Aging and Muscle Fatigability in the Upper Extremity

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AGING AND MUSCLE FATIGABILITY IN THE UPPER EXTREMITY

by

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ABSTRACT
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Aging is accompanied by reductions in strength and contraction velocity, and increased fatigability of limb muscles during high-velocity dynamic contractions. These age-related changes affect functional tasks and are well described for the lower limb, with less known about the upper limb muscles. The aims of the thesis were to compare in young and old men and women: (1) maximal torque and power of the elbow flexor muscles across a range of isokinetic velocities, and (2) the neural (supraspinal) and muscular mechanisms of fatigue induced by high-velocity dynamic contractions of the elbow flexor muscles.

28 young (23.2 ± 2.6 years) men (n = 14) and women (n = 14) and 33 (72.6 ± 5.6 years) old men (n = 18) and women (n = 15) with the elbow flexor muscles performed: (1) maximal isokinetic contractions at 15 velocities to assess strength and power (0-450°/s), and (2) a dynamic fatiguing task involving 80 fast, maximal-effort contractions with a load equivalent to 20% of maximal voluntary isometric torque (MVIC). Before and after the fatiguing task the following were assessed: voluntary activation using motor cortical stimulation as a measure of supraspinal fatigue, and contractile properties evoked with electrical stimulation as a measure of muscular mechanisms.

The elbow flexor muscles of the old adults were weaker and less powerful than young adults across all the velocities assessed ($P<0.01$), although voluntary activation was similar between the age groups ($P>0.05$). Some young and old adults were not able attain higher contraction velocities, primarily driven by the women. Old adults were more fatigable than young adults ($P<0.001$, 15% difference) with now sex differences ($P>0.05$). Old adults exhibited a larger reduction in voluntary activation ($P=0.036$, 7.5% age difference) and greater increase in relaxation in the old adults (55%) than the young (36%) following the fatiguing task.

The elbow flexor muscles of old men and women were weaker and less powerful than young, but this was not due to differences in voluntary activation. The greater fatigability of elbow flexor muscles in the old adults however, was due to both supraspinal mechanisms and slowing of the muscle that occurs with aging.

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CHAPTER I. INTRODUCTION

Between now and 2050, the United States will experience a considerable growth in the number of old adults. It is estimated that by 2050, the number of adults over the age of 65 will almost double current population estimates (Ortman et al., 2014). This exponential growth may result in large economic impacts to both health care systems and individuals. It is therefore imperative to understand the physiological changes occurring due to age to prevent frailty and a loss of independence (Hunter et al., 2016; Reid and Fielding, 2012). Old adults are weaker, slower, and less powerful, leading to overall greater frailty and a loss in independence. Age-related declines in muscle strength and power are associated with losses in mobility, and subsequently predictive of morbidity and mortality (Reid et al., 2012; Metter et al., 2004). Functional changes within the neuromuscular system occur with aging lead to decrements in motor performance (Hunter et al., 2016; Fig 1.1). Ability to perform these tasks can be limited by fatigability of the limb muscles, further exacerbating age-related reductions in strength and power (Justice et al., 2014). Understanding the physiological mechanisms responsible for the age-related reductions in strength and power may help to create solutions to retain strength and keep old adults independent.

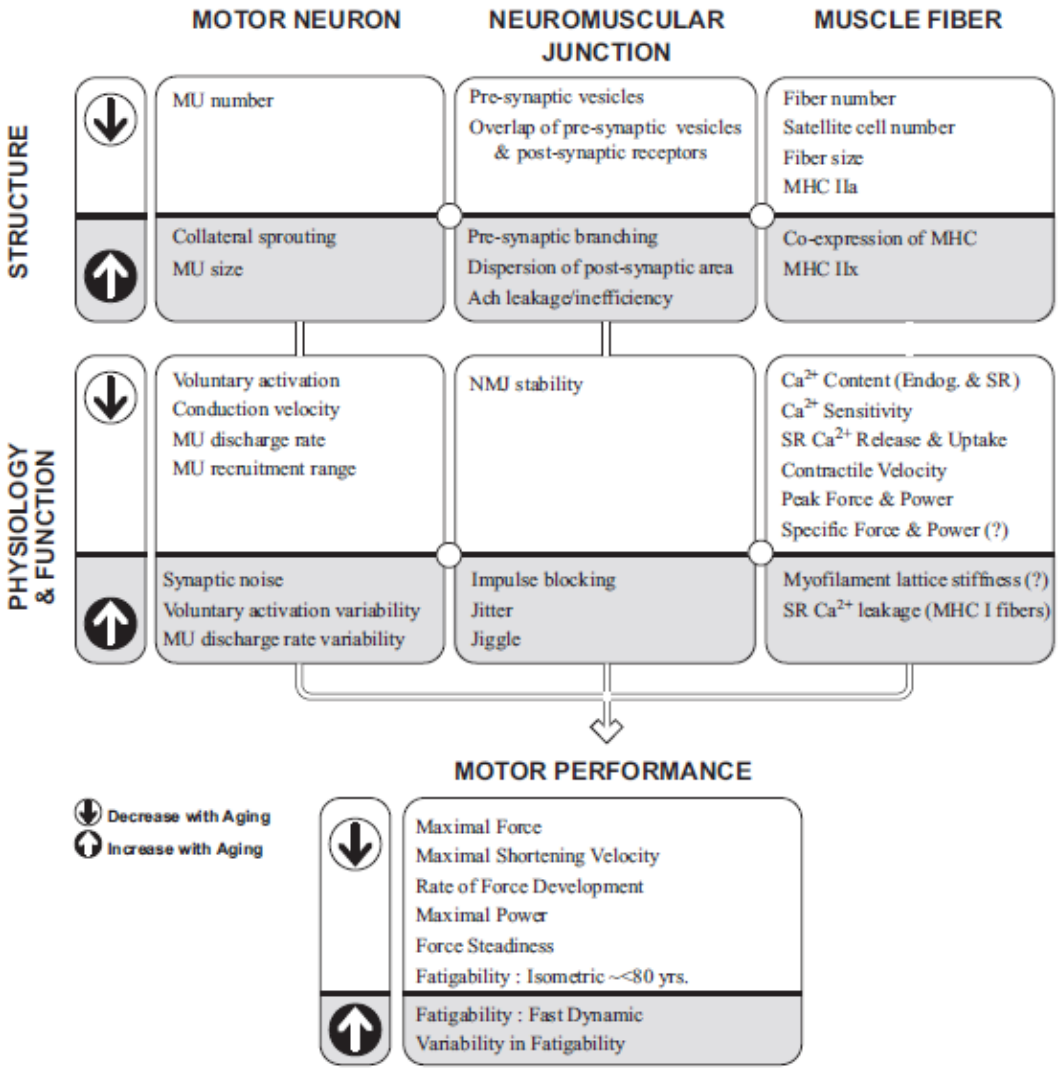

Fig 1.1. Structural and physiological changes due to aging within the motor unit. (Hunter et al., 2016)

Aging and Power

Strength: Sarcopenia is the age-related loss in muscle mass and the associated reductions in muscle strength, power, and function (Fielding et al., 2011). Aging is accompanied by a host of alterations to the neuromuscular system that lead to reduced muscle mass, neural mass, and ultimately a loss in force generating capacity (Raj et al.,

2010; Hunter et al., 2016). Characteristic of this age-related decline is the reduction in skeletal muscle strength within the elderly. This age-related decline in strength has been established over many cross-sectional studies of limb muscles tested under isometric and dynamic conditions, with the knee extensors being the most frequently examined (Doherty, 2003). Studies comparing the knee extensor strength in young and old adults report an average overall decrease in strength of 20-40%, with strength being reduced ~ 10% per decade starting approximately at 40-50 years of age (Doherty, 2003; Hunter et al., 2000). However, these cross-sectional studies may underestimate actual age-related reductions in strength. The few longitudinal studies that have looked at age-related reductions in strength found a greater reduction in strength and a higher amount of variability between individuals with increasing age (Frontera et al., 2000; Metter et al., 2004). There also can be variability in the strength between muscle groups (Hunter et al., 2016). Age-related reductions in isometric strength are typically larger in muscles of the lower extremity compared to the upper extremity (Frontera et al., 2000; Hunter et al., 2000; Raj et al., 2010). This variability may be due, in part to the differing amount of use between the muscle groups (Degens and Korhonen, 2012; Venturelli et al., 2014).

The age-related reductions in isometric strength largely parallel losses in muscle mass (Metter et al., 1999). Aging is accompanied by a loss of innervated muscle fibers and a reduction in the size of the fibers in the surviving motor units (Lexell et al., 1988) (Fig 1.1). The fibers from the existing muscle fibers are, in general, smaller in old adults compared with young adults (Lexell et al., 1988; Hunter et al., 1999). This is particularly true in the lower extremity muscles. However, the age-related reductions in fiber size appear to vary across muscles and men and women. Possible reasons for the differences

seen between muscle groups and genders include physical activity, nutrition, sampling bias in cross-sectional design, variability in muscle biopsy, and small sample sizes in some studies (Hunter et al., 2016). Several studies highlight the reduction in the size of the muscle fiber of old individuals compared to young, showing evidence to a greater amount of atrophy in fibers expressing myosin heavy chain (MHC) II isoforms (Hunter et al., 1999; Lexell et al., 1988; Purves-Smith et al., 2014) and these isoforms are correlated with fast contractile properties. Further, atrophy can be quite marked in all fibers within very old adults (older than ~80 years) (Purves-Smith et al., 2014).

Contractile Velocity. In general, old adults are slower than young adults. Maximal strength produced during isokinetic contractions is also reduced with aging particularly in the lower limb (Lindle et al., 1997) (Fig 1.1). Age-related changes in strength assessed during dynamic contraction however are also dependent on the contraction mode, with less of an age reduction in torque for eccentric (lengthening) compared to concentric (shortening) contractions (Power et al., 2015, 2016). The mechanisms for the relative preservation with age during eccentric (lengthening) contractions is not well understood.

