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Decreased Peak Muscle Power is Associated with Motor Unit Loss in the Lower Limb of Older Adults

Neal B. McKinnon, *The University of Western Ontario*

Supervisor: Dr. Timothy Doherty, *The University of Western Ontario*
A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Kinesiology
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DECREASED PEAK MUSCLE POWER IS ASSOCIATED WITH MOTOR UNIT LOSS IN
THE LOWER LIMB OF OLDER ADULTS

(Integrated Article)

by

Neal B. McKinnon

Graduate Program in Kinesiology

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The School of Graduate and Postdoctoral Studies
The University of Western Ontario
London, Ontario, Canada

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i

ABSTRACT

This study investigated the relationship between motor unit (MU) properties and the strength and power of two lower limb muscles in healthy young and old adults. Twelve older adults (mean age, 77 ± 5 yrs) and twelve young adults (mean age, 24 ± 3 yrs) were studied. MU properties of the tibialis anterior (TA) and vastus medialis (VM) muscles were determined using decomposition-enhanced spike-triggered averaging (DE-STA). Motor unit number estimates (MUNE) of the TA were significantly reduced ($p>0.05$) in older adults (102 ± 76) compared to young adults (234 ± 109), primarily as a result of significantly larger surface-detected motor unit potentials (S-MUP) in older adults. Although VM S-MUP values were larger in older adults (60 ± 31 μV) compared to young (48 ±42), the difference was not significant. Maximal strength and power were significantly larger in both the TA and knee extensors of young adults compared to old. Maximal power output displayed greater deficits than isometric strength in both lower limb muscles of older adults. Results from this study indicate that there are changes in MU properties with age, and that this effect may be greater in the TA muscle. Further, power, especially in the knee extensors, may be a more sensitive measure of neuromuscular health than isometric strength, and should be the focus of exercise programs in elderly subjects.

Keywords: Aging; Decomposition-enhanced spike-triggered averaging (DE-STA); Electromyography (EMG); Motor unit number estimation (MUNE); Power; Tibialis anterior (TA); Vastus medialis (VM)

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

Page

LIST OF ABBREVIATIONS

ADL – Activities of daily living

BW – Body weight

CMAP – Compound muscle action potential

CCAA – Canadian Centre for Activity and Aging

CSA – Cross-sectional area

CoV – Coefficient of variation

DE-STA – Decomposition-enhanced spike-triggered averaging

DQEMG – Decomposition-based quantitative electromyography

EMG – Electromyography

IDI – Inter-discharge interval

Kg – Kilogram

MN – Motor neuron

MPS – Multiple point stimulation

MU – Motor unit

MUNE – Motor unit number estimation

MUP – Motor unit potential

Nm – Newton meter

pps – Pulses per second

QEMG – Quantitative electromyography

RRA – Retirement Research Association

SD – Standard deviation

SE – Standard error

S-MUP – Surface-detected motor unit potential

SNR – Signal to noise ratio

STA – Spike-triggered averaging

TA – Tibialis anterior

VM – Vastus medialis

W – Watts

Chapter 1

General Introduction

1.0   General Introduction

1.0.1 Strength/power loss and sarcopenia

It has been well established that normal human aging leads to a loss of muscle mass and concomitant loss of strength, which has been termed sarcopenia [1, 2]. This loss of muscle mass, and subsequent loss of strength can result in a loss of functional mobility in older adults [1-5]. The ability to walk safely and independently is critical to activities of daily living (ADL) in older adults, and impaired mobility could mean the loss of independence. Thus, any knowledge that may help to further our understanding to potentially mitigate the effects of sarcopenia is of utmost importance to the study of health and aging.

There are several factors that may contribute to the development of sarcopenia which include the disruption of contractile function, genetic predisposition, change in diet, lack of exercise, altered endocrine function, and degeneration of the neuromuscular system [3, 6]. Previous research has demonstrated that the loss of muscular strength in the knee extensors occurs at a rate of 1.5% per year in healthy men over the age of 65 [7]. The same study indicated that the loss of knee extensor power occurs at an even faster rate (3.5% per year). This augmented decrease in muscle power is thought to be largely the result of a decline in the number of type II (fast twitch) muscle fibers [8-11]. Since

type II motor neurons have larger motor axons with increased innervation ratios, and have less oxidative enzymes than type I motor neurons, they may be particularly susceptible to chronic inflammation and oxidative stress with typical aging [11, 12]. The atrophy of fast twitch muscle fibers causes a slowing of whole muscle contraction velocity, which is a fundamental determinant of muscle power [13]. For this reason, power has been described as a more sensitive measure of age-related reduction in neuromuscular performance than isometric strength [3, 10].

Traditionally sarcopenia has been measured by loss of muscle mass. However, some studies suggest that preservation or even increases in muscle mass with age are not enough to counteract age-related weakness [14]. This has led to characterization of muscle not by strength alone but by "muscle quality". Muscle quality refers to the strength per cross-sectional area (CSA) of a muscle and represents the intrinsic force generating capacity of that muscle [6]. Several factors lead to diminished muscle quality with age including altered excitation-contraction coupling, changes in metabolic function, increases in intramuscular lipid content, altered muscle architecture/pennation, and decreased compliance of connective tissue/tendons [3, 6]. In addition to the aforementioned factors contributing to reduced muscle quality with age, changes in the neuromuscular system play a crucial role in the development of muscle weakness with age, and will be the focus of this thesis.

There are many aspects of neuromuscular physiology that contribute to age-related declines in its function including reduced excitability of the corticospinal pathway, increased inhibitory spinal reflex pathways, degeneration of the

neuromuscular junction, and motor unit (MU) loss [3]. Some studies have postulated that increases in agonist/antagonist coactivation with aging may increase the amount of resistance encountered by the agonist muscle, and therefore contribute to the observed decrease in strength [10, 15]; however these findings are not well substantiated [3]. In addition, some research suggests that reductions in neural drive may contribute to age-related weakness [3, 10, 15]. Izquierdo et al [10] showed that muscle quality was significantly reduced in older men compared to younger men. They proposed that these older men might have a reduced ability to voluntarily activate their muscles (i.e. reduced neural drive), resulting in the observed strength deficit. However, others have demonstrated no difference in the voluntary activation of muscles in older adults, and point towards peripheral impairments as the origin of muscle weakness with age [16, 17]. MU loss, on the other hand, is one aspect of neuromuscular physiology that has been extensively studied and is known to result in age-related weakness [1, 6, 18-21].

1.0.2 The motor unit and collateral reinnervation

A motor unit (MU) is comprised of a single α-motor neuron and all of the muscle fibers innervated by its peripheral axon [22]. The MU is the fundamental component of the motor system and is responsible for voluntary and involuntary muscle contractions. The loss of MUs with aging is thought to be one of the main causes of age-related weakness and sarcopenia [6]. MUs are usually well maintained through the first six decades of life, but follow a precipitous decline thereafter [1, 2, 6, 23, 24]. As an individual ages, there is a progressive loss of MUs, starting with larger MUs which typically innervate the fast twitch (type II) muscle fibers. Under

normal circumstances, when a motor neuron dies a nearby surviving motor neuron will sprout a collateral branch in order to reinnervate the orphaned muscle fibers [25]. This compensatory process is known as collateral reinnervation (Figure 1.1). The remodeling of the neuromuscular system through collateral reinnervation attenuates the loss of muscle strength and mass during the early stages of MU loss. However, there is limited capacity for reinnervation of muscle fibers, and with progressive loss of MUs, eventually innervation of some muscle fibers is lost, resulting in a reduction in muscle strength and mass [6, 19].

