DEXTEROUS MANIPULATION CAPABILITIES ARE ASSOCIATED WITH CHANGE IN DISCHARGE RATE PROPERTIES OF MOTOR NEURONS WITH AGE

by

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ABSTRACT

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Aging is accompanied by declines in manual dexterity and fine motor control. The purpose of this research was to compare hand motor control in young and older adults and examine the neuromuscular mechanisms responsible for enabling these interactions. We test force variability during isometric and dynamic contractions, manual dexterity and track motor unit activity to identify the neuromuscular mechanisms responsible for changes in dexterity with age.

26 older adults (66-86 years) and 28 young adults (19 – 38 years) participated in the study. Research participants performed force matching tasks during index finger abduction, precision pinch, static pressing and hybrid force/ motion tasks. The coefficient of variation (CV) during the force-matching task computed. Multichannel high-density EMG was measured from the First Dorsal Interosseus (FDI) and extensor Digitorum Communis (EDC). The EMG signals were decomposed to obtain motor unit discharge rate parameters such as discharge rate and discharge rate variability of the motor neurons was computed. Low-frequency common oscillatory drive to the motor neurons was computed using Principal Component Analysis (PCA) on the motor unit discharge rates. Associations between the force variability, dexterity scores and motor unit parameters were analyzed for group differences and associations.

A higher CV of force was observed in older and younger adults was associated with reduced mean discharge rates, increased discharge rate variabilities and an increase in the low-frequency common oscillatory signal to the motor units. Additionally, the motor unit parameters were associated with performance on tests of manual dexterity such as the box and block test and grooved pegboard test.

Our results showed a change in motor unit properties with age. However, the change in motor performance with age was observed only in two tasks. This may be related to the difference dexterous experience of the young versus the older adults.

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Chapter 1: Introduction

The presence of physiological tremor and a decline in the ability to manipulate objects with the fingers are some of the devastating consequences of aging. These impairments lead to several limitations in performing activities of daily living (ADLs) such as cooking, feeding, dressing, etc., and can eventually lead to dependence and institutionalization (Incel et al. 2009; Ostwald et al. 1989). The number of older adults is projected to double by the year 2060 (Mather 2015) . This increase in the number of older adults, paired with dexterous impairments leading to dependency, will ultimately result in increased healthcare costs. Thus, it is important to examine the mechanisms leading to poor dexterity and explore preventive or rehabilitative measures to alleviate the problem.

Force Steadiness

Tremor, both physiological and pathological, manifests itself as an inability to hold a steady force or maintain a stable movement trajectory. When individuals are asked to hold a steady force, the force is not constant, but instead fluctuates about a mean value. These fluctuations in force can be quantified as the standard deviation (or coefficient of variation) of force and reflect the ability of that person to perform a steady contraction. They also interfere with the ability of an individual to perform the intended task optimally. Previous research has attributed age-related declines in dexterity to a decrease in strength (Ranganathan et al. 2001; Shiffman 1992) and an inability to hold a steady force (Enoka et al. 2003; Marmon et al. 2011). Older adults exhibited greater force variability when isometrically holding a force under 20% maximum voluntary contraction (MVC) (Christou 2011; Galganski, Fuglevand, and Enoka 1993). Force variability during isometric pinch and index finger abduction also increases with age and has been associated with functional measures of dexterity such as the grooved pegboard test (Marmon et al. 2011).

In addition to studying force control during isometric tasks, it is critical to examine motor control on tasks that mimic ADLs. Hybrid force/motion tasks require simultaneous control of forces and movements. For example, tasks such as peeling a fruit, cleaning surfaces, writing and several other ADLs require pressing and moving while manipulating objects and surfaces and are all hybrid tasks. These tasks are challenging for motor control as they require both well-directed forces and movements (Joshi and Keenan 2016; Keenan et al. 2009). Increased force variability on a hybrid task highlights some of the dexterous impairments brought on by advancing age (Joshi 2017). Experimental paradigms involving hybrid tasks are novel and, since they require concurrent control of more than one task constraint, may help reveal additional deficits in motor control that may not be possible with isometric tasks. The proposed project will assess differences in motor performance across isometric and hybrid tasks to examine age-related dexterous impairments.

Interaction between Force and Frictional Properties of Interface

One critical factor influencing steady force production and dexterous manipulation involves the frictional properties of the surface that the fingers contact (Cole and Johansson 1993; Keenan and Massey 2012; Seo et al. 2011). For example, force variability was found to be significantly higher when pressing against a low-friction surface as opposed to a high-friction surface (Keenan and Massey 2012; Seo et al. 2011). Older adults have shown greater impairments than young adults while pressing down with a steady force on a low-friction surface (Keenan and Massey 2012). Another study examining kinematics in young and older adults during a reach - and - lift task found that older adults had higher task failure rate while lifting the slippery object as compared to younger adults (Holt et al. 2013). These impairments stem from the inability to increase the relative safety margin while handling low- versus high-friction surfaces (Cole, Rotella, and Harper 1999). However, when individuals were asked to perform a hybrid task of pressing and moving, both the young and older adults optimized performance on the low-friction surface as compared to the high friction surface, though younger adults exhibited significantly lower force variability than the older adults (Joshi and Keenan 2016; Joshi 2017). Results from our previous work (Joshi 2017) have shown that older adults had lower mean shear forces and shear force variability than young adults. These changes in force variability with age, and frictional properties of the surface may be a result of an increase in skin slipperiness (Cole and Johansson 1993; Johansson 1996) or neuromechanical changes with age. Further research is required to investigate the mechanisms causing these changes in dexterity when interacting with surfaces with different frictional properties.

Effect of Visual Gain on Force Control

Visual feedback of force provided during a force steadiness task also plays a role in performance on the task. Visual gain represents the amount of visual feedback provided and can be changed by altering either the ordinate scale or visual angle. Research has shown that increasing visual gain leads to increased force variability on isometric force and position-holding tasks in older adults (Baweja, Kwon, and Christou 2012; Christou 2011; Kennedy and Christou 2011; Sosnoff and Newell 2006; Keenan, Huddleston, and Ernest 2017). For example, an increase in the visual angle from 0.05˚ to 0.5˚ led to a 43% increase in force variability in older but not young adults (Kennedy and Christou 2011). Similarly, an increase in visual angle led to ~40% in increase in positional variability during an ankle dorsiflexion task in older adults (Baweja, Kwon, and Christou 2012). It has been suggested that this increase in force variability is due to limitations in visuomotor processing or the increased attention demands imposed by high visual gain (Kennedy and Christou 2011; Keenan, Huddleston, and Ernest 2017). Previous research has attributed changes in performance with visual gain to altered modulation of muscle activity (Baweja, Kwon, and Christou 2012; Park, Kwon, and Christou 2017). However, specific neuromuscular mechanisms responsible for performance limitations with increased visual gain are unknown.

Neuromuscular Mechanisms

Aging brings about death of spinal and cortical motor neurons and the loss of muscle mass. Previous research has alluded to a link between this neurophysiological reorganization, increased force variability and poor motor function (Enoka et al. 2003; Erim et al. 1999; Marmon et al. 2011; Moritz et al. 2005; Taylor, Christou, and Enoka 2003). It is not clear what neuromuscular mechanisms are most critical to maintain manual dexterity as many mechanisms have been suggested. For example, age-associated declines in fine motor skills have been attributed to an increase in the variability of motor unit discharge times (Marmon et al. 2011; Moritz et al. 2005). Studies looking to find associations between tremor and manual dexterity have looked at coherence measures to assess common oscillatory inputs to motor neurons, either derived from motor unit discharge times or surface EMGs (Keenan et al. 2007; Semmler, Kornatz, and Enoka 2003). However, coherence is a frequency-domain measure of the linear correlation between two signals and it is unclear how well it represents the global measure of the common inputs to motor neurons (Keenan et al. 2012). Furthermore, studies examining frequency domain properties of motor neurons have drawn conclusions from pairs of motor units (De Luca and Erim 2002; Erim et al. 1999; Semmler, Kornatz, and Enoka 2003). Data from pairs of motor units underestimates the common input signal to the motor unit pool. This signal is best quantified by analyzing cumulative spike trains of several motor neurons (Negro and Farina 2012). A measure of the common inputs to the motor neurons is the low-frequency (< 4Hz) common oscillatory drive (Feeney, Mani, and Enoka 2018; Negro, Holobar, and Farina 2009). Since only low frequency components of the neural drive are reflected in the motor output (Lemon and Mantel 1989), it is critical to study the associations between measures of low-frequency common drive to motor neurons and force variability. A seminal study (Negro, Holobar, and Farina 2009) estimated the low-frequency common oscillatory drive as the first common component of a principal component analysis on motor unit discharge rates. This measure explained ~72% of force variability during an isometric contraction of the abductor digiti minimi in young adults (Negro, Holobar, and Farina 2009). One study (Feeney, Mani, and Enoka 2018) found significant associations between low-frequency common drive and force steadiness on a wrist extension task in young (r^2 = 31%) and older (r^2 = 39%) adults. The present study will examine associations between motor unit discharge rate variability and low-frequency common oscillatory drive and force steadiness on isometric and hybrid tasks as well as tests of dexterity. Findings from this study will corroborate the role of motor unit activity in dexterity and identify changes in neuromuscular function with age.

Statement of Purpose

The purpose of this project was to understand neuromuscular mechanisms underlying hand motor control in healthy young and older (> 65 years) adults. We examined motor performance and motor unit activity within and across muscles, across specific tasks and conditions, which highlight performance differences in young and older adults.

The central hypothesis was that dexterous impairments occurring with age are due to impairments in motor unit activity within and across muscles, and these impairments are associated with deficits in force and movement control. Specifically, we examined changes in low-frequency common oscillatory drive to the motor neurons and motor neuron discharge rate variability with age and across tasks and conditions. This hypothesis was based on previous findings including: 1) increased force variability in older adults as compared to younger adults while performing an isometric as well as hybrid pressing and moving tasks (Christou 2011; Enoka et al. 2003; Joshi 2017; Keenan and Massey 2012), 2) force variability during index finger abduction in young and older adults was positively correlated with time to complete the grooved pegboard test (Marmon et al. 2011), 3) variability in the low-frequency component of the motor unit discharge rate explained ~72% of the variability in force during isometric contractions in younger adults (Negro, Holobar, and Farina 2009), and 4) increased discharge rate variability in older adults as compared to young adults while performing an isometric index finger abduction task (Enoka et al. 2003; Moritz et al. 2005; Taylor, Christou, and Enoka 2003), which was associated with performance on the grooved pegboard test (Marmon et al. 2011). Our *rationale* was based on the concept that older adults have dexterous impairments while performing tasks of fine motor control and those changes in motor unit properties with age have been found to be associated with declines in fine motor skills. While previous research found changes in discharge rate variability and coherence in pairs of motor units, we examined age-related changes in properties of a large sample of motor units. This is possible due to the novel implementation of high-density EMG arrays. Furthermore, assessment of motor performance and neural changes with age and during a hybrid force/motion task is innovative. The use of the hybrid task emphasizes age-related differences in motor control, which highlight the neuromuscular mechanisms causing these changes. To test our hypothesis, we pursued the following *specific aims*:

Specific Aim 1: To examine age-associated changes in neural mechanisms during isometric abduction, pinch grip tasks.