Studies done *in vivo* have shown a lower maximal shortening velocity in healthy old adults compared to young (Labarque et al., 2002; Thom et al., 2005). The whole muscle not only contracts more slowly but also relaxes more slowly with aging. This slowing of the whole muscle with aging has been shown with lower rates of force development such as that in the ankle dorsiflexor muscle (Klass et al., 2008) and slower relaxation rates in the knee extensor muscles of old adults (Hunter et al., 1999). The lower rates of force development and slower relaxation of the muscle is seen in both

voluntary contractions, and evoked contractions (Yoon et al., 2015; Molenaar et al., 2013).

The age-related reductions in maximal torque are larger at higher speeds of concentric contractions, for some muscles such as the knee extensor muscles (Lanza et al., 2003). However, this difference appears to vary across muscle groups (Raj et al., 2010). The muscle fibers of old adults also typically exhibit a reduced contractile speed compared to those of young adults. Lower rates of force development are seen in both active and inactive old adults (Power et al., 2016). Studies have also shown old adults to have lower maximal shortening velocities, although this may not be the case in adults that are active (D'Antona et al., 2003; Krivickas et al., 2001, Larsson et al., 1997). The reduction in velocity of the muscle fibers is associated with overall slower cross-bridge kinetics. Shortening velocity is much faster for myosin heavy chain (MHC) IIa fibers compared to MHC I (Trappe et al., 2003). Advanced age is accompanied by a loss of innervated muscle fibers and a reduction in fiber size in the surviving motor units (Lexell et al., 1988). Old adults generally have been shown to have a smaller proportional area of MHC IIa isoforms compared to young adults (D'Antona et al., 2003; Lamboley et al., 2015). This shift in a reduction of MHC IIa isoforms in old adults would therefore also reduce its contractile speed (Larsson et al., 1997). In addition to the reduction in contractile speed, the rate of muscle relaxation of the whole muscle slows with aging (Callahan and Kent-Braun, 2011). This is likely due to cross-bridge mechanisms and rates of Ca^{2+} uptake in the sarcoplasmic reticulum (Hunter et al., 1999).

Voluntary Activation. The reduced ability of old adults to rapidly develop force during fast contractions, may be due to inadequate activation of the motor units,

contributing to slower force development (Klass et al., 2008). Inadequate activation during maximal contractions may also be responsible for age-related reductions in strength. Voluntary activation of motor units can be assessed by stimulating the muscle or motor cortex during a maximal effort (Taylor, 2009). While it can be measured during slow dynamic contractions, it is most easily attained during maximal voluntary isometric contractions (MVIC). Differences in voluntary activation can depend on contraction velocity, muscle group, physical activity, and practice of the maximal effort (Klass et al., 2007). The literature differs on whether old adults are able to voluntarily activate as well as young adults. Some studies show that old adults have consistently lower voluntary activation levels (De Serres and Enoka, 1998, Hunter et al., 2008, Yoon et al., 2008). Other studies note that old adults are able to voluntarily activate at similar levels to young adults when familiarized with the protocol first (Jakobi and Rice, 2002; Hunter et al. 2008). Practice can help to achieve consistent levels of activation in old adults, but they are still more variable than young adults across trials (Hunter et al, 2008; Yoon et al. 2008). Therefore, the activation levels of old adults may be inadequate for tasks that only allow one attempt (e.g., recovering from a disturbance in balance to prevent a fall). The larger variability in voluntary activation within old adults potentially worsens the age-related declines in strength and power (Hunter et al., 2016).

Power. Power is quantified as the product of torque and velocity. With aging, there are decreases in torque production at moderate to high-velocity concentric contractions, and reductions in the maximal shortening velocity of the muscle (Hunter et al., 2016). The combined reductions in these two measures lead to an overall greater reduction in the power production with older adults (Raj et al. 2010). Power is also more

strongly associated with functional tasks such as stair climbing, ambulation, and rise time from a chair, than the age-related reductions in isometric strength (Reid and Fielding, 2012). Power within the lower extremity during shortening contractions is also predictive of functional tasks and disability (Reid and Fielding, 2012). The age-related reductions in power are greater than the overall reductions in isometric strength (McNeil and Rice, 2007). When young and old adults are matched for cross-sectional area, these age-related differences in power are still present (McNeil et al., 2007) indicating the slowing of muscle has a large influence on the reductions in power and aging. The age difference in power appears to widen as the velocity increases, at least for the knee extensor muscles (Callahan and Kent-Braun, 2011; Lanza et al., 2003). Similar reductions in power have been shown for muscles of the upper extremity (Valour et al., 2003), although muscles within the lower extremity appear to have greater age-related reductions (Raj et al., 2010). The age-related reduction in power at higher velocities is associated with the reductions in shortening velocity of the muscle (Larsson et al. 1997), reduced muscle mass (Reid and Fielding, 2012), and may be furthermore affected by inadequate activation of the surviving motor units (Klass et al., 2008). This work has been primarily conducted on lower limb muscles. This study will investigate whether the age-related reductions in power are greater at the higher velocities of contraction in the upper limb muscles as often observed for the lower limb in both men and women.

Fatigability

Fatigability is the reduction in maximal strength or expected strength or power of a muscle in response to a bout of exercise (Enoka and Duchateau, 2016). Fatigue can

originate from multiple sites along the neuromuscular pathway, some of which are shown in Fig 1.2 (Hunter, 2017).

Central Mechanisms. Central mechanisms of fatigability originate from structures proximal to the neuromuscular junction. The activation of the motor neuron pool involves the integration of synaptic inputs from the descending pathways (Hunter, 2014). During a fatiguing bout of exercise, there is often a failure of voluntary activation. This failure in voluntary activation means that the level of neural drive to the muscle was less than optimal because either the motor units were not all recruited, or the discharge rates were not maximal (Gandevia, 2001). Measurements of the voluntary drive to the motor cortex can be made with a transcranial magnetic stimulus during a voluntary activation (Todd et al., 2003). An observed increase in force evoked by a superimposed stimulation at the cortex during the voluntary contraction implies a failure of voluntary drive superior to the neuromuscular junction and is also known as supraspinal fatigue.

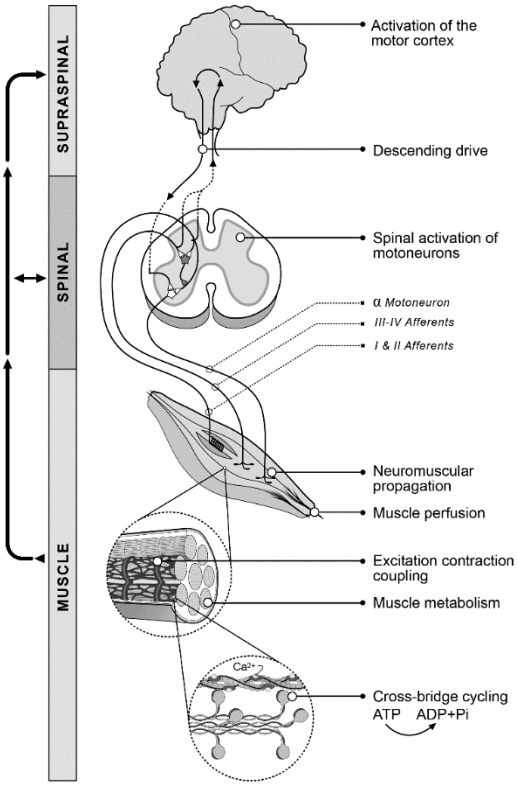

Fig 1.2. *The neuromuscular pathway.* Reductions in fatigue can be due to factors emanating from supraspinal, spinal, and muscular sources (Hunter, 2017).

Peripheral Mechanisms. Peripheral mechanisms of fatigability refer to changes occurring within the muscle, i.e. distal to the motor neuron. Fatigue can occur at several locations within the muscle including the neuromuscular junction, the muscle membrane,

and within contractile properties in the fibers. Estimates of the contributions of these sites can be made through the use of electrical stimulation because force can be evoked independent of the central nervous system (Kent-Braun et al., 2016). Measurements of peripheral fatigue can be made through the reduction in twitch amplitude, the rate of torque development, and rate of relaxation in the electrically induced twitch. These indicate that the force of the muscle is reduced and becomes slower with fatigue (Kent-Braun et al., 2012).

Aging and Fatigability

Isometric Fatigability. Fatigability is an important concept to consider with aging as it further exacerbates the age-related reductions in strength and power in old adults observed before exercise (Hunter et al., 2016). However, the magnitude of the reduction is altered when the demand of the task (such as intensity, velocity, and mode of contraction) changes. Under maximal and submaximal isometric contractions, old adults are typically less fatigable than young adults even when matched for strength (Hunter et al., 2005). Despite young adults typically being stronger, old adults were shown to have a longer time to task failure when completing a submaximal isometric fatiguing task (Hunter et al., 2004). This greater fatigue resistance with aging during isometric contraction is associated with slower contractile properties, a lower proportional number of fibers expressing MHC (myosin heavy chain) IIa isoforms, and less of a reliance on glycolytic metabolism in old adults compared to young (Callahan et al., 2016; Hunter et al., 1999; Hunter et al., 2008; Kent-Braun, 2009). However, the fatigue resistance in older adults may only apply to those <75 years of age; old adults >75 years exhibited greater fatigability in the lower extremity compared to those <75 years (Justice et al., 2014).

Dynamic Fatigability. The velocity and mode of contraction largely alters the magnitude of the age difference in fatigability. The greater fatigue resistance in older adults seen in sustained isometric contractions was diminished when performing a dynamic task at slow to moderate-velocity contractions in the knee extensor (Callahan et al., 2009; Dalton et al., 2012), and elbow flexor muscles (Yoon et al., 2013). When comparing contractions across velocities within the knee extensors, there is a similar reduction in power for slow isokinetic velocities, a greater reduction in the old adults with moderate isokinetic velocities, and even larger reductions during unconstrained (isotonic) contractions (Dalton et al., 2010). The greater reductions in power with the isotonic task highlight the importance of shortening velocity when assessing fatigability during dynamic contractions. Similar studies have found that during high-velocity contractions old adults are more fatigable than the young within the lower extremity (McNeil and Rice, 2007; Dalton et al., 2010).