Conventional measures of sarcopenia (such as muscle mass and isometric strength) do not take into account the reorganization of the neuromuscular system and are not sensitive to collateral reinnervation. Therefore they may not be a valid measure of the progression of sarcopenia until a critical threshold of MUs have been lost. Thus there was a demand to develop a reliable and valid manner of detecting early MU loss.
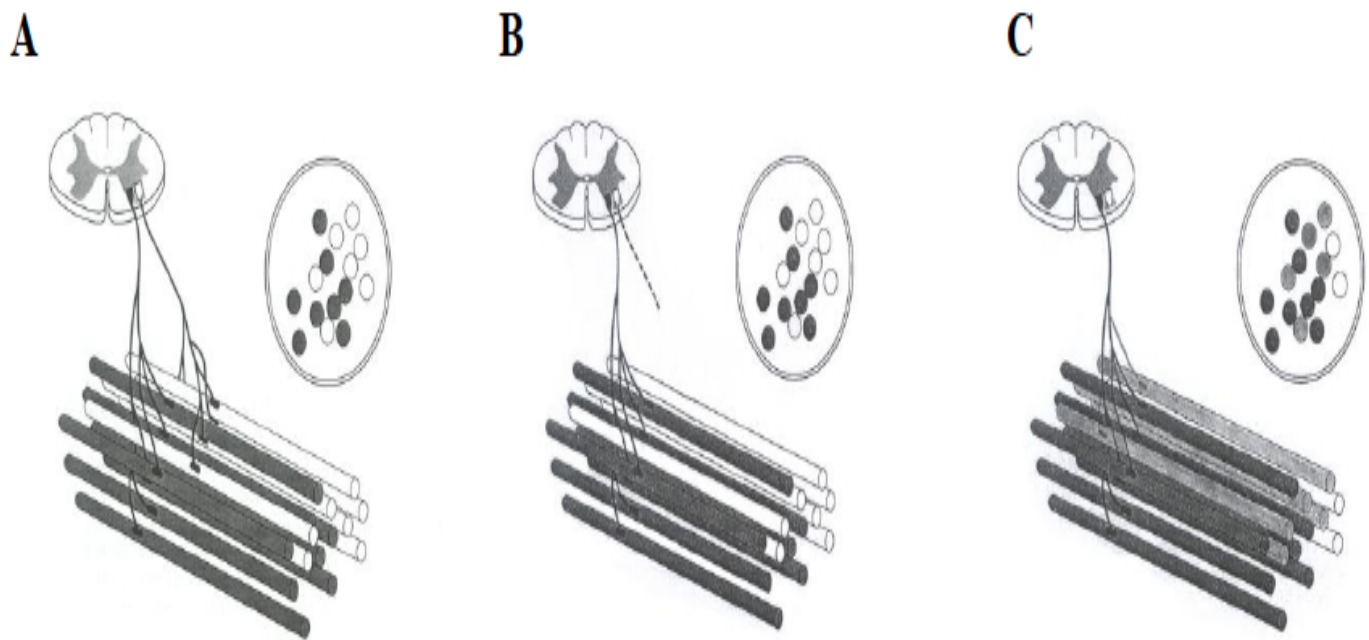
Figure 1.1 Collateral Reinnervation. (A) – Two motor neurons (MN) are depicted within a cross-section of the spinal cord. Their peripheral axons innervate a certain number of muscle fibers within a muscle that comprise the MU of that MN. The muscle fibers of the MU on the left are represented by the dark fibers and the MU on the right by the light fibers. (B) – During typical human aging some MNs die and innervation of the muscle fibers associated with that MU is lost. (C) – Surviving MNs will sprout collateral branches to reinnervate and regain control of some of the lost muscle fibers. This increases the size of the surviving MU. (Modified from Stalberg, E, Falck, B. The role of electromyography in neurology. *Electroencephalogr Clin Neurophysiol.* 1997; 103: 579-98)[25]

1.0.3 Motor unit number estimation

A method of determining a valid and reliable measure of the number of functioning MUs innervating a muscle has been a primary objective of clinical neurophysiology for many years. Although conventional neurophysiological diagnostic techniques such as nerve conduction studies or needle electromyography (EMG) assessment provide qualitative evidence of MU loss (such as increased MU action potential amplitude or duration), they do not indicate the extent to which motor axons have been lost [19, 21]. In 1971 McComas and colleagues [26] developed a revolutionary technique of determining an estimate of the number MUs within a muscle. This technique was initially referred to as motor unit counting, but later termed motor unit number estimation (MUNE). MUNE uses quantitative electrophysiological methods to estimate the number of functioning MUs within a given muscle [21]. Unlike strength and muscle mass, MUNE takes into account collateral reinnervation, making MUNE a more sensitive outcome measure for the early stages of neurodegeneration. Although many different variations of MUNE have been developed, they are all based on the same underlying concept; the compound muscle action potential (CMAP) which is an evoked response to a supramaximal stimulation of the nerve supplying the muscle and represents the combined activation of all MUs in that muscle, is divided by the averaged surface-detected motor unit potential (S-MUP), which represents the average size of a single MU in that MU pool, yielding an estimate of the number of MUs within that muscle [18, 21, 26, 27]. The main difference between MUNE techniques is the manner by

which a representative sample of S-MUPs is collected [18, 21, 27], each with their own inherent strengths and limitations.

1.0.4 Motor unit number estimation techniques

Among the most commonly used MUNE methods are incremental stimulation, multiple point stimulation (MPS), the statistical method, and spike-triggered averaging (STA) (including decomposition-enhanced STA (DE-STA)) [28]. All MUNE techniques use EMG to record the electrical activity of activating MUs. The first three methods defined above involve eliciting an external electrical stimulus to the motor nerve supplying the muscle under study in order to collect a sample of S-MUPs. This limits these MUNE techniques to distal muscles where large sections of the motor nerve can be easily accessed. In contrast STA and DE-STA use both needle and surface EMG recordings during submaximal voluntary contraction to collect a sample of S-MUPs, allowing these techniques to be applied to any muscle from which a maximal m-potential (CMAP) can be determined [19, 21, 27].

1.0.5 Spike-triggered averaging

STA is a quantitative electromyographic technique, which uses both intramuscular and surface EMG recordings to detect muscle activity during low intensity voluntary contractions. As an α-motor neuron fires a train of action potentials travel along its axon branches and into the corresponding muscle fibers [22, 29]. The intramuscular EMG electrodes pick up these action potential impulses and their combined activity is summated and referred to as a motor unit potential (MUP). One needle-detected MUP is selected and isolated from the obtained EMG interference pattern using a level or window-based discriminator. While the

intramuscular concentric needle electrode is collecting MUPs within the muscle, surface electrodes are concurrently used to record surface potentials (S-MUPs). The intramuscular MUP signal is used as a trigger that is time locked to the surface EMG recording [18, 20, 22, 27]. This allows for the extraction of surface EMG activity that is temporally linked to the MUP signal, allowing for the collection of a sample of S-MUPs corresponding to the needle-detected MUP. Adjusting the orientation and/or depth of the needle electrode allows the operator to record from different MUs and collect a representative sample of S-MUPs [19]. Then the S-MUPs are averaged to derive a S-MUP template from which a MUNE can be determined. The application of quantitative EMG (QEMG) to the intramuscular EMG signal complements the findings of STA. QEMG allows for the isolation of activity and firing rates of an individual MUP as well as the determination of the prototypical MUP associated with each MUP train [30]. Each MUP has distinct features (amplitude, turns and phases) that are determined by the morphology of that particular MU [29], thus the quantitative analysis of MUPs in QEMG can provide additional evidence of neuromuscular remodeling.

Although STA has been shown to be a valid and reliable technique for estimating the number of functioning MUs with a muscle [19, 21, 27], it does have some limitations. First, because of the complexity of the interference pattern at high levels of muscle contraction, STA can only be performed on low intensity contractions [31]. According to Henneman's size principle [32], MUs are recruited in an orderly fashion beginning with the smallest motor neurons. This means that STA may be biased towards recording more small MUs and may artificially overestimate

MUNEs. Also because only one MUP can be collected per contraction, STA can be very time consuming and the inclusion of a needle electrode can be invasive and requires considerable patient cooperation.

1.0.6 Decomposition-enhanced spike-triggered averaging

In 2004, Boe and colleagues [18] introduced decomposition-enhanced spike-triggered averaging (DE-STA) as a method of estimating the number of MUs within a muscle. DE-STA uses the same principles as conventional STA but incorporates a series of computer-based algorithms to decompose the composite intramuscular EMG signal. This allows for multiple MUP trains to be extracted from an interference pattern of a single contraction and be represented in a decomposition summary in the specialized computer program Decomposition-based Quantitative Electromyography (DQEMG) (Figure 1.2). The repetitive firings of the isolated MUPs are tracked over the course of the contraction (usually 30 seconds) to form a MUP train. Certain characteristics of the individual MUP waveforms such as amplitude, duration, number of turns, area, etc., are then averaged to create a prototypical MUP template [30], which represents the overall MUP of that particular MU. The computer-based algorithms are also capable of taking more complex interference patterns and decomposing them into their constituent MUP, allowing DE-STA to record MUPs at a higher contraction intensity. Thus, DE-STA both decreases the sampling bias of conventional STA allowing for a more representative sample of S-MUPs to be collected, and increases the efficiency of data collection [33].
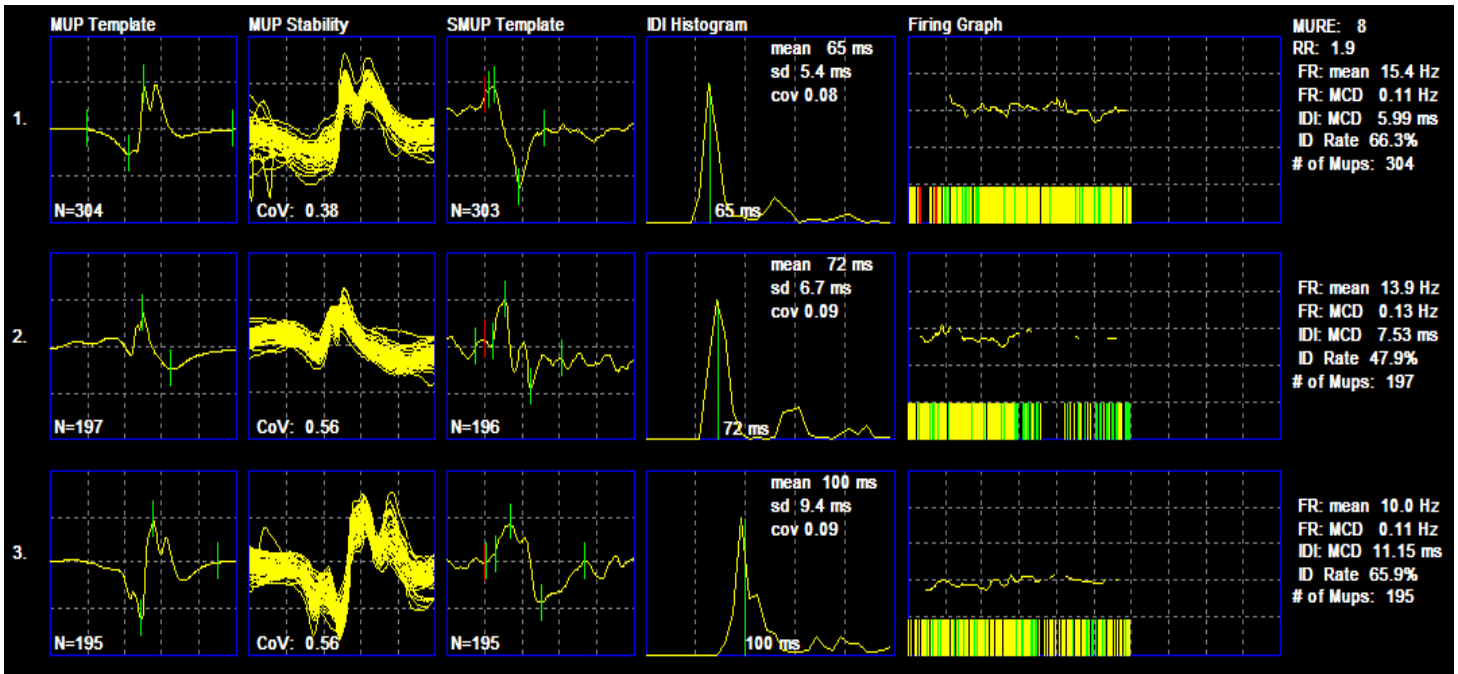
Figure 1.2. DQEMG
Decomposition summary of a single voluntary contraction presented in DQEMG. Each row represents an individual MUP train. The first column depicts the template MUP, which is constructed based on the characteristics of the repeated firings of that MUP. The number in the bottom corner represents the number of firings of that particular MU during the voluntary contraction. The second column is called a shimmer plot and consists of the superimposition of all of the firings of that MUP train. The third column portrays the S-MUP template and the number of firings used to estimate its parameters. The fourth column contains the inter-discharge interval (IDI) histogram as well as the mean IDI and coefficient of variation. Finally the fifth column represents the firing rate graph; with the vertical lines depicting individuals nerve firings and the top trace presenting a plot of the instantaneous firing rate.