Decrease in force steadiness with age during index finger abduction is well-documented (Enoka et al. 2003; Galganski, Fuglevand, and Enoka 1993; Kornatz, Christou, and Enoka 2005; Marmon et al. 2011; Moritz et al. 2005). However, steadiness during precision pinch (Marmon et al. 2011; Sosnoff and Newell 2006) and handgrip tasks have not been studied extensively, particularly across force and visual gain conditions. In addition to index finger abduction, these are primary actions used in several ADLs and thus, changes with age need to be explored for all of these tasks. Furthermore, isometric tasks, being static in nature, yield good quality EMG signals due to minimal movement of the muscle and absence of motion artifact. This in turn will yield good motor unit decompositions that correctly identify motor units. This will allow for examination of specific age-related changes in performance and neural phenomenon within the data and comparisons with previous work in the literature.

Force deficits due to age are greater at low force levels, especially under 20 N (Christou 2011; Galganski, Fuglevand, and Enoka 1993). Previous research studies allude to increased discharge rate variability or greater common modulation of motor unit discharge rate with age (Enoka et al. 2003; Erim et al. 1999). However, these studies used fine wire electrodes to detect motor unit activity; thus, results were based on analysis of pairs of motor units. Moreover, using just a pair of motor units is believed to underestimate the activity across the entire population of motor units (Barry et al. 2007; Negro and Farina 2012), and thus is not sufficient to draw conclusions about activation of the motor unit pool. We will use multichannel EMG to obtain activity from a larger sample of motor neurons to study neuromuscular changes in young and older adults across forces and visual gain conditions. In the following sub-aims:

Aim 1.1: To compare force variability between young and older adults in the index finger abduction and precision pinch tasks at different submaximal forces and visual gain conditions.

Aim 1.2: To compare motor unit activity between young and older adults as they perform the force steadiness tasks and find associations between force variability and motor unit activity.

Hypothesis 1: Older adults will have significantly greater force variability than the young adults in the abduction, and pinch tasks. This difference will be accentuated at low force and high visual gain conditions. Force variability will be associated with low-frequency common drive of motor unit discharge rates and discharge rate variability.

Specific Aim 2: To examine age-associated neuromuscular changes that relate to force control during static and hybrid scratch tasks on a low-friction surface. Previous research comparing motor control between young and older adults found that older adults had 2.54 times greater force variability than young adults while performing a static force matching task on a low friction surface (Keenan and Massey 2012). Furthermore, force variability was significantly higher on a hybrid force/motion task than a static pressing task (Joshi and Keenan 2016; Joshi 2017). Also, older adults had 32% greater variability while performing a hybrid force/motion task than young adults (Joshi 2017). Whether changes in tactile feedback with age (Cole, Rotella, and Harper 1999; Johansson 1996) or neuromuscular changes are responsible for impaired motor performance on the hybrid task is unknown. Pilot data from our lab showed a significant association between discharge rate variability of the FDI motor neurons during index finger abduction to variability on the hybrid task ($r^2 = 0.632$). The hybrid task used in previous studies involved movement about the shoulder and elbow in addition to the index finger. We will use a more constrained scratch task on a Teflon-Teflon interface and limit the degrees of freedom as done by Keenan et. al. (Keenan et al. 2009). This will enable us to study motor unit activity with high density EMG and identify motor unit changes with age across force and visual gain conditions.

Aim 2.1: To compare force variability between young and older adults during static and hybrid tasks and visual gain conditions on the low-friction surface.

Aim 2.2: To compare motor unit activity between young and older adults during the static pressing and hybrid task and find associations between motor unit activity and force variability.

Hypothesis 2: Older adults will have greater force variability than younger adults. This difference will be greatest when older adults perform the hybrid force/motion task and will be associated with an increase in discharge rate variability and increased low-frequency common modulation of motor units.

Specific Aim 3: To examine age-associated changes in performance on tests of manual dexterity such as the grooved-pegboard test, box and block test and the coin rotation task and identify associations between performance, force steadiness and previously identified neuromuscular mechanisms.

Experimental tests examining force steadiness place several constraints on movements such as specific forces and movement trajectories. These tests require calibrated force transducers, signal processing equipment and software for analysis, all of which are costly and require specific skills and expertise to be conducted. In order to extend testing of manual dexterity beyond laboratories, tests need to be portable, cost-effective and easy to administer. To that end, several tests of manual dexterity have been developed and employed in clinics to test dexterity. Tests of manual dexterity such as the grooved pegboard, 9-Hole Peg Test (9-HPT), Purdue pegboard, box and block, Archimedes spiral tracing and Minnesota manual dexterity tests are reliable and sensitive in capturing dexterous impairments with age (Desrosiers et al. 1994; Desrosiers et al. 1995; Heintz and Keenan 2018; Marmon et al. 2011; Martin et al. 2015; Surrey et al. 2003). Furthermore, the National Institutes of Health (NIH) included the 9-Hole Peg Test (9-HPT) as a measure of manual dexterity in the motor battery of tests of the NIH toolbox (Wang et al. 2011). The grooved pegboard test is similar to the 9-HPT incorporated in the NIH toolbox; however, it provides a greater challenge to older adults above the age of 80, and thus may be a better tool to decipher differences with age. Previous research has found associations between force variability on an index finger abduction task and the grooved pegboard and the Purdue pegboard test (Kornatz, Christou, and Enoka 2005; Marmon et al. 2011). One study reported moderate correlation ($r = 0.51$) between performance on the Purdue pegboard test and motor unit discharge rate variability (Kornatz, Christou, and Enoka 2005). A recent study also found associations between low frequency common oscillations to the wrist extensor and performance on the grooved pegboard test in older but not young adults ($r^2 = 0.47$; (Feeney, Mani, and Enoka 2018)). Additional research is required to support these findings.

The box and block test measures gross manual dexterity in healthy and impaired individuals. This test has strong correlation with the Action Research Arm test which includes a battery of tests to assess upper extremity function (Desrosiers et al. 1994). However, associations of box and block performance to force steadiness tasks or motor unit parameters has not been studied. Both, the grooved pegboard and box and block test require significant movement of the upper extremity. Recording EMG during these tasks is a challenge due the presence of motion artifact. In order to identify associations between these measures and motor unit activity, we will correlate the dexterity measures to motor unit activity computed in the previous aims.

A coin rotation task requires coordinated finger movements and is a valid measure of manual dexterity in Multiple Sclerosis and unilateral lesions (Heldner et al. 2014; Mendoza et al. 2009), but not widely used to test impairments in other populations. We assessed the use of the coin rotation task to identify age-related dexterous impairments. In this aim, we examined age-related changes in manual dexterity using the grooved pegboard, box and block and coin rotation tests. We studied associations between manual dexterity and force variability and motor unit activity measures.

Aim 3.1: To identify the association between force variability in isometric, static and hybrid tasks obtained in the previous Aims and the measures of manual dexterity.

Aim 3.2: To determine the association between performance on tasks of manual dexterity and motor unit activity from Aims 1 and 2.

Hypothesis 3: Older adults will have poor performance on tests of manual dexterity than young adults. Force variability, muscle, and motor unit activity during isometric and hybrid tasks will be associated with the measures of manual dexterity.

Delimitations

1. Force steadiness will be assessed at 5 and 15% MVC of the individual subject. Older adults will likely have a lower MVC than their younger counterparts, leading to much smaller submaximal forces. The small value of absolute force might lead to greater force variability and poor EMG and motor unit decompositions. However, EMG at 15% force is expected to have a higher motor unit yield.
2. The novelty of the hybrid task may affect performance. However, participants will be provided several practice trials before, though EMG and performance will be monitored.

Assumptions:

1. Participants will perform tasks as directed and provide at true maximal effort.
2. Participants will be right-handed as identified by the Edinburgh Handedness Test.
3. Age range for young participants is 18 – 49 years, and older adults is 65 – 90 years.
4. Participants will correctly report any neuromuscular or movement impairments that they have had in the past and visual acuity.
5. The hybrid task will involve movement of just the index finger; the rest of the hand will hold a dowel.
6. The tasks will be block randomized.

Significance

As the baby boomer population is aging, the number of older adults aged 65 and over in the US is estimated to increase from 46.2 million in 2014 to 83.4 million in 2040 (AOA https://aoa.acl.gov/Aging_Statistics/Profile/2015/4.aspx). This increase in the number of older adults, paired with dexterous impairments leading to dependency, will ultimately result in increased healthcare costs. Thus, it is important to examine the mechanisms leading to poor dexterity and explore preventive or rehabilitative measures to alleviate the problem.

Changes in several motor unit properties such as mean discharge rate, discharge rate variability, and motor unit synchronization have been associated with age-related increase in force variability. However, these have been studied only in pairs of motor units and not populations of motor units and during isometric tasks. Evidence of association of common oscillatory drive to motor units with force variability in young and older adults is limited. Our study will add to the literature by examining age-related deficits in dexterity during a hybrid task and the neural mechanisms causing these. This work will help better understand dexterous impairments in older adults and inform the design of biobehavioral interventions that can influence motor neuron activity and improve manual dexterity. The techniques developed in this study can be used to further explore the pathophysiological mechanisms underlying the changes in manual dexterity in individuals with stroke, multiple sclerosis, spinal cord injury and Parkinson’s disease.

Chapter 2: Reduced motor unit discharge rate in populations of motor units with age is associated with increased force variability during dexterous tasks

Introduction

The number of individuals aged 65 and over has been increasing across the world. Currently, there are about 49.2 million older adults residing in the US. This number is projected to increase to 94.7 million by 2060 (Vespa, 2018). As life expectancy increases, maintaining health of the elderly is critical to good quality of life. Healthy aging research is concentrated around biomarkers of physiological functions, endocrine function, physical capability, cognitive function, and immune function (Lara et al. 2015). Physical capability includes strength, mobility, balance and dexterity. Among these, dexterity is a key factor in assessing the level of care a person needs (Carment, et al., 2018).