Another important aspect of fatigability that is altered with age is the variability in force or power during a fatiguing task. A greater variability of maximal torque was seen in old women compared to young women when performing a dynamic fatiguing task at a moderate velocity (120°/s) (Kent-Braun et al., 2014). Similarly, maximal velocity was more variable for old adults compared to with young during a dynamic fatiguing task of the knee extensor muscles (Senefeld et al., 2016). However, there were no age-related differences in variability for the same task conducted with the elbow flexor muscles (Senefeld et al., 2016). Further, age-related reductions in power production were recently shown within the upper extremity (elbow flexor muscles), although not to as great of an

extent as the lower extremity (Senefeld et al., 2016) (Fig 1.3). These age-related changes in power were similar for men and women (Senefeld et al., 2016).

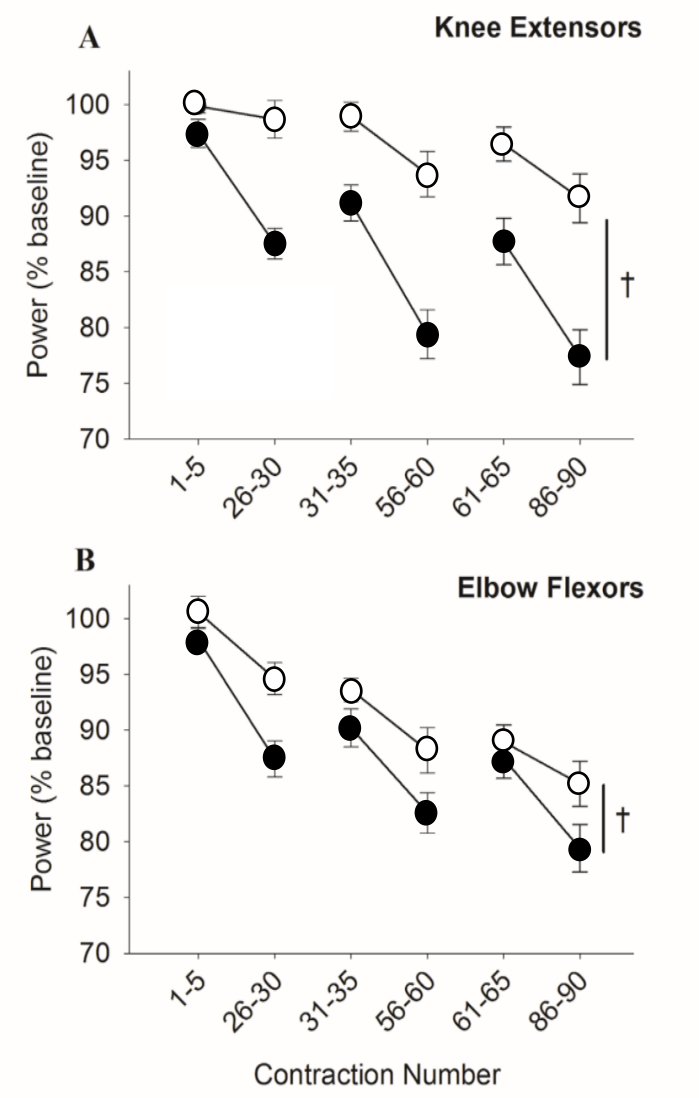

Fig 1.3. Reductions in power in the knee extensor (A) and elbow flexor (B) muscles. Young (○) and old (●) reductions in power over time, during a dynamic fatiguing task. (Senefeld et al., 2016).

The mechanisms for the difference between muscle groups were not identified, although the increased variability in velocity seen in older adults could be indicative of impaired or variable activation of motor units needed for rapid force development (Klass

et al., 2008; Senefeld et al., 2016). The age-related reduction in fatigability during high-velocity contractions in the knee extensor muscles appear to be due primarily to changes within the muscle, with small contributions from central (supraspinal) mechanisms (Sundberg et al., 2016). The mechanisms for the reduced fatigability within the elbow flexor muscles is not well understood. Thus, this body of work will determine the mechanisms for the age-related reductions in power during a fatiguing task with the elbow flexor muscles in men and women.

Specific Aims and Hypotheses

The primary aims of this study were to:

Specific Aim 1: To compare maximal torque and power of the elbow flexor muscles across a range of isokinetic velocities in young and old, men and women.

Hypothesis 1: There will be a large age-related reduction in maximal torque and power, and these age differences will be greatest at higher velocities.

Specific Aim 2: To determine the neural and muscular mechanisms of fatigue induced by high-velocity dynamic contractions of the elbow flexor muscles in young and old, men and women.

Hypothesis 2: Older adults will be more fatigable during a high-velocity fatiguing task with the elbow flexor muscles primarily due to mechanisms within the muscle and with small contributions from supraspinal fatigue.

CHAPTER II. METHODS

Subjects

Twenty-eight young adults (19-29, 23.2 ± 2.6 years; 14 men and 14 women) and 33 old adults (72.6 ± 5.6 years; 18 men and 15 women) participated in the study. All subjects were healthy, community dwelling men and women with no known neurological diseases or contraindications to exercise. Participants were screened and excluded for use of medication affecting the central nervous system and hormonal status (e.g. hormone-replacement therapy). Prior to the experiment, each subject provided written informed consent. The protocol was approved by the Marquette University Institutional Review Board and was conducted according to the Declaration of Helsinki.

Each participant visited the laboratory for two experimental sessions. The first session involved the assessment of power, torque, and velocity in the elbow flexor muscles, a familiarization of stimulation techniques, and a questionnaire regarding physical activity levels (Kriska et al., 1990; 1992). The second session consisted of a dynamic fatiguing task lasting 4 minutes, with a load of 20% of MVIC in same limb, and stimulations to assess mechanisms of fatigability.

Experimental Setup

Each subject was seated upright in an adjustable chair (Biodex Medical System 4, Shirley, NY). The shoulder was flexed to 50° in the sagittal plane (with 0° considered to be in line with the torso) and the elbow was 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 further attached to the lever arm of a Biodex

dynamometer (Biodex Medical System 4, Shirley, NY). The axis of rotation of the dynamometer was aligned to the anatomical axis of the elbow of each subject. Each participant was secured with padded straps across both shoulders and the waist to minimize extraneous movements during contractions. For isometric contractions, the elbow joint was flexed to 90°. Concentric contractions were performed over an 80° range of motion. Recordings of muscle torque, velocity, and position from the Biodex dynamometer were digitized by a Power 1401 analog-to-digital converter and Spike 2 software (Cambridge Electronics Design, Cambridge, UK) with a sampling rate of 1000 Hz.

Electrical Recordings

Electromyography (EMG) signals were recorded with pairs of bipolar silver chloride circular (8mm diameter) surface electrodes that were placed over the biceps brachii, triceps brachii, and brachioradialis muscles according to recommended placements (Hermens et al, 2000). For biceps brachii, the electrodes were placed between the medial acromion and fossa cubit, 1/3 from the fossa cubit. For triceps brachii, the electrodes were placed on the long head midway between the posterior crista of the acromion and the olecranon at 2 finger widths medial to the line. For the brachioradialis, the electrodes were placed on the muscle belly ~ 4cm distally from the lateral epicondyle. Reference electrodes were placed on the acromion. The EMG signals were amplified (100x) and band-pass filtered (13-1000 Hz; Coulbourn Instruments, Allentown, PA), and recorded online via a Power 1401 analog-to-digital 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 transcranial magnetic stimulation (TMS).

Brachial Plexus Stimulation. The brachial plexus was electrically stimulation to produce a maximal compound muscle action potential (Mmax) of the biceps brachii, brachioradialis, and triceps brachii muscles at rest. Single stimuli (400 V and 100 μs duration) were delivered to the brachial plexus using a constant-current stimulator (model DS7AH, Digitimer, Hertfordshire, UK). A cathode was placed in the supraclavicular fossa and an anode over the acromion. The stimulation intensity was determined by increasing the current until the peak-to-peak M-wave amplitude plateaued, and was then increased to 20% to ensure a maximal electrical response. The stimulation intensity ranged between 50-300 mA and once the intensity was determined, this level of stimulation was used for the remainder of the protocol.

Muscle Stimulation. The biceps brachii muscle was directly stimulated to produce a maximal peak twitch of the elbow flexor muscles. Paired (400 V, 100 μs duration and 100 Hz) stimuli were delivered to intramuscular nerve fibers by a constant-current stimulator (model DS7AH, Digitimer, Hertfordshire, UK) through custom-made electrodes (2.0 x 4.5 cm) attached 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. The anode was placed over the distal biceps tendon. The optimal intensity was set for doublet stimulations (150-550 mA) and was used at rest.

Motor Cortex Stimulation. TMS was delivered via a round coil (13.5 cm outside diameter; Magstim 200, Magstim, Whitland. UK) over the vertex of the motor cortex to evoke motor-evoked potentials (MEPs) in the biceps brachii, brachioradialis, and triceps brachii muscles during isometric elbow flexion contractions. The vertex of the motor cortex was identified and marked to ensure repeatability of coil placement throughout the protocol. The direction of current flow in the coil preferentially activated the motor cortex in the hemisphere opposite of the limb studied. Single stimuli were delivered over the motor cortex at an intensity that produced a large MEP in the agonist biceps brachii muscle (minimum amplitude of 50% of Mmax) but only a small MEP in the antagonist triceps brachii muscle (maximum amplitude of 15% Mmax) during a brief contraction of the elbow flexor muscles at 50% MVC (Todd et al, 2004).