1.0.7 Tibialis anterior and vastus medialis

When investigating denervation and neuromuscular health, the physiology and function of the muscle under study must be considered. For the study of aging in functional mobility, muscles of the lower limb that are particularly active during ambulation are most relevant. For the present investigation two muscle of the lower limb have been selected for study: the tibialis anterior (TA) and the vastus medialis (VM).

The TA resides in the anterior compartment below the knee joint of the lower limb. The TA is proximally attached to the lateral condyle as well as the lateral surface of the tibia and inserts into the base of the first metatarsal and medial cuneiform bone of the foot [34]. Innervated by the common fibular nerve, the TA's primary function is to dorsiflex the foot at the ankle, but it also contributes to inversion of the foot. The TA serves as a suitable model for the study of mobility disability because it is activated throughout differences phases of a typical gait cycle (particularly eccentrically during heel strike and concentrically in order to lift the toes to provide clearance for the swing phase) [35].

The VM muscle is one of the four muscles that make up the quadriceps muscle group. VM originates proximally at the intertrochanteric line and the medial aspect of the linea aspera of the femur and its fibers insert distally into the common quadriceps tendon which runs over the patella and inserts into the tibial tuberosity via the patellar ligament [34]. Innervated by the femoral nerve, the VM muscle works in tandem with the other three quadriceps muscles to extend the leg at the knee joint. The VM muscle was chosen for study because of its role in ambulation,

specifically its contribution to large powerful movements such as climbing stairs or

rising from a seated position. Significant denervation to this muscle could

potentially cause decreases in gait velocity.

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Chapter 2

Decreased Peak Muscle Power is Associated with Motor Unit Loss in the Lower Limb of Older Adults

2.0   Introduction

As a consequence of typical human aging, there is a loss of muscle mass and subsequent loss of muscular strength. This process has been termed sarcopenia, which means "poverty of flesh" [36]. This age-related weakness is a critical factor leading to the loss of functional ability in older adults and potentially resulting in their loss of independence and quality of life. Thus, understanding the mechanisms of sarcopenia and developing novel interventions to attenuate its progression is an integral aspect of the research of mobility and aging. There are several mechanisms that contribute to the development of sarcopenia including excitation-contraction uncoupling, genetic predisposition, altered diet and exercise, and changes in endocrine function [3, 6]; however motor unit (MU) loss is one aspect of typical human aging that has been extensively studied [1, 2, 6, 18, 23, 24] and is known to contribute to age-related muscle weakness and sarcopenia. MU loss is typically gradual throughout the first six or seven decades of life but follow a precipitous decline thereafter[1, 2, 19, 21, 37]. This occurs because of a process known as collateral reinnervation (described in detail in Chapter 1). As the neuromuscular system ages MUs begin to atrophy and die, typically starting with the larger (type II) MUs [9]. When a MU dies, control of the muscle fibers associated with that MU is lost. However, through the process of collateral reinnervation a nearby surviving

MU (usually a type I) can sprout a collateral peripheral axon to reinnervate and regain innervation of some of these orphaned muscle fibers [9]. However, there is a limited capacity of collateral reinnervation, and eventually the continued loss of MUs overwhelms this process. The reinnervation of lost MUs results in a relative preservation of muscular strength and mass that often masks the early stages of MU loss. Thus, a quantitative estimate of the amount of functioning MUs within a muscle is essential to the understanding of the progression of MU loss and sarcopenia and can be accomplished electrophysiologically through a technique known as motor unit number estimation (MUNE). There are several different MUNE techniques each with their own inherent strengths and limitations (for a review see Bromberg [21]). Decomposition enhanced spike-triggered averaging (DE-STA) is one technique that has been shown to be well tolerated by subjects and provides a valid and reliable estimate of the number of functioning MUs in a given muscle in both healthy subjects and subjects with neuromuscular disease [18, 20, 30, 38-43].

Recently rapid dynamic muscle force generation (i.e. power) has been discussed as a possible measure associated with age-related weakness and sarcopenia [3, 10]. Muscle power is defined as the amount of force produced by a particular contraction multiplied by the velocity of that contraction [4], and represents the muscles ability to rapidly exert force. Due to collateral reinnervation, isometric strength is generally unable to detect MU loss until a critical threshold has been reached. However, since there is a selective atrophy on type II MUs during typical human aging, there may be a slowing of whole muscle contractile speed and thus decrements in muscle power may be more pronounced during the early stages

of neuromuscular remodeling, and power may therefore be a more sensitive measure of neuromuscular degeneration with age than isometric strength [3, 10, 44]. To our knowledge, no study to this point has directly compared a quantitative estimate of the number of functions MUs within a muscle to the power generating capacity of that muscle in the same subject population.

Thus, the objective of this study was to investigate the MU properties using DE-STA of two lower limb muscles of healthy older and young adults and compare these results to isometric strength and power generating capacity of these muscles to determine if subjects with MU loss would demonstrate reduced power capabilities. The muscles chosen for this study were the tibialis anterior (TA) and the vastus medialis (VM) because of their specific roles in mobility and large powerful movements (i.e the VM). We hypothesized that older adults would demonstrate MU loss and consequent reduced maximal strength and power compared to healthy younger adults.

2.1 Methods

2.1.1 Subjects

Twelve older adult subjects (six men, six women) and twelve young subjects (six men, six women) took part in this study (Table 1). All subjects were healthy with no self-reported neuromuscular or musculoskeletal disorders that would affect their gait or ability to perform strong muscle contractions. Subject's health was determined through the inclusion/exclusion criteria of the study protocol as well as an informal screening prior to commencement of the study. Older adult subjects were recruited from the Retirement Research Association (RRA). The RRA is a local

exercise program coordinated by the Canadian Center for Activity and Aging (CCAA) that allows individuals 65 years and older to meet three times a week to go through a wide range of aerobic and anaerobic exercises. This programs aims to maintain health and activity into old age. Young adult subjects were recruited from the Western University undergraduate and graduate student population. Western University's Research Ethics Board approved this study (see Appendix A) and all subjects provided informed written consent to participate.

Table 1. Subject Demographics

Group	Gender	n	Age (yr)	Mass (kg)
Young		12	24 ± 3	71 ± 15
	Male	6	22 ± 2	80 ± 16
	Female	6	25 ± 3	61 ± 7
Old		12	77 ± 5	76 ± 15
	Male	6	76 ± 3	85 ± 13
	Female	6	77 ± 6	68 ± 13

Values are presented as means ± SD

2.1.2 Electromyography data collection

EMG data were collected using the Viking EMG System (Natus Medical Incorporated, San Carlos CA) and subsequently exported into the DQEMG program. Surface EMG information was detected using self-adhering Silver Mactrode® electrodes (GE Medical Systems, Milwaukee, WI), while intramuscular potentials were recorded using 25 mm x 30 gauge TECA™ elite Disposable Concentric Needle Electrodes (CareFusion, Middleton, WI) with a bandpass filter of 20 Hz to 10 kHz and 10 Hz to 10 kHz respectively.