When individuals are asked to hold a steady force, the force is not constant, but instead fluctuates about a mean value. These fluctuations in force can be quantified as the standard deviation (or coefficient of variation) of force and reflect the ability of that person to perform a steady contraction. They also interfere with the ability of an individual to perform the intended task optimally. Previous research has attributed age-related declines in dexterity to a decrease in strength (Shiffman 1992; Ranganathan et al. 2001) and an inability to hold a steady force (Enoka et al. 2003; Marmon et al. 2011). Decrease in force steadiness with age during index finger abduction is well-documented (Galganski et al. 1993; Enoka et al. 2003; Kornatz et al. 2005; Moritz et al. 2005; Marmon et al. 2011). However, steadiness during a precision pinch task (Sosnoff and Newell 2006; Marmon et al. 2011) has not been studied extensively, particularly across force and visual gain conditions. In addition to index finger abduction, pinch is a primary action used in several ADLs and thus, changes with age need to be explored for these tasks. Furthermore, isometric tasks, being static in nature, yield good quality EMG signals due to minimal movement of the muscle and the absence of motion artifact that is a well-documented limitation of EMG. This in turn will yield good motor unit decompositions that correctly identify motor units. Good quality EMG signals and motor unit decompositions will allow for examination of specific age-related changes in performance and neural mechanisms and allow comparisons with previous work in the literature.

Visual feedback provided during a force steadiness task plays an important role in task performance. Visual gain is the term used to quantify the amount visual information provided during a task. It can be changed by manipulating the ordinate axis or adjusting the visual angle. Previous research has demonstrated the increase in force variability on isometric steadiness tasks in older adults dependent on visual feedback (Sosnoff and Newell 2006; Christou 2011; Kennedy and Christou 2011; Baweja et al. 2012; Keenan et al. 2017). This increase in force variability with an increase in visual gain has been attributed to limitations in visuomotor processing in older adults (Keenan, Huddleston, & Ernest, 2017; Tracy, Dinenno, Jorgensen, & Welsh, 2007). However, specific neuromuscular mechanisms resulting in poorer performance are still unclear.

Force deficits due to age are greater at low force levels (Galganski et al. 1993; Christou 2011). Previous research studies allude to increased discharge rate variability or greater common modulation of motor unit discharge rate with age (Erim et al. 1999; Laidlaw et al. 2000; Enoka et al. 2003). However, these studies used fine wire electrodes to detect motor unit activity; thus, results were based on analysis of pairs of motor units. Moreover, using just a pair of motor units is believed to underestimate the activity across the entire population of motor units (Barry et al.

2007; Negro and Farina 2012), and thus is not sufficient to draw conclusions about activation of the motor unit pool.

The present study used a multichannel surface EMG system that identified activity from several motor units, thereby providing a more accurate measure of motor unit population properties. The purpose of our study was to assess the relationship between force variability on abduction and pinch tasks with motor unit parameters including discharge rate, discharge rate variability and measures of low frequency common oscillatory drive. Furthermore, this study aimed at examining age associated differences in motor performance as measured by force steadiness and motor unit activity across force levels and visual gain conditions.

Methods

Ethics statement: The experiments were approved by the Institutional Review Board at the University of Wisconsin-Milwaukee. The local ethics committee approved consent for subjects ranging in age from 18–40 years and 65-90 years. All participants gave their written formal consent before participating in the study.

Participants: 26 older adults (age: 72.4±4.98 years, range: 66-86 years, 14 F, 12 M) and 28 young adults (age: 24.24±5.58 years, range: 19 – 38 years, 16F, 12M) participated in the study. All participants were right-handed as confirmed by the Edinburgh Handedness test (Oldfield 1971), with no reported neuromuscular disorders or hand pathologies volunteered for the study.

Experimental setup: Subjects sat in an adjustable chair with the right elbow resting on a vacuum foam pad (VersaForm pillow, Tumble Forms) to minimize movement. The upper arm was vertical and slightly abducted from the trunk with the elbow at a right angle. The subjects performed the following tasks:

Isometric index finger abduction: The participant's right hand was placed palm down on a rigid surface. A manipulandum held the thumb and the fingers, while isolating the index finger for abduction (Laidlaw et al. 2000; Moritz et al. 2005, Taylor et. al 2003). Subjects abducted their index finger to push into a wooden dowel positioned at the proximal interphalangeal (PIP) joint of the index finger, identical to the approach used in previous studies (Marmon, Pascoe, Schwartz, & Enoka, 2011; Tracy, Maluf, Stephenson, Hunter, & Enoka, 2005; Keenan, Massey, Walters, & Collins, 2012). The dowel was affixed to a force sensor (Nano 17; ATI Industrial Automation) that measured abduction force.

Pinch: The subjects performed a precision pinch task by holding the force sensor (Futek LCM 100, Futek advanced Sensor Technologies Inc.) between their thumb and index finger. The other three fingers were extended by the manipulandum, so they did not assist with the task (Fig 2.1).

Maximal contractions: For each of the tasks described above subjects performed three trials of maximal voluntary contraction (MVC) by slowly ramping up the force to press as hard as they can for 3 - 5s each. Verbal encouragement was provided to ensure that subjects put in maximal effort. If peak force in two subsequent trials differed by more than 5%, additional trials were collected. The peak force in the trial with the highest force was recorded as the MVC and used to calculate submaximal forces.

Submaximal force steadiness: Subjects performed isometric abduction and pinch steadiness tasks at 5% and 15% MVC force levels for 40s. They were asked to hold the force "as steady as possible" with visual feedback. Three trials were recorded at each force level for each task. At least 1 minute of rest was provided between contractions. Forces were sampled at 1000 Hz. The abduction forces were sampled using the ATI A/D converter and pinch forces were sampled using the A/D converter by Coulbourn Instruments (Holliston, MA).

Visual feedback was provided on a 24-in. LCD monitor located 1 m away. The target force for all conditions was displayed as a horizontal black line located in the center of the screen, and the force produced by the subject during the 40 s trial was shown as a horizontal solid blue line. Subjects were instructed to match their actual force with the target force as closely as possible, with the blue line moving up and down on the monitor with increasing and decreasing force, respectively. The low and high visual feedback gain conditions were associated with large and small range of forces displayed to the participant, respectively. For example, if participants are performing a steadiness task at a 5N force, with a low visual gain, the target line is drawn at the center of the monitor and the bottom and top of the screen correspond to 0 and 10 N, respectively. In contrast, for the high visual gain condition, the bottom and top of the screen corresponded to 4.9 and 5.1 N, respectively, with the target line still drawn at the center of the monitor. The visual gain in the high gain condition will be 10 times that in the low gain condition as suggested previously (Schmied et al. 2000).

EMG: We recorded multi-channel surface EMGs with a 5 X 13 electrode grid with 4 mm interelectrode spacing (OTBioelettronica, Torino, IT) positioned on the skin overlying first dorsal interosseus, which is the prime index finger abductor and a 5 X 13 grid with 8 mm interelectrode distance overlying the wrist extensor muscles during the maximal and submaximal tasks. The wrist extensors also have high levels of activity during the abduction and the pinch tasks (Valero-Cuevas FJ, 2005). The 128 channels of EMG were recorded (2048 samples/s; 10 - 500 Hz bandpass filter) using the OT Biolab software from OTBioelettronica (Torino, IT). Research studies identifying associations between motor unit properties and force steadiness

(Negro et al. 2009; Feeney et al. 2018) as well as results from our pilot data (Joshi 2018) confirms the use of these electrode arrays and data processing parameters.

Data Processing: All data were analyzed using a custom written Matlab code. Our primary measure for the abduction and pinch tasks was force steadiness. This was measured as the standard deviation and as the coefficient of variation for force (standard deviation of force / mean force × 100) averaged across the three trials. Additionally, root mean square error (RMSE) was computed for each trial.

The surface EMG was decomposed into trains of motor unit action potentials with the convolution kernel compensation (CKC) technique (Holobar et al. 2010) and manually verified by an experienced operator. Motor unit discharge rates and discharge rate variability were computed. The resulting smoothed and detrended discharge rates from both muscles were arranged in a matrix (time samples × motor unit) and their principal components was computed using the eigenvalue decomposition of the covariance matrix. The maximum eigenvalue of the covariance matrix, which is the first principal component, was used to quantify the strength of the common low-frequency oscillations in motor unit activity. Additionally, coefficient of variance of the first principal component and variance explained by the first principal component were computed to further assess common drive. Associations of discharge rate, discharge rate variability and measures of low-frequency common oscillations with force steadiness measures were examined.

Fig 2.1: Experimental set-up for the index finger abduction task. The PIP joint is aligned with the wooden dowel to perform the abduction task. Movement of the thumb and other fingers is restricted due to the manipulandum.

Statistical analysis. A multivariate analysis of variance (MANOVA) was conducted in SPSS. Performance differences were examined across 2 age groups (young and old), 2 force levels (5% MVC and 15%MVC), 2 gain conditions (High and Low) and 2 muscles (EDC and FDI). The association between the low-frequency modulation of motor unit activity, mean discharge rate and discharge rate variability to force steadiness were quantified by computing the Pearson correlation coefficient in SPSS.

The data were tested for normality. Variables that did not fit the normality criteria were transformed before analyzing data using MANOVA. For the abduction task, inverse transform was used on the discharge rate variability and variability of the first principal component. Force variability was transformed using the square root transform. For the pinch task, a logarithmic transform of the coefficient of variation of force was used for analysis.

Data are reported as mean ± SD in the text and mean ± SE in the figures unless otherwise noted. Normality of the transformed data were confirmed using Shapiro Wilk's test and visual inspection of Q-Q plots. Discharge rate variability and variability of the first principal component did not conform to a normal distribution and were transformed using an inverse transformation for analysis. The standard deviation of force and the coefficient of variability of force during both, abduction and pinch tasks were transformed using a logarithmic transform to conform to a normal distribution (Osborne, 2019). Furthermore, group differences between maximum force during the abduction task were analyzed using a non-parametric, Mann Whitney U test since this measure did not follow a normal distribution.

Results

Participants: Data from 15 older (72.39 ± 5.18 years, range: 67 – 86 years, 8F, 10M) and 16 younger (24.105 ± 5.48 years; range: 19 – 35 years, 12F, 7M) adults were used for analysis. The data discarded was visually examined and had low EMG signal to noise ratio. If included in the analysis this data would contribute to incorrect motor unit detection and parameter scores.