Experimental Protocol

Each participant visited the laboratory for two experimental sessions. The first session assessed torque production over a range of velocities with isokinetic contractions of the elbow flexor muscles. The second session involved a dynamic fatiguing task with a 20% MVIC load in the same limb. M-wave and maximal peak twitch measures were taken at the beginning of both sessions. The protocol then involved measurements of maximal voluntary isometric contractions (MVIC) of the elbow flexor muscles. Four sets of brief isometric contractions (2-3 s for each contraction) for the elbow flexor muscles were performed and separated by two minutes of rest to minimize fatigue. Two sets of MVICs of the elbow extensor muscles, separated by two minutes of rest were performed to normalize triceps EMG activity during the fatiguing contraction. Strong verbal encouragement and visual feedback were provided during each maximal effort.

Isokinetic Contractions. Each participant performed a series of maximal isokinetic contractions (15 sets of 4 contractions) in the elbow flexor muscles. The range of motion for the task was set to 80°, and the test velocities were 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 360, 400, 450°/s. Two minutes of rest separated each velocity to avoid fatiguing the muscle. At each session, the first and last trials were performed at a velocity of 180°/s, all other trials between were randomized. This was done to ensure that the participant did not fatigue during the task. Each participant was instructed to pull as hard as possible throughout the full range of motion for each velocity tested.

Fatiguing Task. A dynamic fatiguing contraction task was performed with the elbow flexor muscles with a weight equal to 20% of MVIC torque. Prior to the start of the fatiguing tasks, subjects were familiarized with the load of the contraction and were verbally encouraged to contract as fast as possible. One contraction was performed every 3 seconds over the 4-minute task for a total of 80 maximal isotonic contractions. Each participant moved the weight through an 80° range of motion in elbow flexion. The subject was then passively returned to the start position within the 3 second time limit. Participants were given verbal encouragement to indicate the start of each 3-second cycle. Visual feedback of position and torque was obscured to prevent participants from contracting prematurely. The fatiguing task was terminated after 4 minutes, and the arm was returned to 90° of flexion.

Voluntary Activation and Contractile Properties. Voluntary activation and contractile properties of the muscle were assessed prior to the fatiguing task, and immediately post (~10 s). Voluntary activation was assessed during MVIC of the elbow flexor muscles with TMS stimulations. Contractile properties were assessed during single

and doublet stimulations at rest following the MVIC contraction. Prior to the fatiguing task, 5 measurements of voluntary activation and contractile properties were taken with 2.5 minutes of rest between each measure. Following the fatiguing task 5 measurements were taken; immediately (~10 s and ~30 s), 2.5 minutes, 5 minutes, and 10 minutes into recovery.

Data Analysis

Isometric Measures. The maximal voluntary isometric torque and the associated RMS EMG of the biceps and triceps brachii muscles were measured during the MVICs without stimulation. For the contractions, measurements were assessed for a 100-ms period during the plateau of the MVIC.

Isokinetic Measures. During each isokinetic contraction, the participants were considered to have reached the target velocity if they were able to consistently reach the peak velocity for four contractions. For all contractions during which the participant was able to achieve the target velocity, peak torque and position were recorded. Peak power was then calculated from the product of the absolute peak torque and the velocity that it was measured at. Power, absolute and relative (% of MVIC) torque-velocity curves were generated for each subject in the elbow flexor muscles.

Fatiguing Task. Fatigability of dynamic contractions was quantified as the percentage reduction in the power during the last 5 contractions, relative to the power produced over the first five contractions of the fatiguing task. Fatigability of the MVIC was quantified as the percentage reduction in the MVIC from baseline measures.

Voluntary Activation. Voluntary activation was assessed using the twitch interpolation technique with TMS (Taylor and Gandevia, 2001; Hunter et al., 2006). The torque following TMS at MVIC (superimposed twitch) was expressed as a fraction of the estimated torque of the response evoked at rest (resting twitch). The estimation of the resting twitch was obtained for each participant by linear regression analysis of the torque of the superimposed twitch at MVIC and subsequent torque production at submaximal contractions of 60% and 80% MVIC. The amplitude of the estimated resting twitch can be determined from three data points with contractions above 50% MVC (Todd et al., 2003). The resting twitch was estimated rather than measured directly due to motor cortical and spinal cord excitability increasing with activity (Thompson et al., 1991). The estimated resting twitch was used to calculate voluntary activation through the following formula: voluntary activation = (1 – superimposed twitch/estimated resting twitch) x 100 (Todd et al., 2003). Majority of the regression measurements taken prior to the fatiguing task were linear ($R^2 > 0.8$), the relationship was not linear for several subjects following the fatiguing task. For this reason, these estimates of voluntary activation were excluded from the statistical analysis (7 young, and 8 older subjects).

Contractile Properties. Contractile properties of the muscle stimulation were assessed at rest prior and following the fatiguing task. The amplitude of the twitch was measured as an index of the force-generating capacity of the muscle. Other measures of including the peak rate of force production, half relaxation time, and contraction time were also assessed.

Statistical Analysis

Data are reported as means ± SD in the text and tables and are displayed as means ± SEM in the figures. Univariate analyses of variance (ANOVAs) were used to compare young and old men and women for the variables: physical characteristics; physical activity; MVIC, twitch amplitude, half relaxation time, voluntary activation, and peak rates of relaxation. For isokinetic trials, three-factor (age, sex, velocity) repeated-measures ANOVA were used to compare groups for absolute torque, relative torque, and power. Statistical analysis included only the velocities that all subjects could achieve. Separate repeated-measures ANOVAs across time, age, and sex were used to compare changes in power during the fatiguing task, and MVIC following. Significance was determined at $P < 0.05$ and all of the analysis was performed with SPSS Statistics (version 24; SPSS, Inc., Chicago, IL).

CHAPTER III. RESULTS

Baseline Measures

Table 3.1 provides the baseline data for anthropometric measures, strength, voluntary activation, and twitch properties. At baseline, there were no differences between young and old adults for height ($P = 0.226$), weight ($P = 0.890$), and BMI ($P = 0.286$). Differences were seen between men and women for height ($P < 0.001$) and weight ($P < 0.001$), but not BMI ($P = 0.331$). Self-reported physical activity levels (PAQ) were similar for both young and old men and women (age effect, $P = 0.952$, sex effect, $P = 0.506$).

MVIC torque of the elbow flexor muscles was lower in old adults compared to young adults (age effect, $P < 0.001$, 19% age difference), and men were stronger than women (sex effect, $P < 0.001$, 53% sex difference) (Table 3.1). At baseline, young adults had a greater amplitude of the resting twitch compared to the old adults ($P = 0.05$, 18% age difference). Men also had a greater amplitude of the resting twitch compared with women ($P < 0.001$, 41% sex difference). Half-relaxation time of the twitch was longer for old adults compared with the young ($P = 0.014$, 17% age difference) and in women compared with the men ($P < 0.001$, 59% sex difference). Peak relaxation rates (fall in force evoked with the TMS during the MVIC) however, was similar between the young and old adults ($P = 0.407$), but the women had lower peak rates of relaxation than the men ($P < 0.001$, 25% sex difference).

Voluntary activation (measured with TMS) was similar between young and old adults (P = 0.606), men had greater activation than the women (P = 0.001, 3% sex difference).

Subject Characteristics

	Young		Old	
	Men	Women	Men	Women
	$n = 14$	$n = 14$	$n = 18$	$n = 15$
Age (yrs) *	24.0 ± 2.2	22.3 ± 2.8	71.9 ± 4.9	73.4 ± 6.4
Height (cm) †	179.4 ± 0.1	164.9 ± 0.1	176.6 ± 0.1	159.2 ± 0.1
Weight (kg) †	81.9 ± 12.1	67.5 ± 12.7	82.3 ± 11.2	64.5 ± 10.3
BMI ($kg \cdot m^{-2}$)	25.4 ± 2.6	24.7 ± 3.7	26.4 ± 2.7	25.4 ± 3.9
PAQ (MET · Hr/week)	50.4 ± 22.5	39.8 ± 25.7	45.1 ± 32.0	45.9 ± 30.7
MVIC (Nm) *†	76.1 ± 17.2	33.8 ± 7.1	58.5 ± 12.0	27.7 ± 4.7
Twitch Amplitude (E-stim) (Nm) *†	15.1 ± 4.0	8.2 ± 2.2	11.5 ± 3.2	7.2 ± 2.1
Twitch Half-Relaxation Time (ms) *†	64.8 ± 13.5	105.1 ± 33.9	84.6 ± 16.4	116.4 ± 27.7
Voluntary Activation (%) †	96.0 ± 3.7	94.2 ± 3.5	96.5 ± 3.0	92.0 ± 4.8
Peak Rate of Relaxation (TMS) (s^{-1}) †	-8.0 ± 2.0	-6.7 ± 2.7	-8.2 ± 1.1	-5.4 ± 1.6

Table 3.1 *Subject characteristics and baseline values.* Data is shown as means (± SD). Age difference, with sexes combined are denoted (*, P < 0.05). Sex difference, with ages combined are denoted (†, P < 0.05). BMI, body mass index; PAQ, physical activity questionnaire; MVIC, maximal voluntary isometric contraction; E-stim, electrical stimulation; TMS, transcranial magnetic stimulation.

Power-Velocity Relationship: Isokinetic Contractions

In some instances, particularly at the higher velocity contractions, some subjects failed to attain the target velocity (Fig. 3.1). Above 210°/s, some old and young adults were unable to reach the velocity (Fig. 3.1A). Overall, more men were able to reach the higher velocities compared with women (Fig. 3.1B). Due to this inability to attain some of the higher test velocities, only the results for velocities up to and including 210°/s were included in the statistical analysis.

Young adults were able to produce more power than the old adults but this difference was larger at the faster velocities of contraction (velocity x age effect, P <

0.01, Fig 3.2A). Men were significantly more powerful than women and this difference was larger at the faster velocities of contraction (velocity x sex effect, $P < 0.01$, Fig. 3.3).