Testing was performed on the dominant limb of each subject. The subject's dominant limb was determined by an informal interview prior to commencement of the study. Subjects were seated comfortably on a medical bed with their backs against a backrest and their legs flat across the surface of the bed. Active and reference electrodes were cut into strips (1 cm x 3.5 cm) however, a full sized (2.5 cm x 3.5cm) electrode was used as a ground. For both the TA and VM the skin was cleaned using 70% isopropyl alcohol wipes prior to the application of surface electrodes. When testing the TA muscle, the active electrode was positioned over the motor point of the TA, approximately 7cm distal to the tibial tuberosity and 2 cm lateral to the anterior border of the tibia. The reference electrode was positioned over the distal tendon of the TA, and a ground electrode was placed on the patella. For the VM muscle, the active electrode was placed over the muscle belly, with the reference electrode positioned over the distal patellar tendon and the ground electrode placed on the patella.

For the TA, an electrical impulse (non-recurrent, 0.1 ms duration) was applied to the common fibular nerve just posterior to the fibular head using a hand held bipolar stimulator. The active electrode was repositioned in order to minimize the rise time and maximize the negative peak amplitude of the CMAP, indicating that the electrode was directly above the motor point of the TA. The intensity of the stimulus was then slowly increased until the negative peak amplitude reached a plateau and no further increase in the CMAP could be elicited. Once an adequate CMAP was recorded, all surface electrodes were secured using surgical tape to prevent any displacement during further testing. Due to limitations in maximally stimulating the femoral nerve, a CMAP was not obtained for the VM and thus MUNE was not calculated.

The concentric needle electrode was then inserted into the muscle under study slightly proximal or distal to the active electrode. The subject was instructed to contract his/her muscle against resistance provided by the experimenter and maintain a contraction intensity between 40-60 pulses per second (pps). A computer screen provided visual feedback of contraction intensity. Subjects also received auditory feedback from the EMG signal as well as verbal feedback from the experimenter. Each contraction was held for 30s in order to gather an adequate amount of MUP firings to produce valid data. After each contraction the depth and/or orientation of the needle electrode was adjusted to sample from different MUs within the muscle. This process was repeated 4-10 times until an adequate sample of at least 20 MUP trains was collected.

2.1.3 Electromyographic signal decomposition and analysis

Once the EMG data were collected and recorded by the Viking System (Natus Medical Incorporated, San Carlos CA) it was automatically exported into DQEMG (Version 3.4) for analysis. In DQEMG the complex EMG signal was decomposed into its constituent MUPs by computer algorithms. The process and algorithms used to decompose this signal have been described previously[18, 30].

In short, the complex interference pattern was broken down into multiple MUP trains. These MUPs were then used as triggers and time-locked to the surface EMG signal. This allowed the computer to extract the surface EMG associated with each MUP firing. The S-MUP associated with each MUP was then extracted through ensemble averaging of the surface EMG signal.

Once data collection was completed, MUPs and their associated S-MUPs were inspected to ensure they met the acceptable eligibility criteria. First, MUP trains were required to contain 51 or more discharges. Also MUP train firing rates were inspected to ensure they were consistent and within physiological range. This was assessed by reviewing the interdischarge interval (IDI) histogram to ensure it followed a Gaussian (normal) distribution with a coefficient of variation (CoV) of less than 30%, as well as a visual inspection of the instantaneous firing rate plot. Any MUP trains that did not meet these requirements were excluded from further analysis. Finally MUP discharges were visually inspected to ensure they did not represent cannula potentials (inverted potentials that result from the recording of the cannula in the needle electrode). Cannula potentials were excluded from further analysis, however their associated S-MUPs were retained since their ability to serve

23

as an appropriate trigger to the surface detected signal was still valid. Occasionally, the computer would identify two MUP trains as "disparate", indicating that these MUPs never fired at the same time and were likely derived from the same MU. In this case the experimenter visually examined the two MUPs, and if deemed to be similar the MUP train with fewer discharges was excluded from analysis.

Once a MUP was deemed acceptable the experimenter visually inspected and repositioned (when applicable) markers for the onset, negative peak, positive peak, and offset of the MUPs as well as the negative onset, negative peak, and positive peak of the S-MUPs. S-MUPs with a signal to noise ratio (SNR) less than ten were excluded from analysis. A final check was made to ensure that the negative onset of the S-MUP occurred within 10 ms of its trigger MUP. Computer algorithms then calculated descriptive statistics based on all included MUPs and S-MUPs and a mean S-MUP template was created based on a data point-by-data point average. Finally, a MUNE was determined by dividing the negative peak amplitude of the CMAP by the negative peak amplitude of the calculated S-MUP template.

2.1.4 Strength and power data collection/analysis

Strength and power of the TA and knee extensor muscles were determined using the Biodex System 3 Dynamometer (Biodex Medical Systems, Shirley, NY). For the TA, subjects were seated comfortably in the dynamometer with the dominant ankle positioned at 30° plantar flexion and hip and knee joint angles of 90°. Velcro straps were fixed across the dorsum of the subject's foot to secure it to the dynamometer footplate. Seatbelts were fastened across the subject's waist to prevent any excess movement during activities. Before testing began subjects

performed a few moderate intensity dynamic contractions in order to warm up and reduce the chance of injuries. Participants were then asked to perform a series of three maximal effort isometric dorsiflexion contractions in order to determine an MVC of the TA muscle. For these contractions subjects were instructed to contract their TA as strong as possible for three to four seconds. During this contraction subjects received verbal encouragement from the experimenter as well as visual feedback of force production on a computer screen. Contractions were separated by at least one minute of rest to prevent fatigue. The strongest of the three contractions was recorded as the subjects MVC. If a large disparity was observed between successive MVC attempts, additional contractions were performed, separated by at least one minute, until consecutive contractions differed by less than 5%. Once an adequate MVC was determined, the experimenter calculated 0, 10, 20, 30, 40, and 50% of that MVC. The dynamometer was then set to isotonic mode and subjects were asked to perform a series of rapid dynamic concentric contractions with mechanical resistance provided by the dynamometer arm equal to those sub-maximal MVC values. Subjects were instructed to contract as quickly as possible concentrically against the resistance, and then passively return to the starting position. The order subjects performed each load was randomly selected before testing commenced, in order to reduce any practice effect in the results. As subjects contracted torque and velocity information from the dynamometer was concurrently channeled into Spike 2 (Version 6, Cambridge Electronic Design, Cambridge, UK) for further analysis. The same protocol was followed for knee extensor strength and power using a different attachment to the dynamometer that

strapped around the subject's leg approximately 2 cm above the lateral malleolus. The subjects were again seated in a confortable position with hip and knee joint angles of 90° and a seat belt fastened across their waist, and performed maximal effort knee extension contractions.

During offline analysis on the Spike 2 (Version 6, Cambridge Electronic Design, Cambridge, UK) program, the experimenter adjusted markers to find the peak torque and velocity measure at each sub-maximal contraction, and subsequently multiplied these values to determine peak power. The contraction that yielded the highest value for power was considered the subject's peak power output at each submaximal load. All strength and power measurements were divided by the subject's body weight (BW) in kilograms (kg) to represent a normalized value of strength/power (newton meters (Nm)/kgBW and watts (W)/kgBW respectively).

2.1.5 Statistics

All statistics were analyzed using Statistical Package for the Social Sciences (Version 21; IBM SPSS Inc., Chicago, IL). An independent samples t-test was used to identify any differences between groups for all EMG and strength/power data. Effects sizes were calculated using the Cohen's d for the S-MUP negative peak amplitudes of the TA and VM. A two way repeated measures analysis of variance (ANOVA) was performed to investigate a potential difference on peak power at each submaximal isotonic load in the TA and the VM. If a significant difference was detected a post hoc analysis was performed with a Bonferonni adjustment to determine where the difference exist. A significance level of $p \leq 0.05$ was used for all statistical tests. All values are reported in mean ± standard deviation (SD).

2.2 Results

2.2.1 Motor unit properties

2.2.1.1 TA

For young subjects, on average 23 ± 6 acceptable S-MUPs were acquired (from 28 ± 4 MUP trains) using 6 ± 1 contractions per subject. Older adults took an average of 5 ± 1 contractions to attain 20 ± 4 acceptable S-MUPs from 25 ± 4 MUP trains. Therefore an average of 3.8 ± 1 and 4.3 ± 1 S-MUPs were obtained per contraction for young and old adults respectively. MU firing rates and contraction intensity did not differ ($p > 0.05$) between young and old adults, indicating that subjects were contracting similar relative intensities. There was no difference ($p > 0.05$) in CMAP negative peak amplitude of the TA between young and old subjects; however, S-MUP negative peak amplitudes were significantly larger in older adult subjects compared to young subjects, ($p < 0.05$, effect size = 1.5). Due to the significantly larger S-MUP values in older adults, MUNEs of the TA were significantly smaller in older adults compared to young adults, ($p < 0.05$). MU properties are reported in Table 1. Results for CMAP, S-MUP and MUNE are depicted in Figure 1.

Table 2. MU properties of the TA.

Group	CMAP Neg Peak Amp (mV)	S-MUP Neg Peak Amp (µV)	MUNE (#)	MU Firing Rate (Hz)	Intensity (pps)
Young	5.4 ± 1.2	27 ± 14	233 ± 109	11.2 ± 1	49 ± 7
Old	4.7 ± 0.9	63 ± 29 *	102± 76 *	10.4 ± 1.6	50 ± 11

Values are presented as means ± SD. * Indicates a significant difference between young and old adults.