Performance on abduction test: Age related differences were observed across force and motor unit parameters. The Mann Whitney U test showed no differences in the maximum abduction between young and older adults ($p = 0.232$; Fig 2.2). There was an age × visual gain interaction in standard deviation of force. In the low visual gain condition, the SD of force was significantly greater in older adults (8.09 ± 5.414) vs younger adults (6.33 ± 3.86), f (1, 98) = 5.418; $p = 0.022$). There was no age-associated difference in the SD of force in the high visual gain condition. There was a main effect of age on the SD of force (f (1,98) = 4. 141; $p = 0.045$; Fig

2.2). Force variability measured as the SD of force was significantly greater in older adults (7.586 ± 1.099 N) as compared to younger adults (5.95 ± 1.073 N).

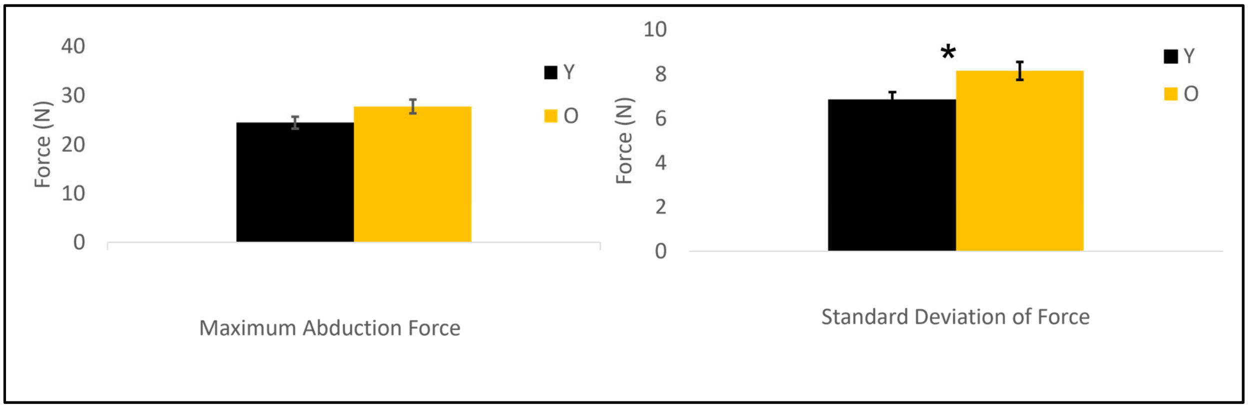


Fig 2.2: Age-associated maximum abduction force and force variability. Maximum abduction force was not significantly different in older adults versus younger adults. The standard deviation in the older adult group was significantly greater than younger adults (p = 0.045).

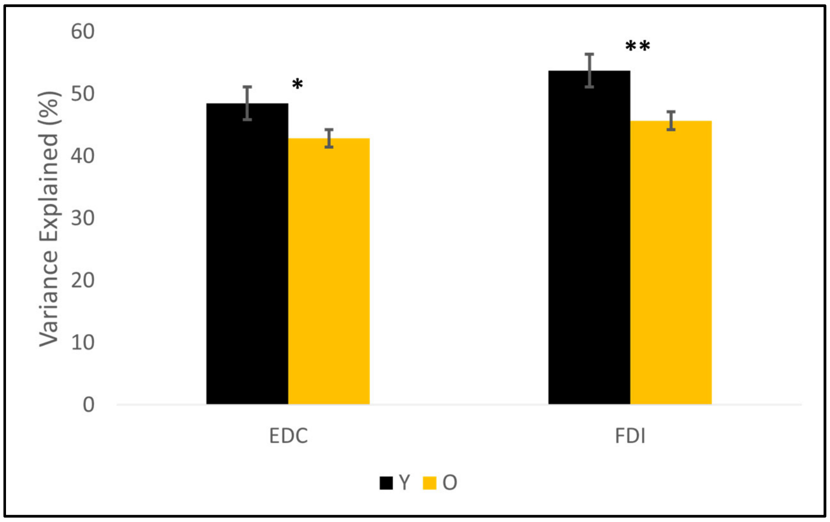


Fig 2.3: Variance explained by the first principal component in young and older adults on the abduction task. The variance explained was significantly greater in older adults than younger adults in both the EDC (p = 0.01) and FDI (p = 0.033).

Variance explained by the first principal component represents common variance in the motor unit discharge rates. The variance explained was significantly greater in young (51.153 ± 1.282) vs older adults (43.781 ± 1.787; f (1,98) = 10.773, p = 0.002; Fig 2.3).

Age associated changes were observed in discharge rate and the strength of the first principal component (Fig 2.4). There was a group × gain × muscle interaction in these variables. Discharge rate and the strength of the first principal component were significantly higher in the FDI muscle of young versus older adults during the low visual gain condition but not during the high visual gain condition.

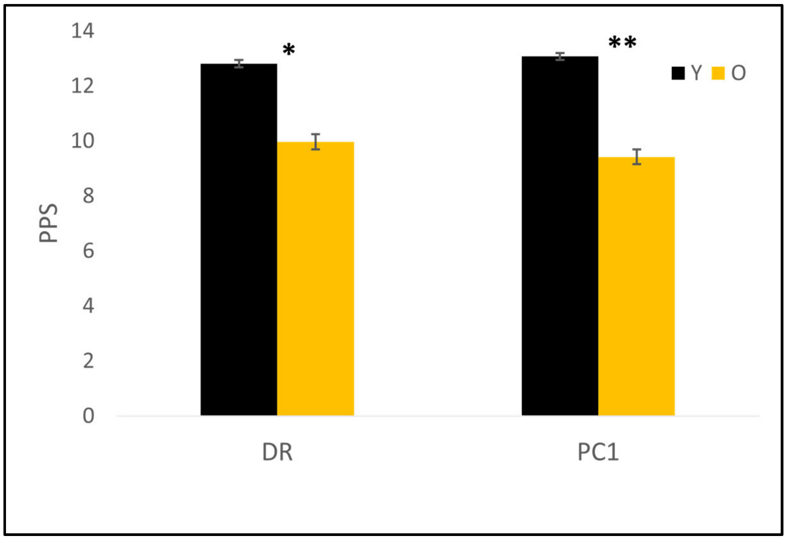


Fig 2.4: Age-associated differences in discharge rate and first principal component in the FDI muscle during the abduction-low gain condition. The discharge rate ($p = 0.002$) and the strength of first principal component ($p = 0.001$) were significantly greater in young adults than in the older adults than younger adults in the FDI.

In younger adults, the motor unit properties did not differ across the FDI and EDC muscles. However, motor unit properties in the older adults were significantly different across the 2 muscles (Fig 2.5). Discharge rate ($p < 0.001$) and the first principal component ($p < 0.001$) were significantly greater in the EDC muscle than the FDI. Discharge rate variability (p = 0.013) and variability of the first principal component (p = 0.045) were greater in the FDI than in the EDC.

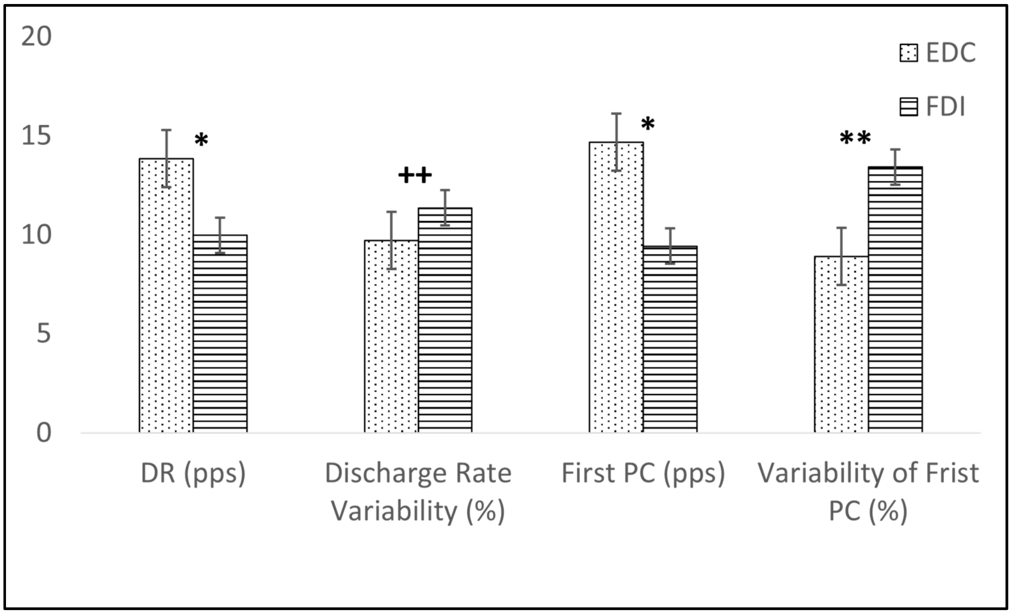
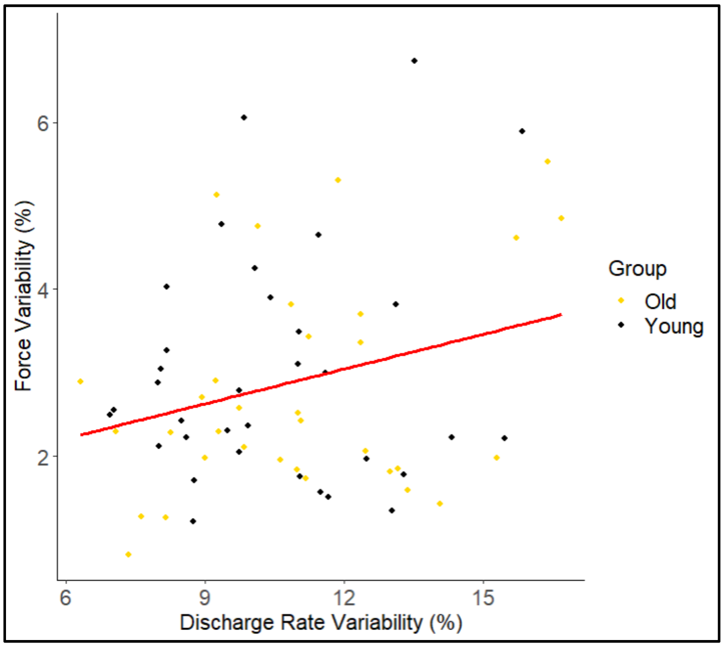


Fig 2.5: Motor unit characteristics in EDC and FDI muscles of older adults on the abduction task. Discharge rate and first principal component were significantly greater in the EDC and the variability of discharge rates and the first principal component were significantly greater in the FDI

Correlation analysis revealed significant associations between force variability measures and motor unit parameters across all the force levels and visual gain conditions. Force variability was associated with discharge rate variability (r = 0.261, p = 0.033; Fig 2.6), discharge rate (r = -0.295, p = 0.014; Fig 2.7) and the first principal component (r = -0.270, p = 0.025; Fig 2.8).