Young adults produced higher peak torques compared with the old adults (age effect, $P < 0.01$), (velocity x age effect, $P < 0.01$, Fig. 3.2B) and men produced higher peak torques compared to women (sex effect, $P < 0.001$, Fig. 3.3B). All groups had decrements in torque with increasing velocities (velocity effect, $P < 0.001$).

Torque was also quantified relative to each participants MVIC to account for differences in maximal strength between the groups. Relative torque (%MVIC) was similar across age groups (age effect, $P = 0.670$, Fig. 3.2C) across all the velocities of contraction. Furthermore, there were no differences between the men and women (sex effect, $P = 0.205$, Fig. 3.3C) across the different velocities.

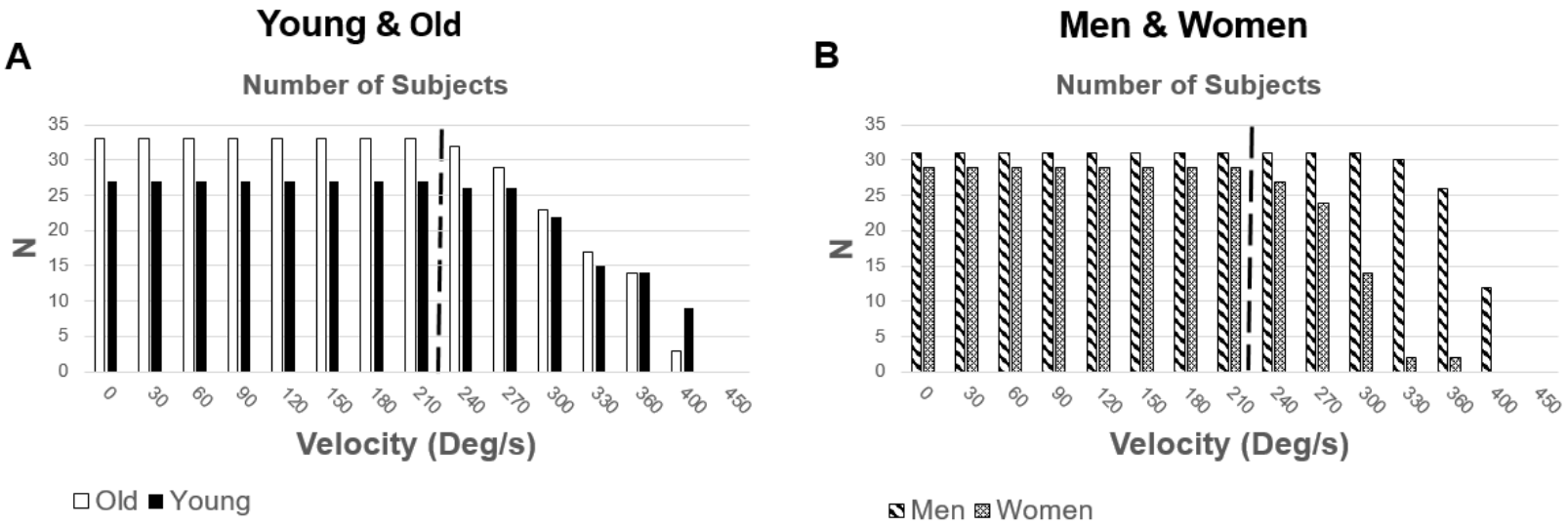

Fig. 3.1. Number of subjects that attained each velocity. Number of young and old participants that were able to attain each isokinetic velocity in the elbow flexor muscles (A) and the number of men and women (B). All subjects were able to complete velocities up to 210°/s as marked by the dashed line.

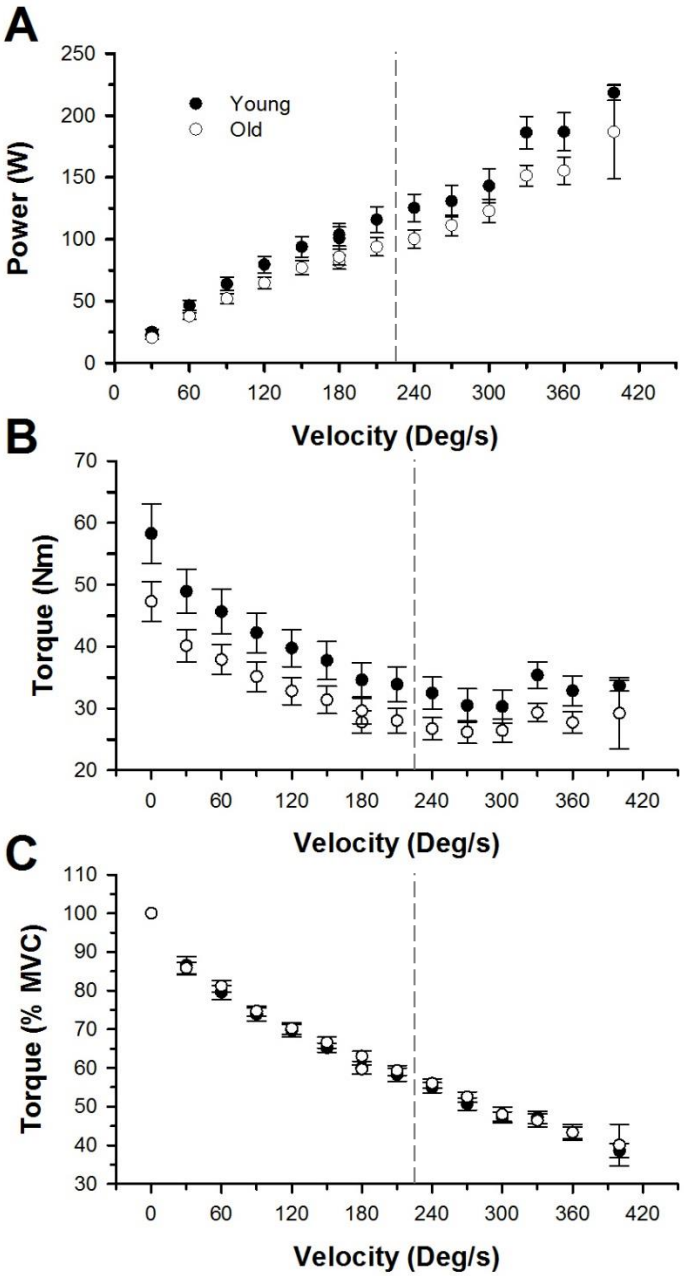

Fig. 3.2. *Torque-velocity relationship of the elbow flexor muscles.* Power production in young (●) and old (○) adults over a range of isokinetic velocities (A). Old adults were less powerful than young adults across the velocities up to and including 210°/s (age effect, $P < 0.01$). Absolute (B) and relative (C) torque production. Young adults produced more absolute torque across the different velocities (age effect, $P < 0.01$), but when taken relative to their MVIC there was no age difference ($P = 0.670$). Shown are means (± SEM). All participants completed velocities up to the vertical dashed line.

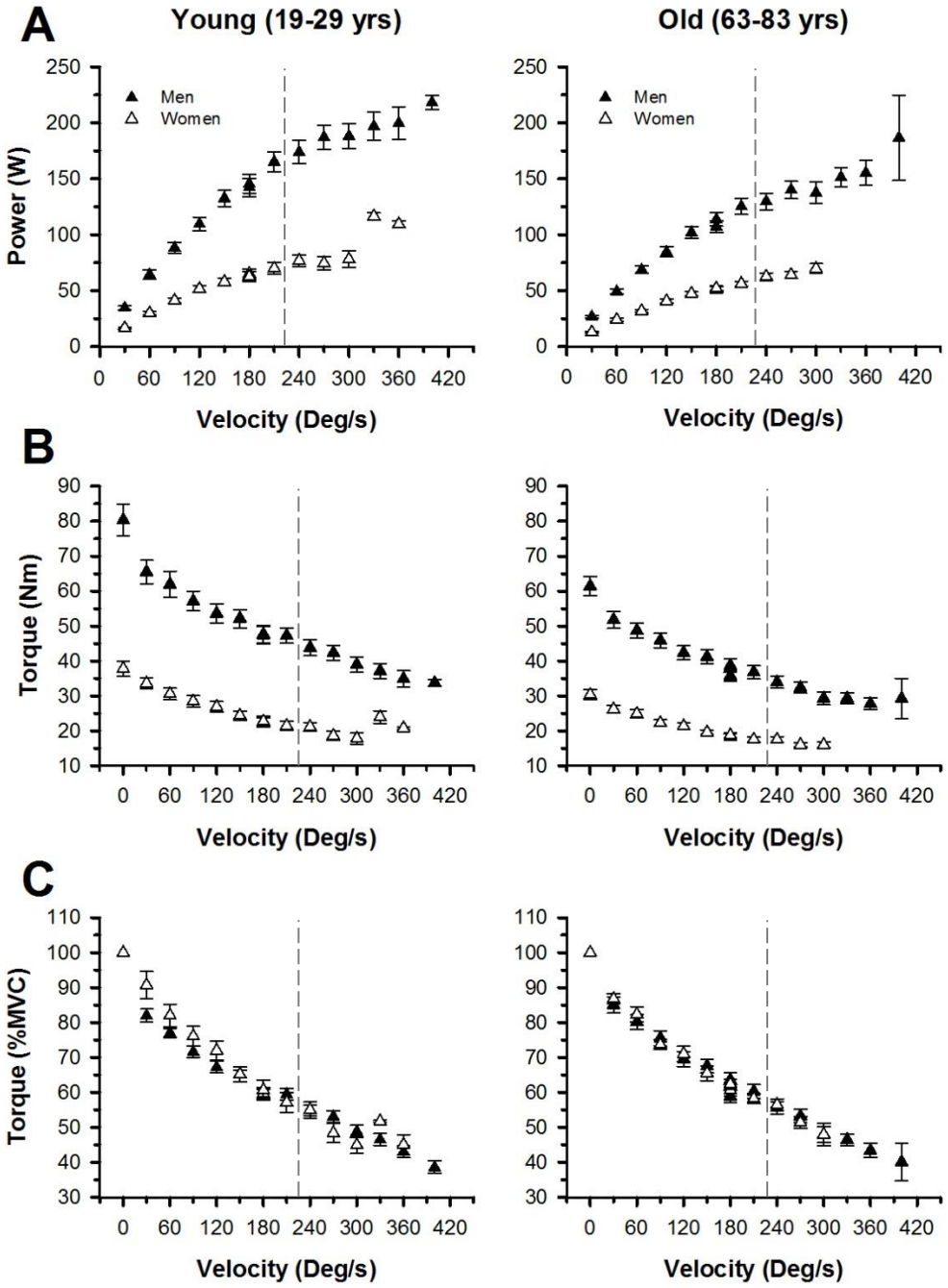

Fig 2.3. Sex-differences in torque x velocity relationship. Power production in young and old men (▲) and women (Δ) (A). Both young and old men were more powerful than the women (sex effect, $P < 0.01$), produced higher peak torques (sex effect, $P < 0.01$) (B), but showed similar amounts of torque production when taken relative to MVIC ($P = 0.205$). Shown are means (± SEM). All participants completed velocities up to the vertical dashed line.