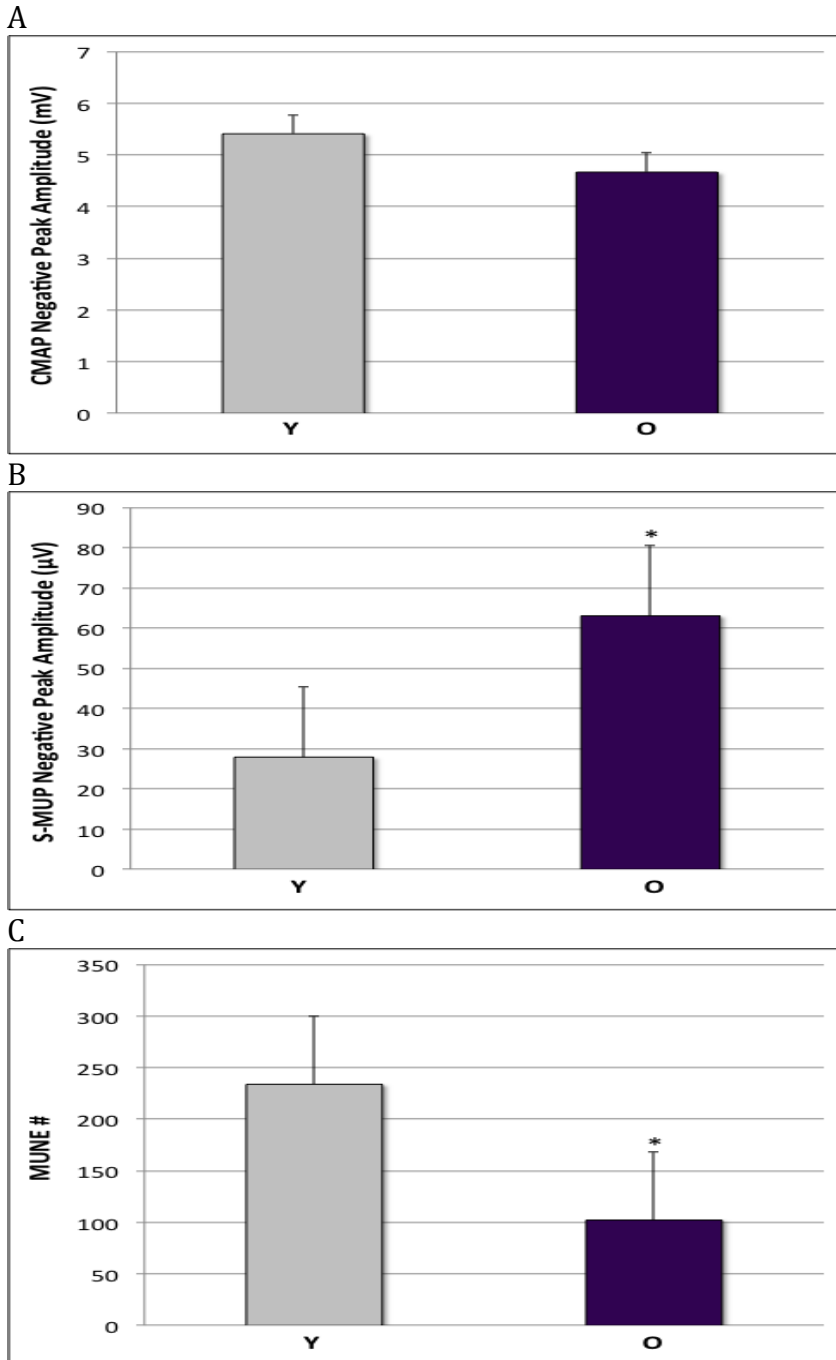**Figure 1. Derived MUNE of the TA**
A- CMAP negative peak amplitude did not differ between young (Y) and old adults
(O). B- Older adults demonstrated significantly larger S-MUP negative peak
amplitudes compared to young adults. C- Young subjects displayed significantly
larger MUNEs compared to older adults. Values are reported as means ± SE.
* indicates a significant difference between young and old adults.

2.2.1.2 VM

For young subjects, 5 ± 2 contractions yielded an average of 29 ± 5 MUP trains from which 29 ± 7 acceptable S-MUPs could be obtained. Older adults had an average of 20 ± 4 acceptable S-MUPS (from 21 ± 3 MUP trains) acquired from 5 ± 1 contractions. Therefore young adults had an average of 5.6 ± 0.7 valid S-MUPs per contraction, whereas older adults on average had 4.2 ± 1.1 valid S-MUPs per contraction. MU firing rates did not differ ($p > 0.05$) in the VM between young and old adults. There was a significant difference ($p < 0.05$) in contraction intensity between young and older adults, indicating that older adults may have been working at a lower relative rate than young subjects ($p < 0.05$). Although S-MUP negative peak amplitudes values of the VM muscle were 48.4 ± 21.6 µV and 60.1 ± 30.5 µV for young and old adults respectively, this difference was not significantly different ($p > 0.05$, effect size = 0.44). MU properties are presented in Table 2. S-MUP negative peak amplitudes of the VM are displayed in Figure 2.

Table 3. MU properties of the VM.

Group	S-MUP Neg Peak Amp (µV)	MU Firing Rate (Hz)	Intensity (pps)
Young	48 ± 22	10.4 ± 1.1	49 ± 7
Old	60 ± 31	10.2 ± 1.5	41 ± 10 *

Values are presented as means ± SD. * indicated a significant difference between young and old adults.
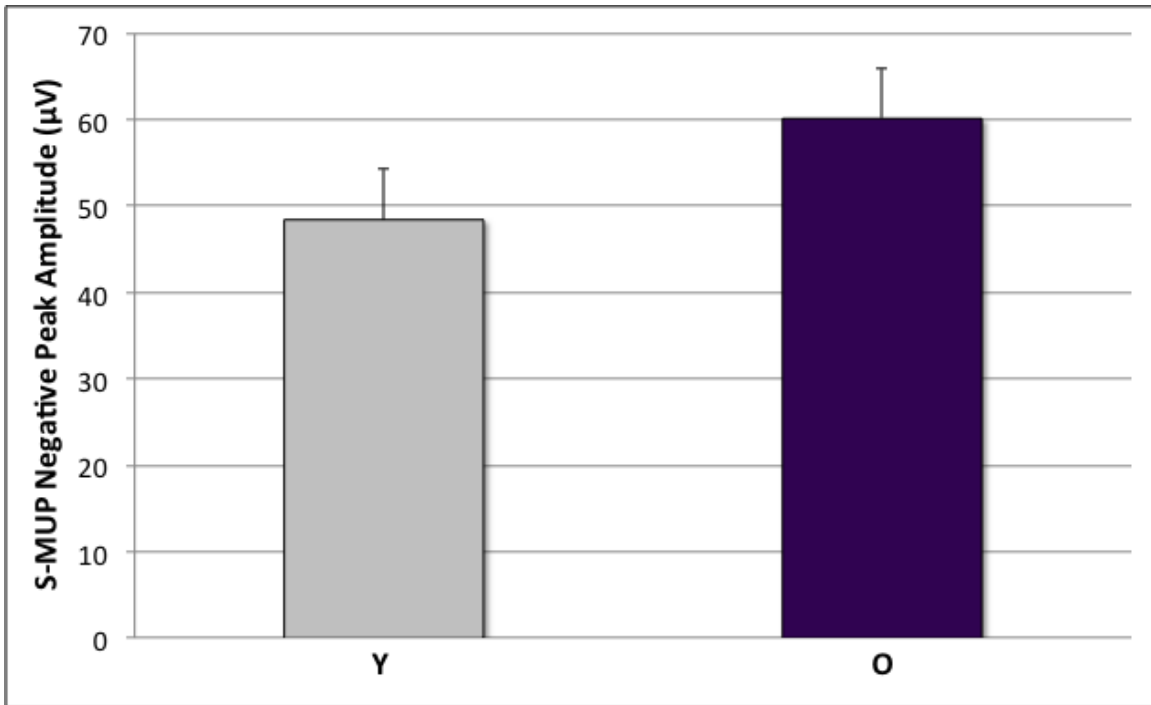
Figure 2. S-MUP negative peak amplitude of the VM
S-MUP negative peak amplitude was not significantly different between young (Y) and old (O) adults in the VM muscle. Values are presented as mean ± SE.

2.2.2 Strength and power

2.2.2.1 TA

The average strength (MVC) for young subjects was 40 ± 12 Nm, which was significantly stronger than older adults who had an average MVC of 30 ± 7 Nm ($p<0.05$). As shown in Figure 3, when normalized to subjects' BW, maximal isometric strength of the TA was significantly larger in young subjects (0.56 ± 0.1 Nm/kg) compared to older subjects (0.4 ± 0.1 Nm/kg BW) ($p<0.05$). Peak muscle power of the TA was also larger in young adults (33 ± 9 W) compared to older adults (26 ± 10 W). There was no interaction effect detected between age and power achieved at submaximal loads in the TA ($F_{(5,100)} = 0.7$, $p>0.05$). There was a main effect of maximal power detected in the TA ($F_{(5,100)} = 10$, $p<0.05$), with significant differences between young and older adults at all submaximal isotonic loads ($p<0.05$) except 10% MVC and 20% MVC ($p>0.05$). Peak power output of the TA was achieved at 20% MVC for young subjects and 30% MVC for older adults (Figure 4).

