb however, did not differ to that of young adults, despite the increased age-related variability across all contraction types. Thus, the age-related decrease in strength during isometric and dynamic contractions in the elbow flexor muscles is primarily due to a reduction in muscle mass and was not due to a difference in supraspinal activation. The minimal sex differences in activation and its variability also indicate older men and women had similar neural drive from supraspinal sources during dynamic contractions. The findings however, of increased age-related variability of activation, suggest that the measurement of mean levels of voluntary activation may mask small neural deficits of even healthy old adults who have lower predictability and consistency of voluntary activation that originates from supraspinal sources. This increased variability may be indicative of subclinical changes in the central nervous system that are a precursor to demise in the capacity and consistency of activation with advanced aging.

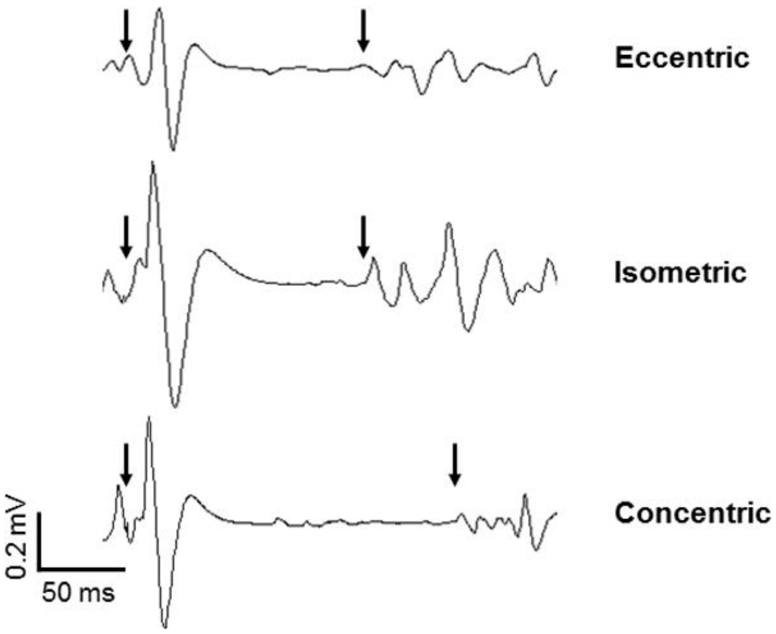

Fig. 6 Typical traces of EMG response to transcranial magnetic stimulation during eccentric, isometric and concentric contractions. The first vertical arrow indicates the time at which the stimulation was delivered and the second one indicates the end of the silent period. The amplitude of the MEP was smaller during eccentric

contractions than during isometric and concentric contractions (both $P < 0.001$). The silent period was longer during concentric contractions compared with eccentric and isometric contractions (both $P < 0.001$)

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