Fig 2.6: Association between abduction force variability and discharge rate variability of FDI motor units in young and older adults. r = 0.261, p = 0.033.



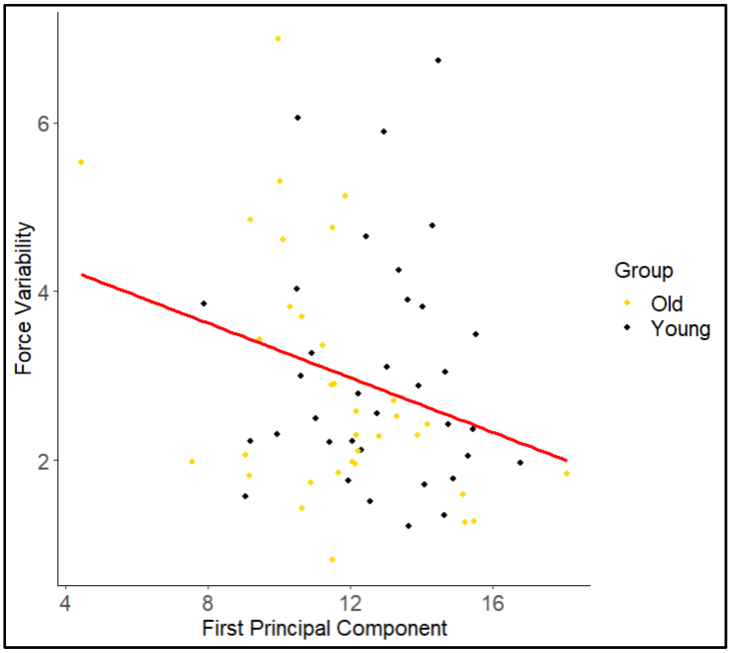


Fig 2.7: Associations between abduction force variability and first principal component of FDI motor units. r = -0.295, p = 0.014

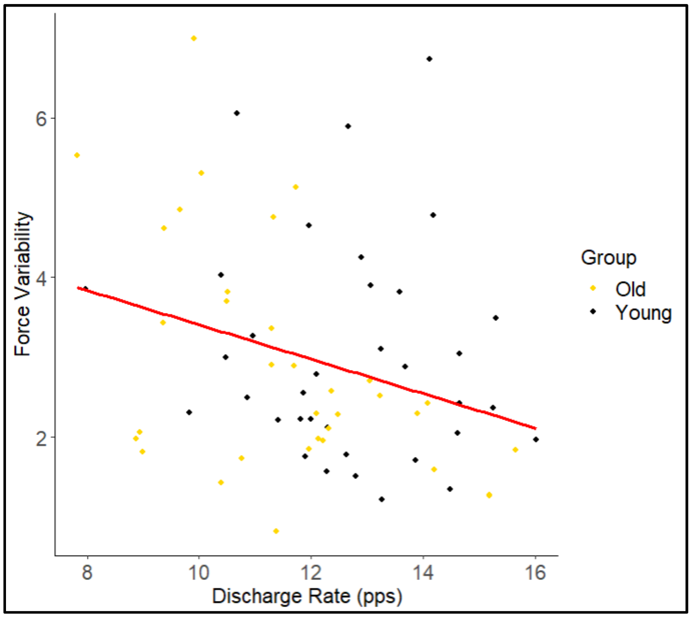


Fig 2.8: Associations between abduction force variability and discharge of FDI motor units. r = -0.270, p = 0.025.

Performance on pinch task: Maximal pinch force and force variability on the pinch task were both similar across young and older adults. Age-associated differences were seen in the variance explained by EDC motor units during the pinch task (Figure 2.9; p = 0.030). Variance explained by the FDI motor units was significantly greater than that in the EDC motor units in both young (p = 0.05) and older adults (Figure 2.9; p <0.001). Additionally, the variability of the first principal component in the FDI motor units was significantly greater than the EDC motor units in the older adults (Figure 2.10, p = 0.04).

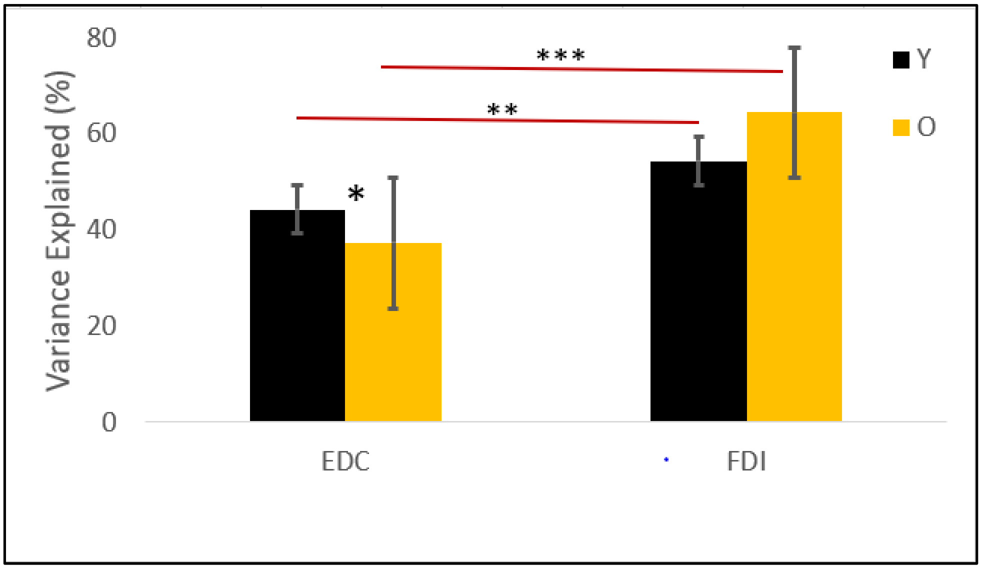


Fig 2.9: Differences in variance explained in EDC and FDI motor units in young and older adults on the pinch task. Younger adults had significantly greater variance explained than older adults in the EDC motor units (*, p = 0.030). Variance explained by the FDI motor units was significantly greater than the EDC motor units in young (**, p = 0.05) and older adults (***, p < 0.001)

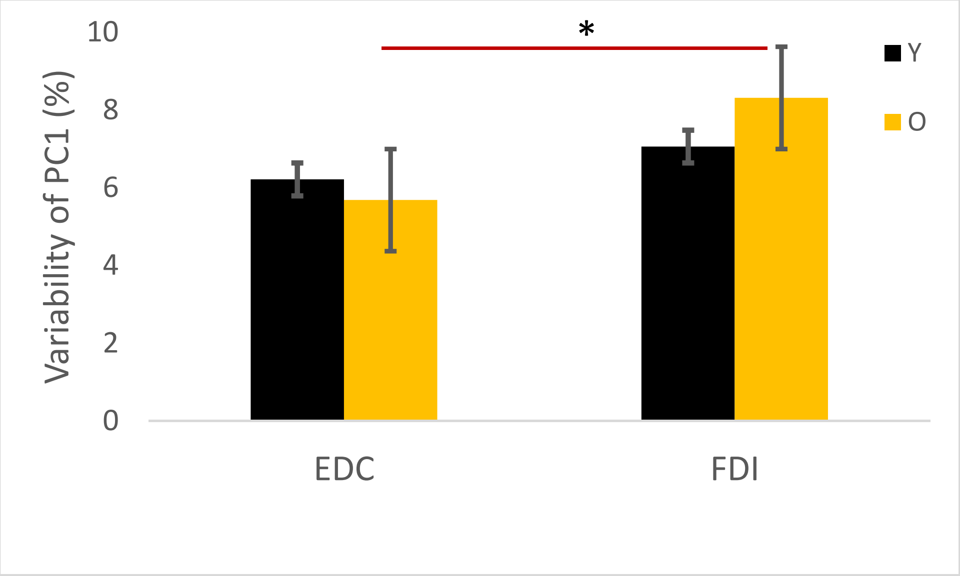


Fig 2.10: Differences in variability of the first principal component of the EDC and FDI motor units in young and older adults on the pinch task. The variability of the first principal component in the FDI motor units was significantly greater than the EDC motor units in the older adults (p = 0.04).

Discussion

Our data shows greater force variability in the older adults on the abduction, but not on the pinch task. Associations between motor unit parameters and force variability could help explain changes in dexterity with advancing age.

Force Steadiness: Maximal abduction force was not different between the young and older adults, in our study. Thus, the standard deviation of force is used as an estimate of force variability like previous research (Cole, 2006; Joshi & Keenan, 2016). Furthermore, force steadiness on the index finger abduction task was greater in young versus older adults. This result agrees with previous research (Marmon, Pascoe, Schwartz, & Enoka, 2011; Galganski, Fuglevand, & Enoka, 1993)

The pinch task demonstrates the challenge of holding a force with two digits, thus bringing to fore the role of coordination. Steady pinch force production requires producing well directed forces by all the digits involved (the thumb and the index finger). Studies have found increased misdirection of forces in older adults as compared to younger adults (Cole, 2006). The use of 2-digits requires muscles to co-contract and generate forces that are in opposite directions. Weakness in either of these muscles can lead to misdirected forces, thereby causing greater force variability in older adults, as seen in our data. These deficits are highlighted in a study examining pinch in stroke survivors by Seo et. al. (2010). They found that individuals with stroke had a 2.5 times greater misdirection of force as compared to healthy young adults, which was accompanied by lower activation of the EDC and FDI muscle and an overactive FDS muscle. Our data did not show any age-associated changes in pinch force variability.