Fatiguing Task

At the start of the fatiguing task, the initial power production over the first five contractions was larger for the young adults than the old adults (P = 0.004, 30% age difference, Fig. 3.4A). Young men produced more initial power than young women (P < 0.001, 53% sex difference, Fig. 3.5A), and old men produced more initial power than old women (P < 0.001, 58% sex difference, Fig. 3.5B).

Power declined for both groups between the first and last five contractions (time effect, P < 0.001). Power during the last 5 contractions of the elbow flexor muscles (relative to the initial five contractions) was larger for the young adults than for the old adults (P < 0.001, 15% age difference, Fig. 3.4B) indicating a greater fatigability for the old adults than the young. However, the reduction in power (relative to initial power) was similar for the young men and women (P = 0.734, Fig. 3.5C), and old men and women (P = 0.153, Fig. 3.5D).

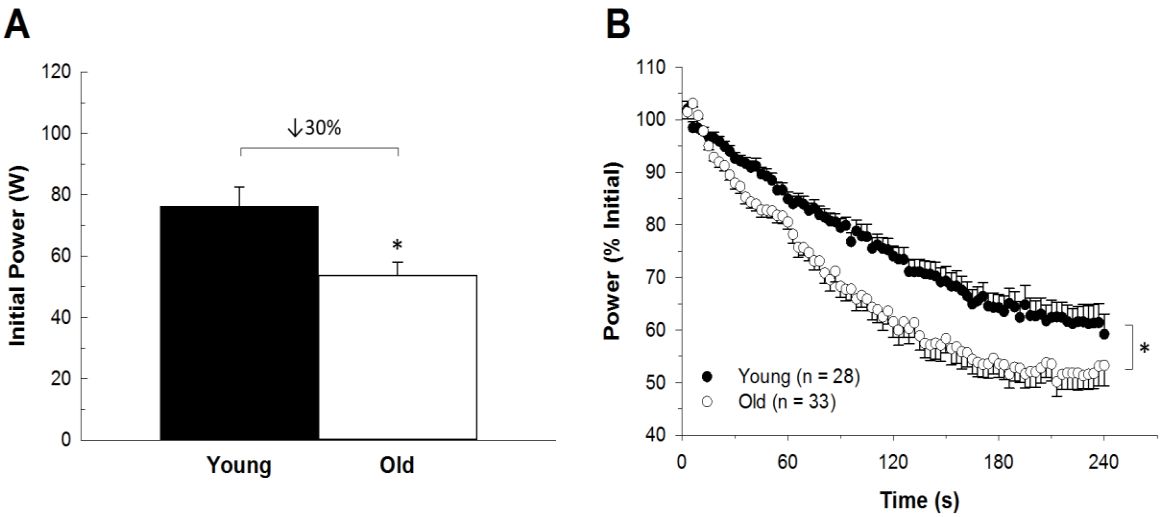

Fig. 3.4. *Fatigability: Power reductions during a high-velocity dynamic fatiguing task with the elbow flexor muscles.* Initial power (A) over the first 5 contractions was larger for young adults (P = 0.004, 30% difference) compared to old. Power as a percentage of the first 5 contractions in young (●) and old (○) (B) was reduced more in the old adults than the young (*, P < 0.001, 15% age difference). Shown are means (± SEM).

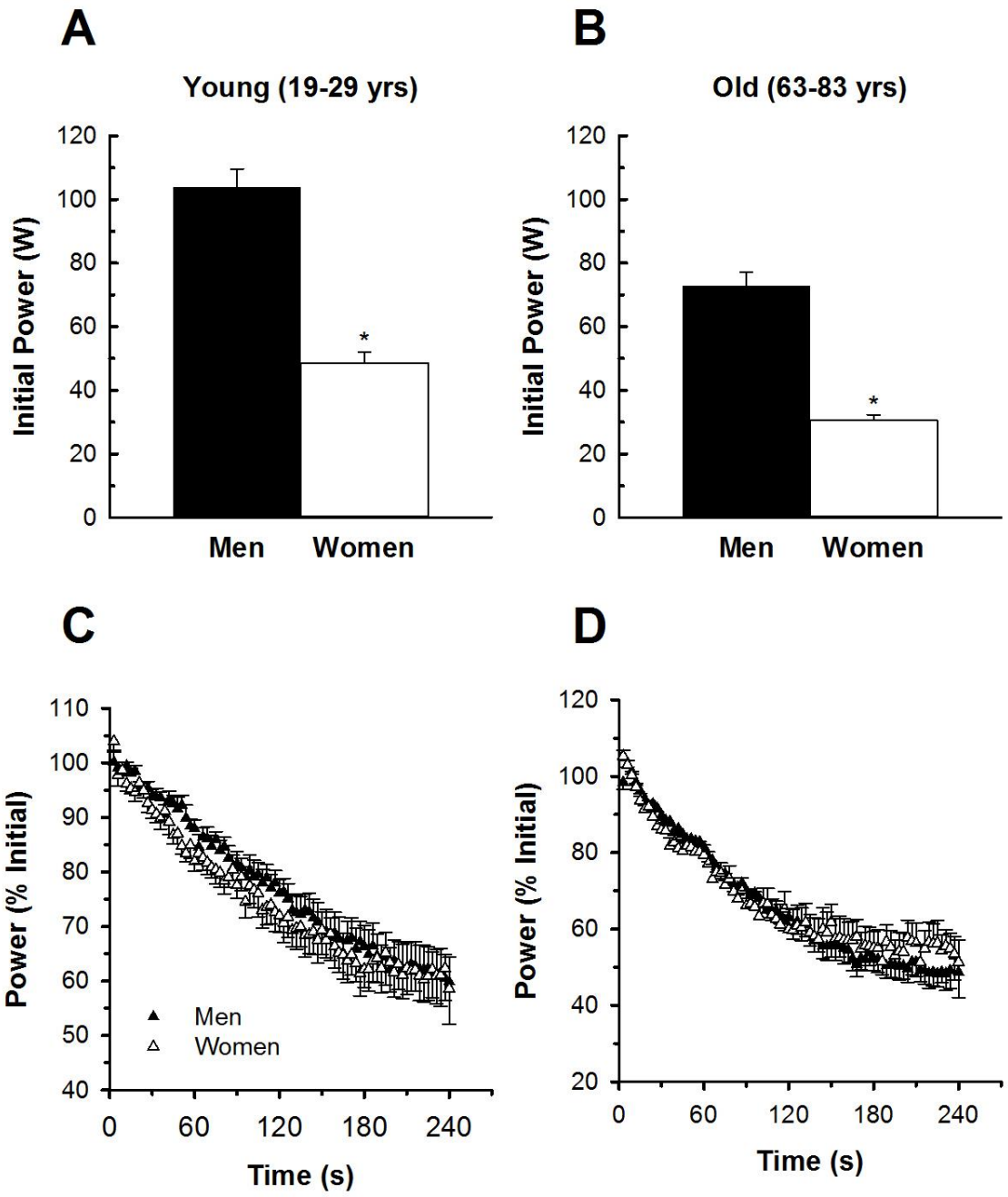

Fig. 3.5. *Fatigability: Power reductions during a high-velocity dynamic fatiguing task with the elbow flexor muscles in men and women for the two age groups.* Initial power production over the first 5 contractions was lower in young (A) ($P < 0.001$, 53% sex difference) and old women (B) ($P < 0.001$, 58% sex difference). Similar reductions in power over the fatiguing task were seen in both young (C) ($P = 0.734$) and old (D) ($P = 0.153$) men and women. Data is shown as means (± SEM).

MVIC torque following the fatiguing task decreased from control (baseline) by 21.2% ± 12.4% ($P < 0.001$). The relative decline was similar for the young and old ($P = 0.106$, Fig. 3.6) immediately following the fatiguing task (TE1) and then 15 seconds later (TE2). MVIC torque increased during the recovery period, and the increase in MVIC was similar for young and old adults at 2.5 minutes ($P = 0.335$), 5 minutes ($P = 0.498$), and 10 minutes ($P = 0.797$) into recovery (Fig. 3.6).