2.2.2.2 Knee extensors

For the knee extensor muscles, young adults had an MVC of 160 ± 79 Nm, which was significantly greater ($p<0.05$) than the MVC of 105 ± 34 Nm observed in older adults. When normalized to subject's BW, young adults were significantly stronger (2.2 ± 0.7 Nm/kgBW) in the knee extensors compared to older adults (1.3 ± 0.4 Nm/kgBW), $p<0.05$ (Figure 5). Peak power of the knee extensor muscles was 357 ± 120 W for young adults and 224 ± 73 W for older adults ($p<0.05$). There was a significant interaction effect between age and power achieved at submaximal

isotonic loads ($F_{(5,100)}$ = 13, $p<0.05$). Post hoc analysis indicated significant differences between young and old adults at all submaximal loads except for 0% MVC, with peak power achieved at 40% MVC for young subjects and 30% MVC for older adults (Figure 6).

2.2.2.3 Age/muscle interaction

There was a significant interaction effect ($p<0.05$) between age (young/old) on peak power attained at submaximal isotonic loads in the VM but not in the TA ($p >0.05$). As shown in Figure 4 peak power in the TA peaked around 20-30% MVC in both young and old then began to decline thereafter. In contrast, the knee extensors peak power of older adults plateaus at about 20% MVC, whereas peak power in young adults continued to increase until about 40% MVC.
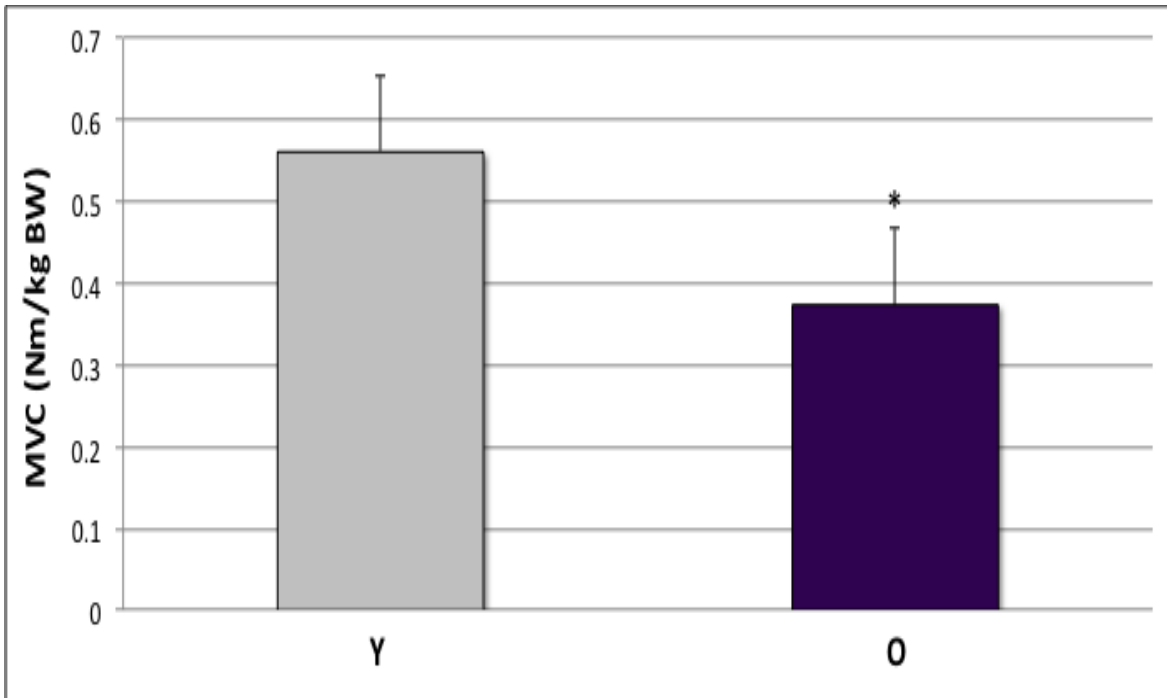
Figure 3. Strength of the TA
MVCs of the TA normalized to subjects BW of young (Y) and old (O) adults. Older adults were significantly weaker than young adults (p<0.05). Values are presented as means ± SE. * represents a significant difference between young and old.

Figure 4. Peak Power of the TA
Peak power of the TA for young (diamonds) and old (squares) adults. Power was significantly reduced ($p < 0.05$) in older adults across all submaximal loads except for 10% and 20% MVC. Peak power output was achieved at 20% MVC for young adults and 30% MVC for older adults. Values are presented as means ± SE.
* indicates a significant difference between young and old.
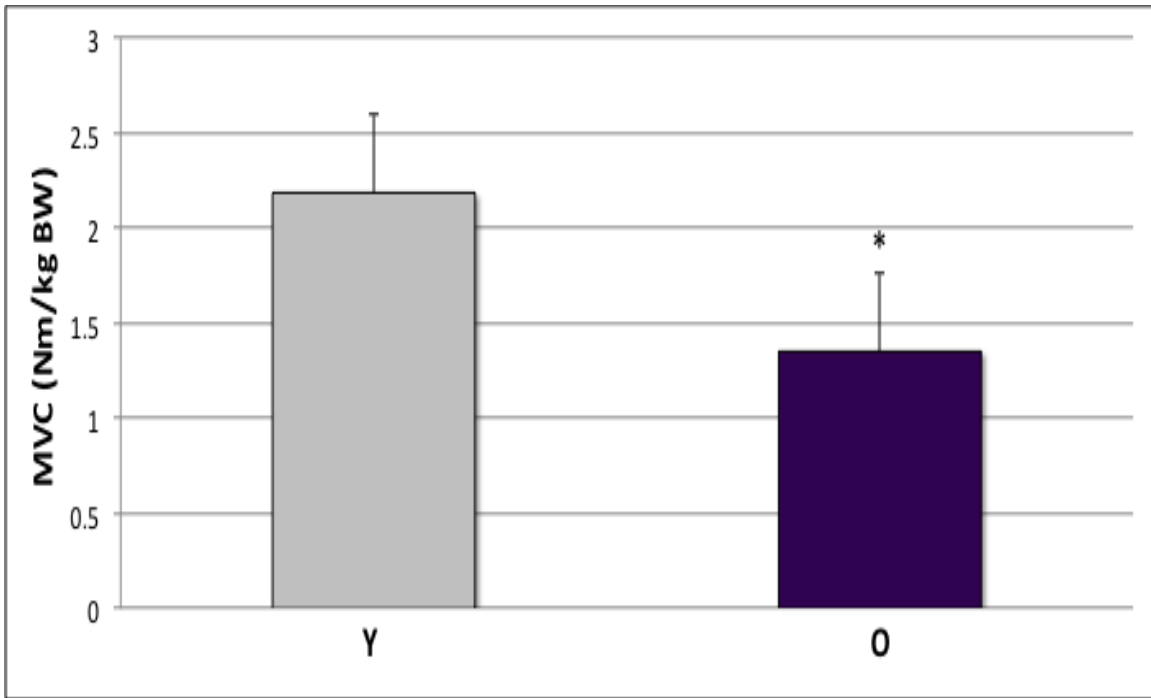
Figure 5. Strength of the VM
MVCs of the knee extensors normalized to subjects BW for young (Y) and old (O) adults. Young adults were significantly stronger than older adults. Values are presented as means ± SE. * indicates a significant difference between young and old.
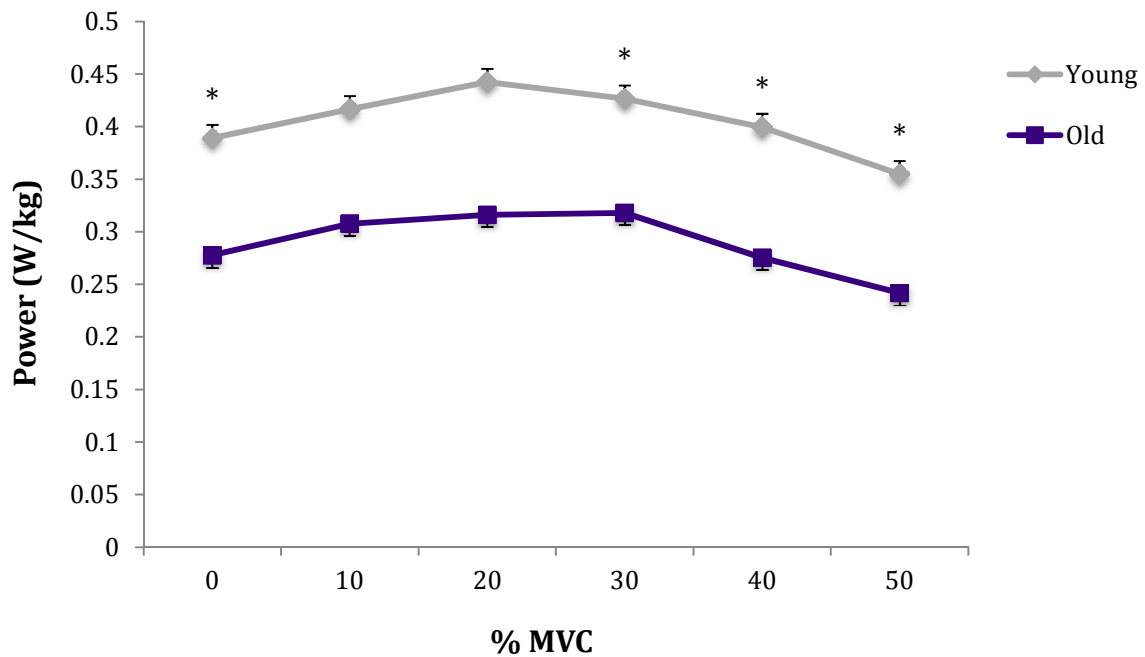
Figure 6. Peak Power of the VM
Peak power of the knee extensors of young (diamonds) and old (squares) adults.
Power was significantly reduced in the older adults across all submaximal loads.
Peak power was achieved at 40% MVC for young subjects and 30% MVC for older
adults. Values are presented as means ± SE. * indicates a significant difference
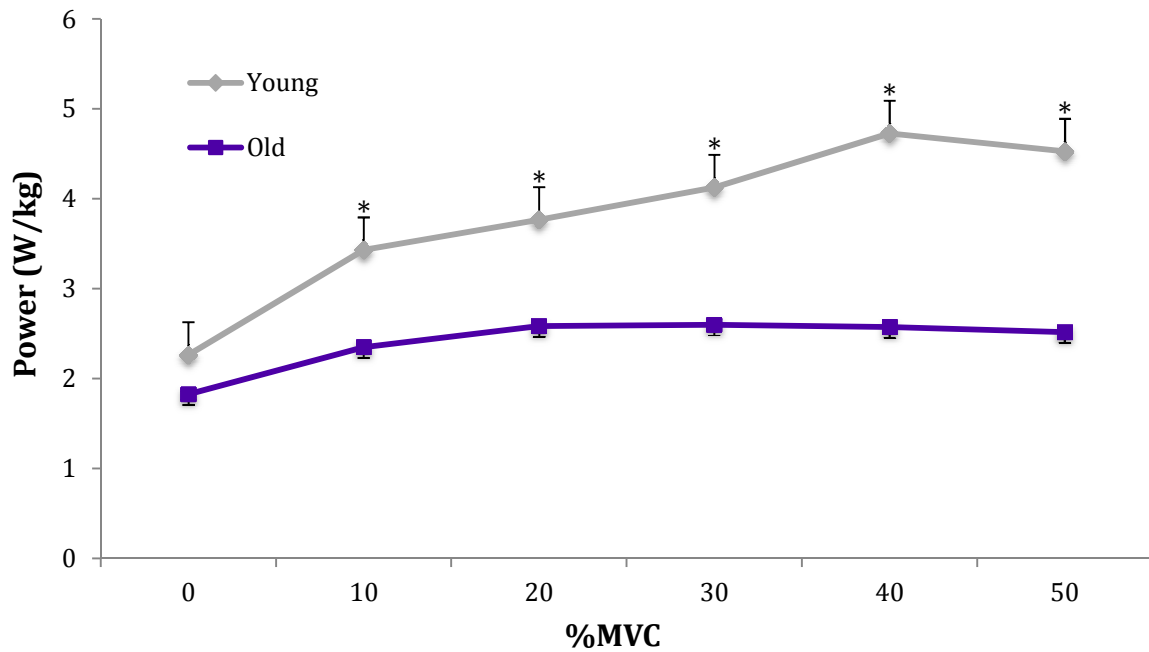between young and old.