Neural factors influencing motor control: Literature looking at changes in fine motor control with age has attributed the performance on a force steadiness task to changes in discharge rate and discharge rate variability (Tracy, Maluf, Stephenson, Hunter, & Enoka, 2005; Erim Z, 1999). Our data showed a similar pattern. On the abduction task, the discharge rate, as well as the first principal component of motor unit discharges which represents the neural drive to the muscle were greater in in FDI muscle of the young adults as compared to the older adults. Aging leads to a decrease in the number of motor neurons, which in turn causes a reorganization of the motor system. While the recruitment pattern stays the same the derecruitment of motor neurons is disrupted leading to changes in the discharge rate properties (Erim Z, 1999). Decreased discharge rate and increased discharge rate variability have been documented in several studies (Christou 2011; Enoka et al. 2003; Moritz et al. 2005; Taylor and Enoka 2004). Barry et al. (2007), reported average FDI discharge rates of 7.1 pps in older adults compared to 12.1 in the younger adults. These numbers are similar to our data where older adults had an average discharge rate of 9.7 pps and the younger adults had an average discharge rate of 13.1 pps. This data was combined across 5% and 15% MVC, in the high and low visual gain conditions.

Additionally, the correlation analysis showed a positive association between force variability and discharge rate variability, and a negative correlation between force variability and measures of neural drive as represented by the average discharge rate and eigen value first principal component. Both these findings align with previous findings (Erim Z, 1999; Tracy, Maluf, Stephenson, Hunter, & Enoka, 2005).

Another interesting finding from our data was the differential activation patterns of the EDC and FDI motor units. While the FDI is the prime mover for the index finger abduction task, data from older adults showed a higher discharge rate of EDC motor units as compared to the FDI motor units. Also, the eigen value for the EDC motor units was greater. Conversely, the discharge rate variability and the variability of the first principal component were higher for the FDI motor units. Furthermore, pinch data in older adults showed greater variability in the first principal component of the FDI motor units as compared to the EDC motor units. This difference between the motor units of the 2 muscles was not observed in the younger adults. Previous research has pointed to a decrease in coordination patterns in older adults. Specifically, a study by Olafsdottir et. al (2007) showed a decrease in adjustment in motor synergies in older adults. The differential activation of FDI and EDC motor units in our data likely point to a diminished coordination pattern present with age.

In addition to changes to motor neuron properties, changes in the common oscillatory drive to the motor neurons with age has also been suggested as a cause of change in motor function with age (De Luca & Erim, 1994; De Luca & Erim, 2002). The motor neurons receive inputs from several spinal and supraspinal sources. Some of these inputs are common to across the motor neuron pool and some are independent. The common oscillatory inputs to the motor neurons may help with coordination across multiple muscles. Common oscillatory inputs across groups of motor neurons can be examined by analyzing discharge rates of groups of motor units (Negro, Holobar, & Farina, 2009; Negro & Farina, 2011) or by running a coherence analysis to estimate the common spectral content in the signals (Keenan, Massey, Walters, & Collins, 2012; Semmler, Sale, Meyer, & Nordstrom, 2004; Baker, Kilner, Pinches, & Lemon, 1999). In our data the variance explained by the first principal component is of interest as it may explain the common oscillatory inputs to the motor neurons. The variance explained by the first principal component was significantly greater in young adults in the EDC and FDI motor units during abduction and in the EDC motor units during pinch. A higher value would indicate a more heterogenous motor neuron pool, while a smaller variance could point to a more homogeneous motor neuron pool. Previous research has attributed the decrease in manual dexterity to a greater common oscillatory drive to the motor neurons (Enoka et al. 2003; Erim et al. 1999; Keenan et al. 2007; Semmler, Kornatz, and Enoka 2003) in older adults. So, a lower variance explained by the first principal component in older adults likely points to the existence of a greater commonality in motor unit discharges of older adults as compared to younger adults. This common input makes force control challenging in fine motor tasks such as the ones used in this study. Tasks such as these require coactivation of agonist and antagonist muscles to achieve precise force control. Thus, future studies should examine independent and common motor neuron inputs across pairs of agonist-antagonist muscles for a movement.

Chapter 3: Age-associated changes in motor unit discharge rate properties during static pressing and hybrid force/ motion tasks.

Introduction

The number of older adults is projected to double by the year 2060 (Mather, 2015) . This increase in the number of older adults, paired with dexterous impairments leading to dependency, will ultimately result in increased healthcare costs (Carment, et al., 2018). Thus, it is important to examine the mechanisms leading to poor dexterity and explore preventive or rehabilitative measures to alleviate the problem.

Research looking at mechanisms that lead to impaired manual dexterity typically examine force control on isometric tasks such as abduction and pinch (Enoka et al. 2003; Moritz et al. 2005; Taylor, Christou, and Enoka 2003, Feeney, Mani, and Enoka 2018). In addition to studying force control during isometric tasks, it is critical to examine motor control on tasks that mimic ADLs. Hybrid force/motion tasks require simultaneous control of forces and movements. For example, tasks such as peeling a fruit, cleaning surfaces, writing as well as using a smartphone all require pressing and moving while manipulating objects and surfaces and are all hybrid force/ motion tasks. These tasks are challenging for motor control as they require both well-directed forces and movements (Joshi and Keenan 2016; Keenan et al. 2009). Experimental paradigms involving hybrid tasks are novel and, since they require concurrent control of more than one task constraint, may help reveal additional deficits in motor control that may not be possible with isometric tasks. Data from our previous studies compared force variability between young and older adults on a static pressing and a hybrid force/motion tasks (Joshi and Keenan

2016; Joshi 2017). Older adults had 32% greater variability while performing a hybrid force/motion task than young adults (Joshi 2017). This increased force variability on a hybrid task may highlight some of the dexterous impairments brought on by advancing age. Pilot data from our lab shows an association between force variability on a hybrid task with that on pinch and grip tasks, the grooved pegboard test, and discharge rate variability of FDI during index finger abduction in older adults ($r^2 = 0.632$) (Joshi 2018). These associations provide a preliminary evidence of a hybrid task force control as being a useful tool to assess dexterity. However, further research is needed to assess whether changes in tactile feedback with age (Johansson 1996; Cole et al. 1999) or neuromuscular changes are responsible for impaired motor performance on the hybrid task.

Visual feedback provided during a force steadiness task plays an important role in task performance. Visual gain is the term used to quantify the amount visual information provided during a task. It can be changed by manipulating the ordinate axis or adjusting the visual angle. Previous research has demonstrated the increase in force variability on isometric steadiness tasks in older adults dependent on visual feedback (Sosnoff and Newell 2006; Christou 2011; Kennedy and Christou 2011; Baweja et al. 2012; Keenan et al. 2017). This increase in force variability with an increase in visual gain has been attributed to limitations in visuomotor processing in older adults (Keenan 2017, Tracy 2007). However, specific neuromuscular mechanisms resulting in poorer performance are still unclear.

Frictional properties of the surface that fingers contact have an effect on force control. Previous research comparing dexterous control of movement between young and older adults found that older adults had 2.54 times greater force variability than young adults while performing a static force matching task on a low friction surface (Keenan and Massey 2012).

Additionally, force control on a high- and low- friction surface across static and hybrid task in young (Joshi and Keenan 2016) and older adults (Joshi 2017) was examined in our lab. This task was performed on an iPad surface with and without a screen protector acting as low- and high-friction surfaces, respectively. Pressing and moving on a high friction surface showed greater force variability as compared to the low friction surface (Joshi and Keenan 2016). The hybrid task used in previous studies involved movement about the shoulder and elbow in addition to the index finger. EMG and motor unit data have not been recorded during a hybrid task previously, due to the movements involved in the task which can introduce unwanted artifact in the EMG recordings. The present study will use a more constrained scratch task on a Teflon-Teflon interface and limit the degrees of freedom as done by Keenan et. al. (2009). This task will allow us to examine motor unit activity with high density EMG and identify motor unit changes with age across force and visual gain conditions.

Methods

Ethics statement: The experiments were approved by the Institutional Review Board at the University of Wisconsin-Milwaukee. The local ethics committee approved consent for subjects ranging in age from 18–40 years and 65-90 years. All participants gave their written formal consent before participating in the study.

Participants: 26 older adults (age: 72.4±4.98 years, range: 66-86 years, 14 F, 12 M) and 28 young adults (age: 24.24±5.58 years, range: 19 – 38 years, 16F, 12M) participated in the study. All participants were right-handed as confirmed by the Edinburgh Handedness test (Oldfield 1971), with no reported neuromuscular disorders or hand pathologies volunteered for the study.

Experimental setup: Subjects sat in an adjustable chair with the right elbow resting on a vacuum foam pad (VersaForm pillow, Tumble Forms) to minimize movement. Subjects grasped a horizontal dowel with all fingers while the thumb stayed in an extended position. The index finger, which was free to extend and flex along a low-friction Teflon® surface. The Teflon® surface was attached to a rectangular pedestal mounted on a 6-axis force-torque ATI Gamma sensor (ATI technologies, Apex, NC). Height of the dowel with respect to the surface was adjusted such that the index finger was in a neutral ad-abduction posture and could flex and extend completely across the pedestal. Subjects wore a custom-molded thermoplastic on the fingertip, with a thin Teflon® strip secured along the centerline of the index fingertip. This custom-molded cover with the attached Teflon® strip helped remove the discontinuity at the fingernail, and provided minimal resistance to sliding at any speed (Teflon-Teflon friction coefficient ≈ 0.04,Keenan et al. 2009). Figure 1 shows the experimental set-up.

Range of motion for each participant was determined by asking them to perform maximal extension and flexion on the Teflon® surface with their right index finger. Points corresponding to the maximal flexion and extension were marked. Using these as the reference, the center location was marked at 50%, and 25% (extension) and 75% (flexion) of the total range of motion were also marked with tape visible to the participants. Methods will be similar to previous research (Keenan et al. 2009).

Figure 3.1: Experimental set-up for the static pressing and hybrid force/ motion tasks.

<u>*Experimental Paradigm:*</u>

Static Contractions: Subjects pressed down isometrically on the Teflon® with their index finger at the 25% (extension) position. Three trials of maximal voluntary contraction (MVC) by slowly ramping up the force to press as hard as they can for 3 - 5s each. Verbal encouragement was provided to ensure that subjects put in maximal effort. If peak force in two subsequent trials differed by more than 5%, additional trials were collected. The peak force in the trial with the highest force was recorded as the MVC and used to calculate submaximal forces.

The static steadiness task was performed by pressing and holding a steady force at 5%, and 15% MVC force levels for 40s with visual feedback on a screen 1 m away. Three trials were recorded at each force level. At least 1 minute of rest was provided between contractions. All trials were conducted at a high and low visual gain condition. Visual gain was altered by changing the ordinate axis on the feedback.

Hybrid task: The hybrid force/motion task was performed by moving between the 25% and 75% points at a cadence of 50bpm, while holding a steady force. The force target for the hybrid task was set at 5 and 15% of MVC recorded during static pressing at the center of movement. Visual feedback of force was provided.