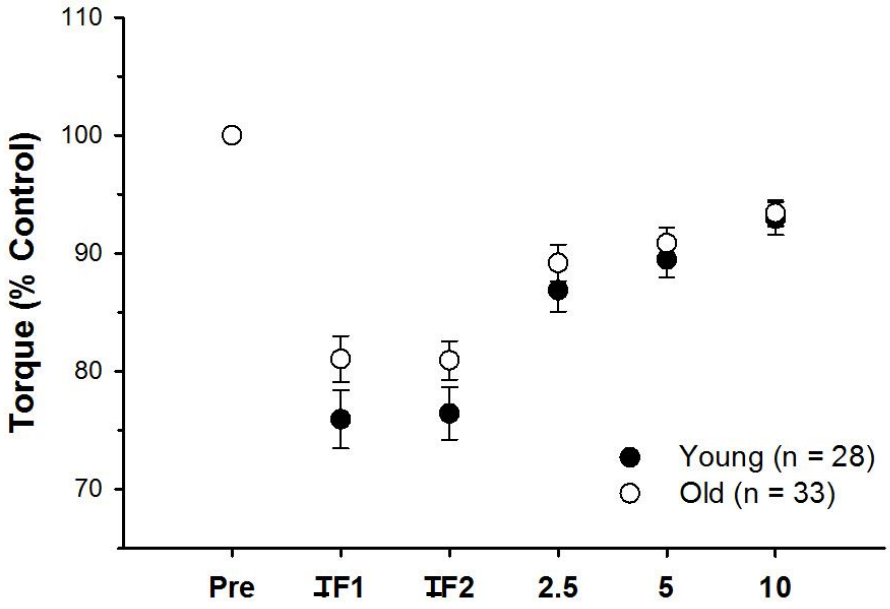

Fig 3.6. *MVIC reductions following fatigue.* MVIC torque following the fatiguing task was reduced on average by 21.2% ± 12.4% ($P < 0.001$) in young and old. The relative decline was similar between the young and the old immediately following the task (TF1 and TF2, $P = 0.106$), 2.5 minutes (2.5, $P = 0.335$), 5 minutes (5, $P = 0.498$), and 10 minutes (10, $P = 0.797$) into recovery. Data is shown as means (± SEM). Pre, baseline; TE1, task end; TE2, task end 2 (15 seconds later); 2.5, 2.5 minutes into recovery; 5, 5 minutes into recovery; 10, 10 minutes into recovery.

Voluntary Activation: Following the fatiguing task, voluntary activation was quantified during the MVICs. Voluntary activation declined from baseline levels for all age groups, but the young adults were able to voluntarily activate more than old adults at task end (P = 0.036, 7.5% age difference, Fig. 3.7). Compared to baseline values, young men and women's voluntary activation decreased by 5%, whereas old men saw a 16% reduction, and old women had an 18% reduction. Furthermore, at task end, old adults were more variable between subjects in their voluntary activation (Fig 3.7B).

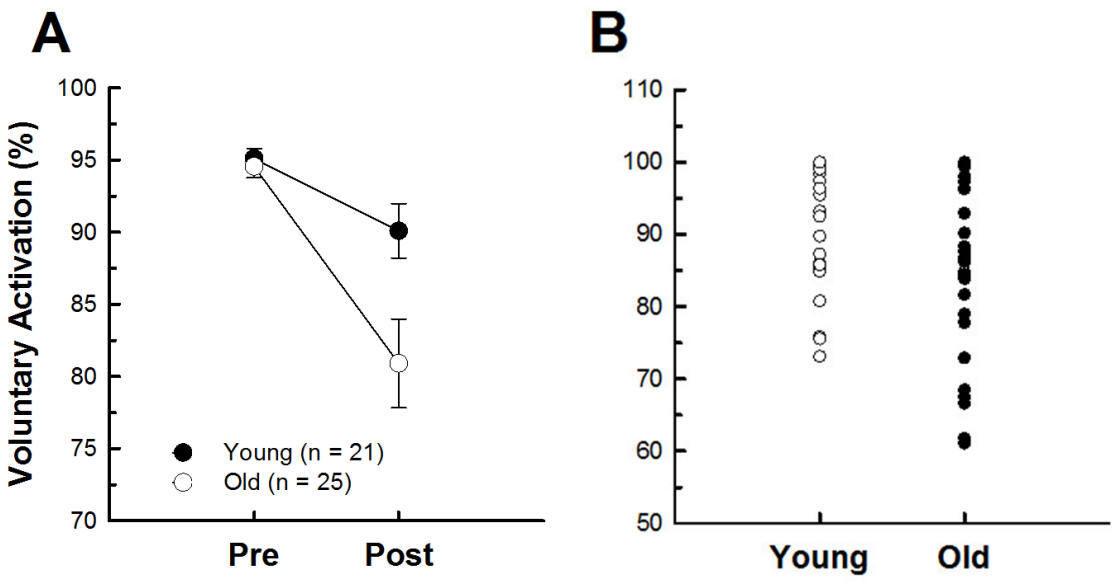

Fig 3.7. *Voluntary activation before and after fatigue.* Young adults are able to voluntarily activate more than older adults following a fatiguing task (A) (P = 0.036, 7.5 % age difference). Ranges of voluntary activation following the fatiguing task (B). Data is shown as means (± SEM).

Contractile Properties: Potentiated resting twitch amplitude decreased following the fatiguing task for all groups. The reductions in the twitch amplitude however was similar between young and old (P = 0.128, Fig. 3.8). Compared to baseline values; the

young men and women had a 34% reduction in twitch amplitude, and the older men and women had a 32% reduction.

Relaxation time of the electrically evoked twitch increased following the fatiguing protocol in all groups ($P < 0.001$). However, the increase in half-relaxation time was greater in the old adults (age effect, $P = 0.021$) than the young. Old adults increased the half relaxation time from 99.1 ± 27.1 to 153.9 ± 65.3 ms ($P < 0.001$, 55% increase) and young adults from 84.9 ± 32.6 to 115.53 ± 54.0 ms ($P < 0.001$, 36% increase).

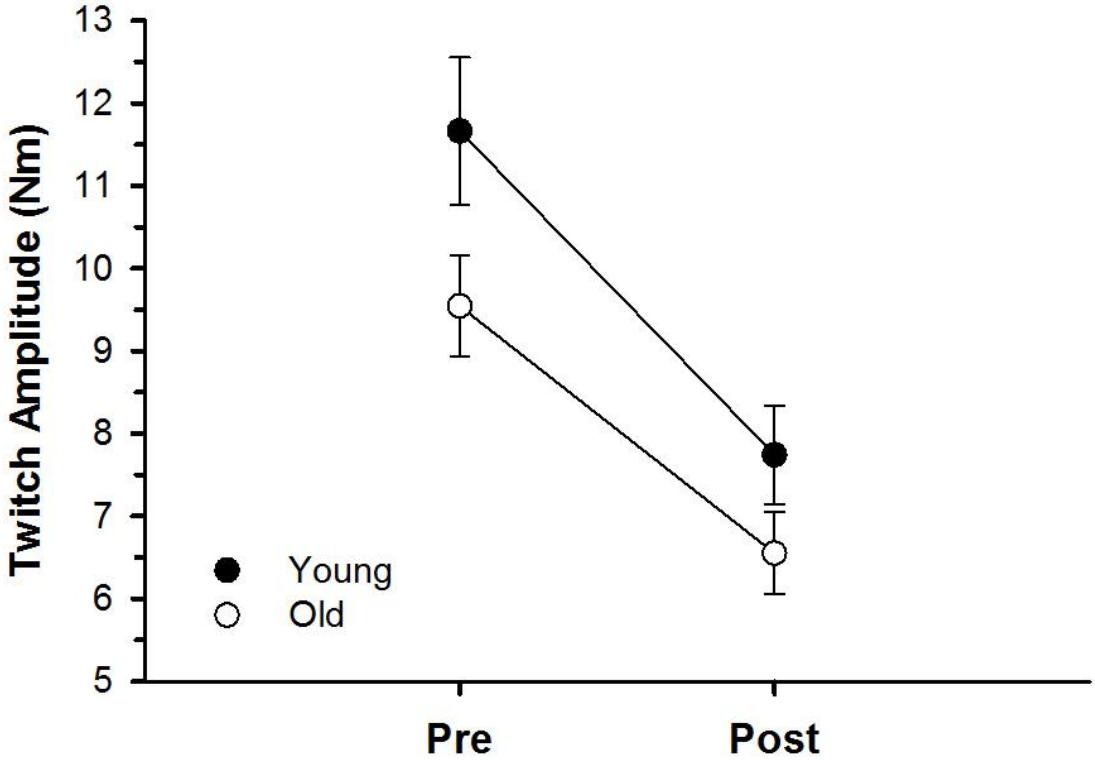

Fig. 3.8. *Reductions in resting twitch amplitude before and after a fatiguing task.* Data is shown as means (± SEM). Twitch amplitude following fatigue was similar between young and old adults ($P = 0.128$), with a 34% reduction in the young and a 32% reduction in the old. Data is shown as means (± SEM).

CHAPTER IV. DISCUSSION

This study investigated the age-related differences in elbow flexor muscle power and fatigability during a high-velocity dynamic task. The novel findings of this study were for the elbow flexor muscles: 1) older adults were weaker and less powerful than the young adults across the entire range of velocities able to be achieved, with greater age differences at the higher velocities of contraction; 2) both young and old adults were not able to achieve velocities > 210°/s during the dynamic contractions, with both young and old women having the least rate of success; 3) old adults were more fatigable than young adults during a fast dynamic fatiguing task, due to a larger reduction in voluntary activation and greater slowing of the muscle of the old adults following the task. There were also large sex differences in that men were stronger and more powerful than the women in both age groups and this sex difference was larger at the higher velocities of contraction. However, men and women showed no sex difference in fatigability during and in recovery from the dynamic contractions when assessed as a maximal isometric torque or as the reduction in power.