2.3 Discussion

This study was designed to test the hypothesis that older adults, who show indices of MU loss, would have reduced power capabilities compared to healthy younger adults. In accordance with our hypothesis, we found that older adults not only had significant indications of MU loss, but also demonstrated significant declines in power production and isometric strength in both the TA and VM muscles. These results demonstrate that older subjects with MU loss also exhibit reduced muscle power, indicating that reductions in muscle power may be a sensitive measure of MU loss and neuromuscular remodeling associated with typical human aging.

Reductions in MUNEs have been reported in a number of upper limb [23, 37, 45-47], and lower limb [1, 2, 48, 49]muscle studies. Previous work by McNeil and colleagues [1], investigated MUNEs in the TA of young (~25 years), old (~65 years) and very old (>80 years) subjects. Their results were similar to that of the present study reporting MUNEs of 150 ± 43, 91 ± 22, and 59 ± 15 MUs for the young, old, and very old groups respectively. Although McNeil et al [1] found no difference in strength between the young and old subject groups (whereas in the present study we observed significantly lower MVCs in older adults), they did report a significant drop in strength between the young and very old adults. The researchers concluded that MU loss does not result in strength loss in the TA muscle until a critical threshold of MUs are lost, and at this point the progressive loss of MUs outpaces the compensatory process of collateral reinnervation. Based on their results this threshold appears to exist between 40-60% MU loss. The decline in strength

observed in the older adults of the present study may be explained by the age range of the older subjects recruited. In the current study older adults ranged in age from 68 – 85 years old (mean: 76.8 years), with four of the twelve subjects being greater than 80 years old. Therefore, it is plausible that these older adults (which would apply to McNeil et al's [1] very old group) could have been beyond the critical threshold of MU loss, and skewed the average isometric strength value of the older adult population towards a lower value. However, our obtained values for MU properties are in accordance with previously reported data on the TA; CMAP negative peak amplitude did not differ between young and old adults but due to significantly larger S-MUP values in older adults (78.2 ± 19.3 µV reported by McNeil et al [1], and 63 ± 29 µV reported here), MUNEs were significantly reduced.

Several other studies have also measured MUNEs of the TA muscle in health, age, and disorder [2, 20, 43, 48-55]. Power et al [2] used DE-STA in the TA to investigate the effects of long-term physical activity on MU loss. The authors performed MUNEs on young, old, and old master runners (>60 years old who regularly competed in long distance races throughout their lives), and found that master runners exhibited MUNEs similar to those seen in young adults, concluding that lifelong physical activity may attenuate MU loss. Although the healthy older adults in this study were slightly younger (mean age: 66 ± 3) than that of the present investigation, their reported MU parameters are in agreement with the values reported here. Trojaborg and colleagues [48] used the statistical method to derive MUNEs of the TA of 24 subjects aged 21-80 years old. They reported values for CMAP negative peak amplitude of 6.2 ± 0.2 mV, S-MUP amplitude of 32 ±2 µV,

and MUNE of 194 ± 5. Given the fundamental differences in the underlying assumptions of DE-STA and the statistical method, coupled with the large age range included in a single sample in that study, their results are remarkably similar to those presented here. Additionally, Doherty and Stashuk [20] collected DE-STA data on the TA of a heterogeneous sample of young adults (aged 23-45 years). Although no MUNE calculation was performed in this study, the authors reported various MU parameters in this group of subjects. The S-MUP amplitudes reported in their study are within the scope of those observed in the present study, however they more closely resemble those of the older adults than that of our younger group. It is important to note that Doherty and Stashuk [20] did not regulate contraction intensity during their data collection. More recent work has suggested that contraction intensity has a profound effect on the S-MUP amplitude obtained using DE-STA [18, 56], and recording from relatively low or relatively high contraction intensities will artificially over- or underestimate a MUNE calculation respectively. Therefore, it is possible that the results reported by Doherty and Stashuk [20] have been artificially inflated by a relatively high contraction intensity during data collection causing them to resemble that of typical older adults.

In contrast, relatively few studies have investigated MU properties of the VM muscle. An investigation by Berger et al [42] recorded MU properties using DE-STA of the VM in healthy adults (mean age: 62 ± 6) and age matched osteoarthritis (OA) patients. Although some of the MUP parameters (i.e. MUP durations and thickness) reported in that study indicated an increase in the average MU size in OA patients, S-MUP negative peak amplitude values did not differ between healthy and OA patients

and are similar to those presented here (41 ± 29 μV). Conwit et al [56] used DE-STA to examine the effects of contraction intensity and test-retest reliability of S-MUP amplitudes in the VM muscle of a group of adults aged 21-70 years. At 20- and 30% MVC (which most closely resemble the intensity used for the present investigation) the authors reported an average S-MUP negative peak amplitude of 41.3 ± 4.4 and 53.5 ± 5 μV respectively. These values are similar to those presented here (48.4 ± 21.6 μV in young adults and 60.1 ± 30.5 μV in older adults), especially considering the heterogeneity of their sample population. Additionally, Doherty and Stashuk [20] recorded S-MUP negative peak amplitudes from the VM muscle using DE-STA and reported values higher (87 ± 43 μV) than those seen here or by Conwit et al [56]. However, as described previously, this disparity may be explained by the lack of modulation in contraction level in this study leading to a biased sample of relatively large S-MUPs.