Forces were sampled at 1000 Hz using the ATI A/D converter. The abduction forces were sampled using the ATI A/D converter and pinch forces were sampled using the A/D converter by Coulbourn Instruments (Holliston, MA). EMG was recorded for static and hybrid steadiness tasks from the FDI and EDC muscles.

Visual feedback was provided on a 24-in. LCD monitor located 1 m away. The target force for all conditions was displayed as a horizontal black line located in the center of the screen, and the force produced by the subject during the 40 s trial was shown as a horizontal solid blue line. Subjects were instructed to match their actual force with the target force as closely as possible, with the blue line moving up and down on the monitor with increasing and decreasing force, respectively. The low and high visual feedback gain conditions during the static task were associated with large and small range of forces displayed to the participant, respectively. For example, if participants are performing a steadiness task at a 5N force, with a low visual gain, the target line is drawn at the center of the monitor and the bottom and top of the screen correspond to 0 and 10 N, respectively. In contrast, for the high visual gain condition, the bottom and top of the screen corresponded to 4.9 and 5.1 N, respectively, with the target line still drawn at the center of the monitor. The visual gain in the high gain condition will be 10 times that in the low gain condition as suggested previously (Schmied et al. 2000).

EMG: We recorded multi-channel surface EMGs with a 5 X 13 electrode grid with 4 mm interelectrode spacing (OTBioelettronica, Torino, IT) positioned on the skin overlying first dorsal interosseus and a 5 X 13 grid with 8 mm interelectrode distance overlying the wrist extensor muscles during the maximal and submaximal tasks. The 128 channels of EMG were recorded (2048 samples/s; 10 - 500 Hz bandpass filter) using the OT Biolab software from OTBioelettronica (Torino, IT). Research studies identifying associations between motor unit properties and force steadiness (Negro et al. 2009; Feeney et al. 2018) as well as results from our pilot data (Joshi, 2018) confirms the use of these electrode arrays and data processing parameters.

Data Processing: All data were analyzed using custom written Matlab code. Our primary measure for the static and hybrid tasks was force steadiness. This was measured as the standard deviation and as the coefficient of variation for force (standard deviation of force / mean force × 100) averaged across the three trials.

The surface EMG was decomposed into trains of motor unit action potentials with the convolution kernel compensation (CKC) technique (Holobar et al. 2010) and manually verified. Motor unit discharge rates and discharge rate variability were computed. The resulting smoothed and detrended discharge rates from both muscles were arranged in a matrix (time samples × motor unit) and their principal components was computed using the eigenvalue decomposition of the covariance matrix. The maximum eigenvalue of the covariance matrix, which is the first principal component, was used to quantify the strength of the common low-frequency oscillations in motor unit activity (Negro, Holobar, & Farina, 2009; Negro & Farina, 2011). Additionally, coefficient of variance of the first principal component and variance explained by the first principal component were computed to further assess common drive (Negro, Holobar, & Farina, 2009; Negro & Farina, 2011). Associations of discharge rate, discharge rate variability and measures of low-frequency common oscillations with force steadiness measures were examined.

Statistical analysis: Age-associated differences in the MVC were analyzed using a t-test. A multivariate analysis of variance (MANOVA) was conducted in SPSS. Performance differences were examined across 2 age groups (young and old), 2 force levels (5% MVC and 15% MVC). The association between the low-frequency modulation of motor unit activity, mean discharge rate and discharge rate variability to force steadiness were quantified by computing the Pearson correlation coefficient in SPSS.

Data are reported as mean ± SD in the text and mean ± SE in the figures unless otherwise noted. Normality of the transformed data were confirmed using Shapiro Wilk's test and visual inspection of Q-Q plots. Discharge rate variability, variability of the first principal component, variance explained by the first principal component and force variability did not conform to a normal distribution. Data on the variability of the first principal component were transformed using an inverse transformation for analysis. The other variables were transformed using a logarithmic transformation to conform to a normal distribution (Osborne, 2019).

Results

Participants: Data from 15 older (72.39 ± 5.18 years, range: 67 – 86 years, 8F, 9M) and 18 younger (24.105 ± 5.48 years; range: 19 – 35 years, 12F, 5M) adults were used for analysis. The data discarded had a low EMG signal to noise ratio when visually inspected. Including these in the analysis would contribute to incorrect motor unit identification. Furthermore, due to the dynamic nature of the task, motor unit data was obtained from 15 EDC and 9 FDI muscles for the static task, and 15 EDC and 6 FDI muscles for the hybrid task.

The data were tested for normality. Variables that did not fit the normality criteria were transformed before analyzing data using MANOVA. Motor unit discharge rate variability, variability of the first common component, and force variability parameters like root mean square error, coefficient of variation of force and standard deviation of force were transformed using a logarithmic transform. The variability of the first principal component was transformed using the inverse transform.

MVC during static pressing was not significantly different between older adults (25.1 ± 10.02) and younger (22.7 ± 9.322.04) adults (t (31) = 1.281, p = 0.243).

An age X force level X task X muscle MANOVA was performed. Force variability was significantly greater on the hybrid as compared to the static task across both age groups (F (1,131) = 403.771, p <0.001, Figure 3.2). No age-associated differences were seen.

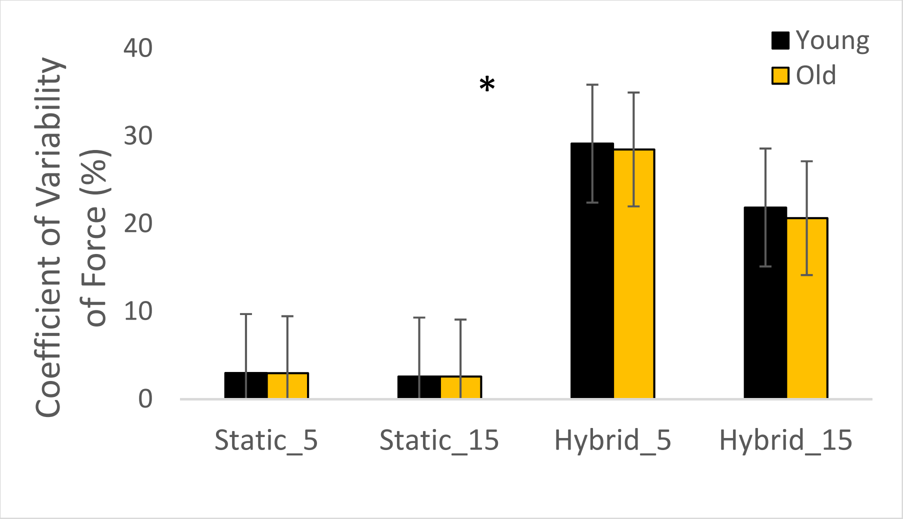


Figure 3.2: Force variability was greater on the hybrid task as compared to the static task in both young and older adults.

A significant age X task interaction was observed for the discharge rate (F (1,131) = 4.178; p = 0.043) and the first principal component (F (1,131) = 5.676; p = 0.019). The discharge rate and the first principal component combined across both the muscles were significantly greater in young versus older adults on the hybrid task. Furthermore, there was a main effect of muscle activity and force level for the discharge rate (F (1,131) = 8.662; p = 0.004, F (1,131) = 4.067; p = 0.047) and the first principal component (F (1,131) = 8.053; p = 0.005, F (1,131) = 4.197; p = 0.043; Figures 3.3 and 3.4). The discharge rate and the first principal component of the EDC motor unit discharge rates was significantly greater than that of the FDI in older adults. A group X muscle interaction and a main effect for task was observed for discharge rate variability (F (1,131) = 5.292; p = 0.023, F (1,131) = 52.393; p < 0.001, figure 3.5). The discharge rate variability was significantly greater in the EDC muscle of older adults as compared to younger adults. In younger adults, FDI motor units had greater discharge rate variability than the EDC motor units during the static task (p = 0.044).

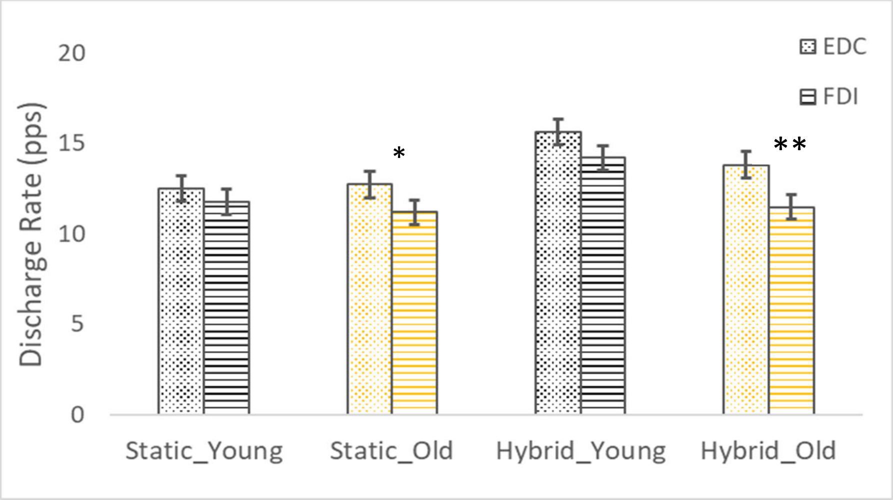


Fig 3.3: Discharge rate of motor units of the EDC and FDI muscles in young and older adults. The discharge rate was significantly different between the 2 muscles in older adults, for static (*, p = 0.009) and hybrid tasks (**, p = 0.012).