Torque-Power-Velocity Relationship

Maximal torque decreased with an increase in velocity of shortening contraction in both the young and old adults as expected. This relationship is due to the inability of the cross bridge to form as the velocity of contraction increases (Miller et al., 2013). However, old adults produced less torque than the young across the velocities studied, although this was not the case when the torque was expressed relative to peak isometric torque (Fig. 3.2C). The absolute decrease in maximal torque of old adults was expected,

due to the reductions in muscle mass that are typically seen with aging (Lexell et al., 1998). In this cohort the primary reason was probably a reduced muscle mass with aging, because the young and old adults had a similar ability to voluntarily activate their muscles at baseline. The similar levels of relative torque (% MVIC) in the elbow flexor muscles are particularly interesting as this finding differs from previous studies in the lower extremity. With the knee extensor muscles, others have shown a difference in torque production relative to isometric strength between young and old adults, particularly during high-velocity contractions (Lanza et al., 2003; Sundberg, Kuplic, Hunter, unpublished findings). The ability of the old adults to produce similar levels of torque (%MVIC) to the young adults, even during high-velocity dynamic contractions, suggests that aging may not significantly impact the upper limb as much as the lower limb. This is consistent with studies that show lesser age-reductions strength of the upper limb compared with the lower limb muscles (Hunter et al 2000; Raj et al 2010).

Maximal power across the different velocities of contraction was also less with aging. To assure that these reductions were aging, rather than fatigue with the multiple trials, the trials were randomized and two trials of 180°/s concentric contractions were performed, one at the beginning and the other at the end of the torque-velocity protocol. Because there was no difference between the maximal torque during the first and last set of contractions at 180°/s, we can assume the age related reductions in torque and power occurred independent of fatigue. There are several physiological changes that might be affecting this decreased power of the elbow flexor muscles seen in older adults. First, there is typically a reduction in total muscle mass typically with aging (Lexell et al., 1998, Larsson et al., 1997). We showed that maximal torque and twitch amplitude was

less in the old adults indicating lower strength due to reduced muscle mass. Decreases in muscle cross-sectional area largely parallel the loss in maximal isometric strength (Metter et al., 1997), although decreases in power are still shown when matched for cross-sectional area (McNeil et al. 2007). Because power is the product of torque and contraction velocity, additional reductions in power are likely due to changes within the muscle and a slowing of the muscle and an inability to rapidly develop force. Consistent with this finding was that the old adults had slower contractile properties than the young, shown in the longer relaxation times at baseline (Table 3.1). An inability to activate the motor units during high-velocity contractions may also contribute to the decrements in power (Wallace et al., 2016). However we saw no differences in the ability of young and old adults to voluntarily activate their muscle under isometric conditions.

An important finding of this study was the inability of participants to attain some of the higher target velocities. The isokinetic setup of the dynamometer provided an upper limit to the velocity reached during each contraction, but it did not guarantee that the subject would always attain it. We found an inability of subjects to reach some of the higher velocities set by the dynamometer beginning at 210°/s. The decrease in the number of subjects at each velocity following 210°/s was relatively similar between young and old adults (Fig 2.1A). Rather, the decreased number of subjects reaching higher velocities in the elbow flexor muscles was due to an inability in both young and old women to contract as quickly as required. This may be explained by slower contractile properties typically seen in women compared to men as indicated in the slower peak relaxation rates seen in women (Table 3.1).

Fatigability

We demonstrated an age-related difference in fatigability within the elbow flexor muscles during high-velocity fatiguing contractions. Previous studies to date have focused on age-related differences in fatigability during dynamic contractions of the lower extremity including the knee extensor and ankle dorsiflexor muscles (Dalton et al., 2015, McNeil and Rice, 2007), with some comparisons between the upper and lower extremities (Senefeld et al., 2016). We observed that fatigability of the elbow flexor muscles during a high-velocity dynamic task was greater for old adults than it was for young adults (~15% difference in power production at the end of the fatiguing task). Initial, absolute power production was greater for young adults compared to older adults, consistent with previous research observing power during a dynamic fatiguing task (Sundberg et al., 2016). However, the greater age-related fatigability for the fast dynamic contractions are in contrast to those found during tasks of sustained isometric contractions and slow dynamic contractions (Kent-Braun, 2009). During tasks of sustained isometric contractions, old adults are less fatigable than young in the elbow flexor muscles (Hunter et al., 2004, Yoon et al., 2008). When performing slow velocity contractions (~60°/s) in the elbow flexor muscles, old and young adults demonstrate similar patterns of fatigue (Yoon et al., 2015). The importance of contraction velocity has been discussed previously in the literature, although this has been primarily studied in the lower extremity. Similar to the results found within the lower extremity (Dalton et al., 2015; Callahan et al., 2011), we have found that old adults are more fatigable than young when preforming high-velocity contractions in the upper extremity, although the age difference was less (Senefeld et al., 2016).

Research comparing the reductions in fatigability between the upper and lower extremities has shown similar reductions in old adults for the elbow flexor muscles (~10%) (Senefeld et al., 2016). However, greater reductions in fatigability are typically seen within the knee extensor muscles (~20-35% reductions in power). This limb difference in fatigability may be due to changes in physical activity that may affect the lower limb more so than the upper (Kern et al. 2001, Senefeld et al., 2016). Regardless of physical activity, greater reductions in fatigability persist between young and old adults matched for physical activity (Dalton et al., 2012). Likewise, we saw greater reductions in fatigability of old adults despite similar self-reported levels of physical activity (~45 MET*HR/week), indicating that physical activity may not completely explain the age differences in fatigability. Other mechanisms regarding these differences have begun to be explored within the lower extremity muscles. Greater reductions in potentiated twitch amplitude in the knee extensor muscles seen in old adults indicate muscular mechanisms were involved in the age difference. This reduction in potentiated twitch showed high correlations with the reductions in power, i.e. fatigability (Sundberg, Kuplic, Hunter, unpublished findings). In that study, small reductions (~5%) were also seen in the voluntary activation elicited with motor cortical stimulations of old adults following the fatiguing task in the knee extensors. These findings would suggest that the primary mechanisms of fatigability in the lower extremity are related to fatigue occurring within the muscle, with small supraspinal contributions. However, these conclusions do not fully explain the differences in fatigability we have seen within the elbow flexor muscles.

In the current study measurements of twitch amplitude, via electrical stimulation, were measured at baseline, prior to and also immediately following the fatiguing task.

Baseline values were highlighted in Table 3.1 showing an 18% age-related difference in amplitude of the potentiated twitch. Following the high-velocity fatiguing task, old and young adults saw a similar decrease in the amplitude of the potentiated twitch (32% and 34% reduction, respectively). Thus, despite overall greater decrements in power during the fatiguing task, old and young adults had similar reductions in the size of the stimulated twitch. However, age-related differences were seen in the half-relaxation time following the fatiguing task. Old adults had an increase in half relaxation time of 55%, whereas young adults increased by 36%. The increase in half-relaxation time shown here for the elbow flexors parallels results that were observed within the knee extensor muscles after a dynamic fatiguing task (67% increase for old adults, and 30% increase for young adults) (Sundberg et al., 2016). The reduced rate in muscle relaxation following the high-velocity fatiguing task may be indicative of age-related differences in cross-bridge mechanics and rates of Ca^{2+} uptake in the sarcoplasmic reticulum (Hunter et al., 1999). Thus, although the reduction in twitch amplitude was similar for the young and old adults, the half relaxation showed age differences that are consistent with the greater fatigability and slowing of the old adults compared with the young during the dynamic fatiguing task.

Fatigue within the central nervous system occurred following the dynamic contraction task. Supraspinal fatigue was assessed with the measurement of voluntary activation with TMS and there was a decrease in this after the dynamic task. Voluntary activation was assessed during the MVIC (superimposed twitch) and the evoked force response was expressed as a fraction of the estimated torque of the resting twitch, with the resting twitch being estimated through a regression analysis (Todd et al., 2003). To

try and decrease the variability seen in older adults with measures of voluntary activation (De Serres and Enoka, 1998), practice trials were performed during the first session to familiarize the participants with the task. Prior to fatigue, young and old adults were able to voluntarily activate at similar levels. Following the fatiguing task, both young and old adults saw decreases in their ability to voluntarily activate, with greater decrements in voluntary activation occurring in the old adults (17% reduction in old) compared with the young adults (5% reduction). Furthermore, the range of voluntary activation at task end was considerably larger for old adults following the fatiguing task than it was for young adults (Fig. 3.7B). Previous results shown in the knee extensor muscles indicated no reductions in voluntary action with young adults, and only slight reductions (5%) within the old adults (Sundberg et al., 2016). These findings together suggest that supraspinal fatigue has a larger contribution to the fatigability of old adults during high-velocity dynamic tasks with the elbow flexor muscles than the knee extensors.

In addition to the reduction in power following the fatiguing task, we found a reduction in MVIC torque (Fig. 2.6). Young and the old had a similar decrease in torque of ~22% following the fatiguing exercise, and followed a similar pattern of recovery over 10 minutes. These reductions in MVIC in both young and old adults was less than the overall reductions in power. While there may be disparate findings across muscle groups regarding the reductions in MVIC torque in relation to power following a dynamic fatiguing task, previous research on the elbow flexor muscles has shown similar reductions between young and old adults (Yoon et al., 2013, Senefeld et al., 2016).

Conclusion

Old adults were weaker and less powerful in the elbow flexor muscles than young adults, and this reduction occurred for both men and women. Further, there was an inability to attain higher velocities in both the young and the old, primarily driven by an inability of women in both groups to contract quickly. Despite the decreases in absolute torque, old adults were able to produce similar levels of relative torque as the young, indicating that age may have less of an effect on the reduction in torque in the elbow flexor muscles compared to muscles of the lower limb.

Fatigability of the elbow flexor muscles was greater among old adults than young adults. Old men and women were 15% more fatigable than the young adults during a fast dynamic fatiguing task with the elbow flexor muscles. This age-related increase in fatigability was due to a greater reduction in voluntary activation quantified with motor cortical stimulation, and also a greater slowing of the muscle of the old adults evidenced with slowing of relaxation from electrically evoked contractions following the fatiguing task. These results indicate that the increased fatigability with old adults during high-velocity contractions is due to supraspinal mechanisms, with some contributions from contractile slowing.

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