Although mean S-MUP negative peaks amplitudes were 48.4 ± 21.6 μV in young adults and 60.1 ± 30.5 μV in older adults, this difference was not statistically significant. Apart from the obvious large variation between subjects within age groups, there are several factors that may have contributed to this result. One possible explanation is that the contraction intensity was significantly lower in VM of the older adults than the young adults (Table 2). As suggested by Henneman's size principle [32], motor neurons are recruited in an orderly fashion, beginning with the smaller motor neurons which innervate relatively fewer muscle fibers. Additionally, multiple studies have reported a significant contraction level effect on S-MUP amplitudes using DE-STA [18, 56]. Therefore, it is possible that the older

adults contracting at a lower intensity may have biased their recording towards recruiting smaller MUs, which would result in smaller S-MUPs. Notably, even with a significantly lower level of contraction, older adults displayed much higher average S-MUP amplitude than young adults, providing further evidence of significant neuromuscular reorganization in this VM of this group. Additionally, it has been established that older adults have increased subcutaneous and intramuscular adipose tissue [6], and that adipose tissue can diminish surface EMG signals [57]. Therefore, it is possible that the increased intramuscular lipid content in the thigh of older adults may have attenuated the surface EMG signal, leading to reduced S-MUP amplitudes. Finally, the non-significant result presented here could be a result of the limitations of the surface electrodes recorded S-MUP to accurately reflect MU size from the very large VM muscle. Traditionally, MUNE techniques have been developed for use of distal limb muscle where large sections of the motor nerve can be easily accessed and muscles are relatively small with simple innervation zones [19, 21, 26, 46]. Due to the size of the VM, it has a more complex innervation zone, which makes it more difficult to record an accurate measure of mean S-MUP size. It is possible that due to the spatial dispersion of axon branches in the VM the surface electrode is simply not capable of recording all of the potentials associated with a MU within this muscle (especially in an older muscle which presumably has significant neuromuscular reorganization and larger MU territories). Since large powerful muscles, such as the VM, are very functionally relevant to mobility and aging and are often the target of exercise/training programs, further investigation

into obtaining valid and representative indices of MU loss from these muscles is warranted.

Overall our findings on MU properties suggest that although older adults demonstrate indications of MU loss and neuromuscular reorganization in both the TA and VM muscles, the differences in MU properties appear to be larger in the TA muscle. This result is in accordance with previous research, which has shown greater age-related changes in the neuromuscular system of more distal muscles [47, 58, 59]. Taylor and colleagues [59] have attributed this to a discontinuity in functional nerve synapses due to the increased length of axonal paths. This deterioration of functional connections between longer axons could explain the greater neurogenic changes in distal muscles with age described here and in previous work.

As predicted by our hypothesis, we observed reduced strength and power in both the TA and the knee extensor muscles. Previous research has demonstrated knee extensor strength to decline at a rate of approximately 1.5% per annum, while knee extensor power declines at approximately 3.5% per annum [7]. As discussed previously (Section 1) the accelerated loss of muscle power is thought to be a result of the selective atrophy of type II MUs during the early stages of MU loss, leading to a progressive shift to a more type I dominated MU pool [8-11]. The present findings provide additional support for this paradigm. While both strength and power were reduced in older adults, power exhibited a more precipitous decline in both the TA and VM muscles. Although we did not control for muscle quality (strength/power per CSA) in the present study, it is reasonable to suggest based on previous research

44

[7, 8, 10, 16, 44, 50] that deficits in muscle power resulted from a decreased proportion of fast twitch muscle fibers present in older muscles.

For the present study we chose to calculate power isotonically rather than isokinetically for two principle purposes: First is that velocity has been shown to be a critical factor in determining muscle power[13], and previous research shows that aged subjects may be unable to attain the high velocities required for isokinetic power calculation[60]. Secondly, isotonic contractions are more functionally relevant and thus more applicable to daily activities[61]. In the present study we found a significant interaction between muscle and age on peak power. For the TA muscle, young and old adults followed a similar pattern in which peak power was attained at approximately 20-30% MVC then declined thereafter. However, for the knee extensors, peak power in older adults plateaued at approximately 20% MVC, whereas peak power of young adults continued to increase until 40% MVC. Additionally the greatest difference in power between young and old adults was observed at 20% MVC for the TA and 40% MVC for the knee extensors. These results are significant when you consider the underlying function of these muscles; The TA, which is usually active at relatively low levels of force during foot clearance in the swing phase of gait, and eccentrically during heel strike [35], is most inhibited in older adults during loads of 20% MVC. Whereas the knee extensors, which are responsible for more powerful movements such as climbing stairs and standing from a seated position, are most impaired with age at higher isotonic loads. Thus, it appears that in both the TA and the knee extensors muscles, the greatest deficit in power generation occurs at loads that are specifically relevant to the functionality of

45

that muscle. In addition to declines in muscle strength and power, previous work has reported reductions in postural stability and proprioceptive acuity with age [62], which implies there may be a systemic degradation of the neuromuscular system with age. Together, these results underscore the importance of exercise programs that specifically target increases in muscle power over functionally relevant muscular loads. Although some studies have demonstrated significant improvements in muscle power with specific power and velocity training programs [63, 64], these results are not unanimous[65]. Therefore future research should aim to elucidate the effects of power/velocity training programs on improvements in muscular power, specifically implementing isotonic loads that are applicable to functional mobility.

One limitation to the present study is the homogeneous comparison between men and women. It is well documented that men are stronger and more powerful than women [6, 44, 66, 67], even when controlling for muscle volume [68]. Previous work has suggested that post-menopausal women have significant declines in contractile function and muscle quality compared to similarly aged men, although men tend to express greater deceases in muscle mass [6, 66]. In order to mitigate gender-related effects in the present study we ensured that an equal number of men and women were present in each population as well as normalized all strength and power measures to the subject's body weight, allowing for a more practical comparison between men and women. Additionally, previous work using STA reported no difference in typical MU parameters between male and female subjects [23]. Another potential limitation to this study is the sample size. Although previous

work in this lab and others have been able to detect significant differences in MU properties with samples of ten to twelve subjects [1, 2], considering the large degree of variability in the S-MUP amplitudes of the VM, a relatively small sample of twelve subjects used in the present study may have contributed to the non-significant result observed.

In summary, the data presented here demonstrates that older adults, who exhibit indices of MU loss, have significant reductions in peak power capacity in the TA and the VM muscles. To our knowledge this is the first study to directly document a quantitative reduction of the number of functioning MUs within a muscle with reduced peak muscle power. This experiment further validates the utility of muscle power as a sensitive measure of neuromuscular remodeling with age. Future investigations should focus on improving muscular power (especially in the lower limb) over functionally relevant isotonic loads of the muscle under study in order to increase functional mobility in older adults.

2.4 References

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APPENDIX A

Principal Investigator:Dr. Tim Doherty
File Number:103980
Review Level:Full Board
Approved Local Adult Participants:60
Approved Local Minor Participants:0
Protocol Title:Comparing Neuromuscular Function in Mobility Impaired and Healthy Older Adults
Department & Institution:Schulich School of Medicine and Dentistry\Clinical Neurological Sciences,St. Joseph's Health Care London
Sponsor:
Ethics Approval Date:July 19, 2013
Ethics Expiry Date:August 01, 2014

Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Western University Protocol		
Letter of Information & Consent		2013/07/09

This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request form.

Member of the HSREB that are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature

Ethics Officer to Contact for Further Information

Erika Basile (ebasile@uwo.ca)	Grace Kelly (grace.kelly@uwo.ca)	Shantel Walcott (swalcott@uwo.ca)

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Curriculum Vitae

Neal McKinnon

Post-Secondary Education and Degrees

Western University (September 2012 – Present) - London, Ontario
- MSc Candidate Kinesiology

Wilfrid Laurier University (September 2008 – April 2012) - Waterloo, Ontario
- Honours BSc Kinesiology

Honours and Awards

Southern Ontario Neuroscience Association (SONA) Poster Award (2014)
Ontario Graduate Scholarship (2013-2014)
University of Western Ontario Graduate Research Scholarship (2012-2014)
Dean's List Wilfrid Laurier University (2012)

Related Work Experience

Graduate Teaching Assistant – (January 2014 to April 2014)
    Kinesiology 1080: Introduction to Psychomotor Behaviour
    Department of Kinesiology
    Western University

Graduate Teaching Assistant – (September 2012 to April 2013)
    Kinesiology 2230: Introductory Exercise Physiology
    Department of Kinesiology
    Western University

Research Assistant – (May 2012 to August 2012)
    Department of Kinesiology and Physical Education
    Wilfrid Laurier University

Student Volunteer – (September 2011 to February 2012)
    Sun Life's Movement Disorders Research and Rehabilitation Centre (MDRC)
    Waterloo, Ontario

Athletic Therapist – (August 2010 to November 2011)
    Men's varsity rugby team
    Wilfrid Laurier University

Publications

McKinnon, NB, Graham MT, Tiidus PM. Effect of creatine supplementation on muscle damage and repair following eccentrically-induced damage to the elbow flexor muscles. *Journal of Sports Science and Medicine. 2012; 11: 653-659*

Presentations and Conferences

McKinnon, NB and Doherty TJ. Comparing neuromuscular function in healthy older and young adults. Southern Ontario Neuroscience Association (SONA) Annual Meeting. London, Ontario. (May 5th, 2014). (Poster)

McKinnon, NB, Graham MT, Tiidus PM. Effects of creatine supplementation on muscle damage and repair following eccentrically- induced damage to the elbow flexor muscles. Canadian Society of Exercise Physiology (CSEP) Annual Meeting, Regina, Saskatchewan. (October 10th-13th, 2012). (Oral).

McKinnon, NB, Graham MT, Tiidus PM. Effects of creatine supplementation on muscle damage and repair following eccentrically- induced damage to the elbow flexor muscles. 3rd Annual Muscle Health Awareness Day, Toronto, Ontario. (May 25th, 2012). (Poster).

McKinnon, NB, Graham MT, Tiidus PM. Effects of creatine supplementation on muscle damage and repair following eccentrically- induced damage to the elbow flexor muscles. Ontario Exercise Physiology Conference, Barrie, Ontario. (January 20-22nd, 2012). (Oral).