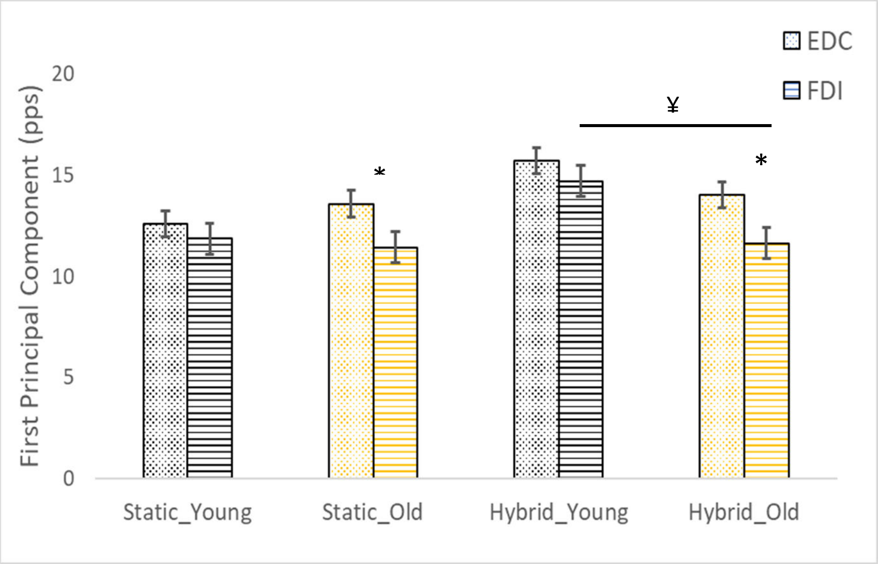


Fig 3.4: The first principal component of the motor unit discharge rates (PC1) of the EDC and FDI muscles in young and older adults. The PC1 was significantly different between the 2 muscles in older adults, for static (*, p = 0.001) and hybrid tasks (**, p = 0.014). PC1 of FDI motor units was significantly greater in young versus older adults (¥, p = 0.047).

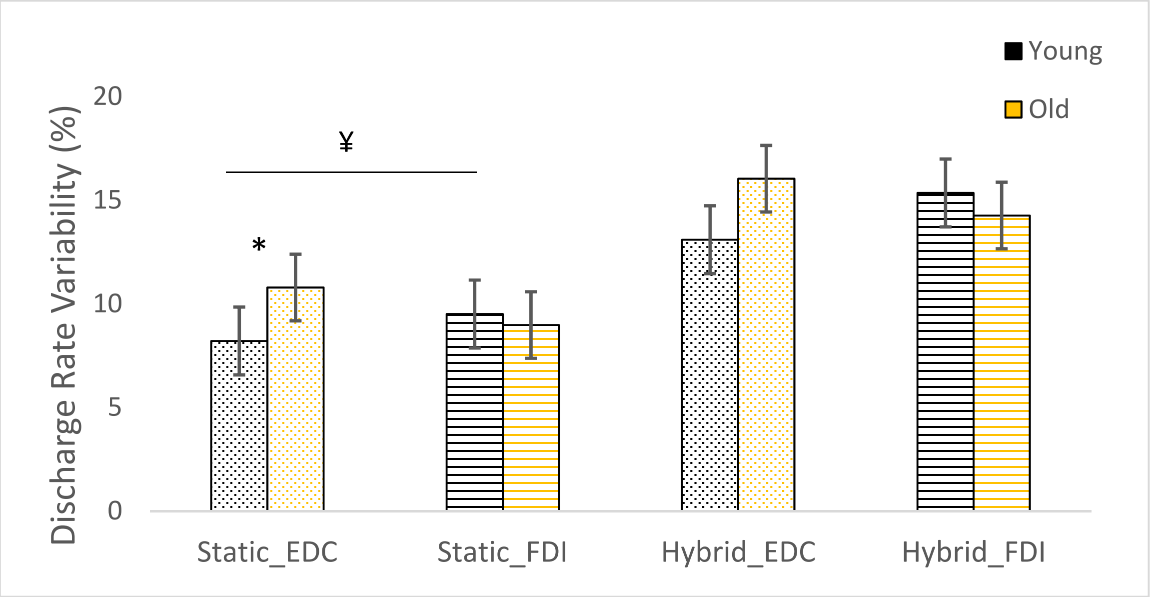


Fig 3.5: Age associated differences in discharge rate variability across EDC and FDI muscles. The discharge rate variability was significantly greater in the EDC of older adults as compared to younger adults (*, $p = 0.014$). In younger adults, FDI motor units had greater discharge rate variability than the EDC motor units during the static task (¥, $p = 0.044$).

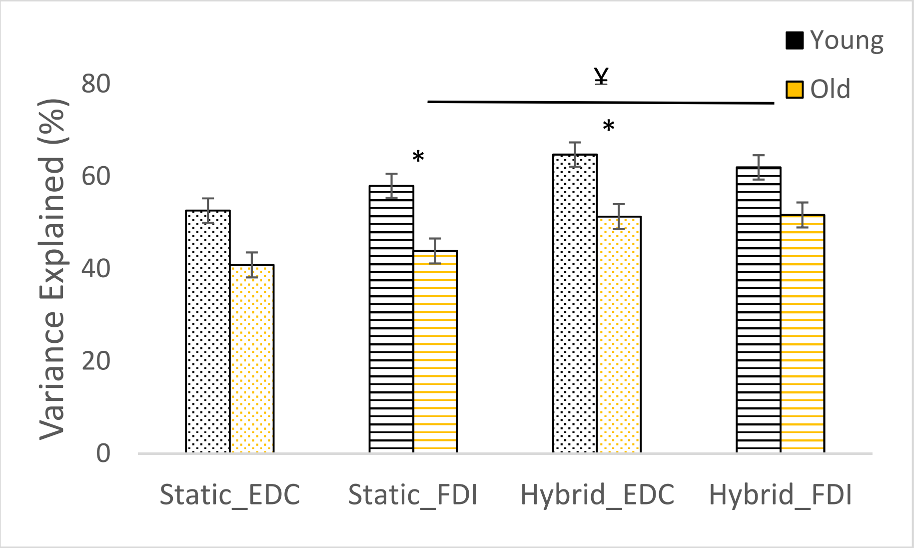


Fig 3.6: Age associated differences in variance explained by the first principal component across EDC and FDI muscles. *, $p < 0.001$; ¥, $p = 0.001$

Variance explained by the first principal component had a main effect across age groups (F (1,131) = 21.415 p < 0.001) and tasks (F (1,131) = 10.568 p = 0.002, Figure 3.6). The variance explained was significantly greater in young versus older adults in the EDC and the FDI during the static pressing task (p <0.001). Variance explained by the EDC and FDI motor units was greater in young versus older adults during the static task (p <0.001). In older adults, variance explained by the EDC motor units was significantly greater during the hybrid task as compared to the static task (p = 0.001).

Significant associations were observed between force steadiness measures and motor unit parameters on the hybrid task. There was a significant positive correlation between force variability and discharge rate variability of the FDI motor units (r = 0.611, p = 0.035, Figure 3.7).

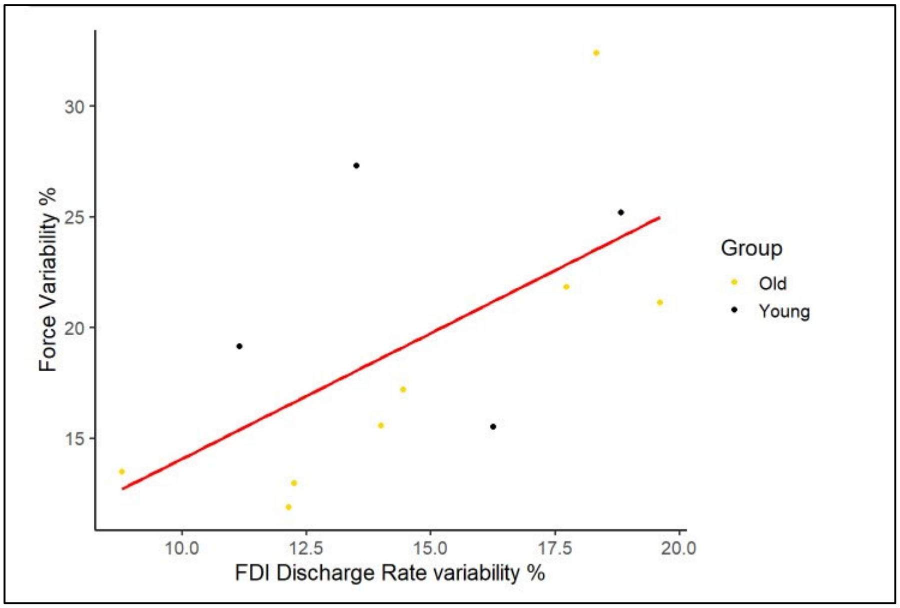


Fig 3.7: Positive correlation between force variability hybrid task and discharge rate variability of FDI motor units (r = 0.611, p = 0.035).

Discussion: The results from this study did not show a significant age-associated effect on force steadiness across the static and hybrid tasks. However, the task influenced force steadiness. Changes in the motor unit properties across age and tasks were also observed.

Force steadiness: Our data did not show any age-associated changes in force steadiness. The static task required pressing down while holding a steady force, which was easy for both the age groups, even at a low force level and a high visual gain condition. The hybrid task was performed at 5% and 15% MVC, at a low gain condition. This task was challenging for participants across both groups as reflected in our data. Though previous data (Joshi 2017) showed a higher variability on the hybrid task in older adults, the task was done with the index finger a touch screen surface. The change in cutaneous properties with age could have likely affected the results. Furthermore, interaction of the skin with the touch screen surface leads to a higher coefficient of friction, than is present in this study. In the present study, participants had a thermoplastic cover at the end of their finger, and the movement involved interaction on a Teflon – Teflon interface. This created a very low-friction interface that challenges motor control (Keenan & Massey, 2012; Keenan, Santos, Venkadesan, & Valero-Cuevas, 2009) and minimizes the influence of cutaneous feedback. The complexity of the movement and the low-friction nature of the interface together made the task challenging and may have eliminated any age-related effects. The challenge posed by the complex nature of the hybrid task was evident in the high variability of the force while performing the task in both young and older adults. The hybrid task requires simultaneous control of force and motion. This task mimics everyday activities and has been studied in the context of robotic arms. The challenges of hybrid force/ motion tasks in this context have been reported (Raibert, Playter, & Krummel, 1998; Chhatbar & Francis, 2013; Delph, et al., 2013; Jara, Pomares, Candelas, & Torres, 2014), where two different control systems simultaneously calculate both the required joint torques to produce the needed motion and maintain desired contact forces. Furthermore, the control of force and motion in these hybrid tasks is reported to have independent neural origin (Venkadesan & FJ, 2008; Chib, Krutky, Lynch, & Mussa-Ivaldi, 2009)and the fluctuations associated with the control of motion during a hand tracking task are the primary source of force variability during hybrid tasks (Chib, Krutky, Lynch, & Mussa-Ivaldi, 2009). This may explain the increased variability from the static to the hybrid task across all participants.

Neural factors influencing motor control: The discharge rate and the first principal component of the EDC motor unit discharge rates was significantly greater than that of the FDI in older adults. Both these parameters provide information about the activation of the neural drive to the muscles during the task. There was differential involvement of the 2 muscles in older adults but not the younger adults. This result concurs with the changes in coordination pattern with age (Martin JA, 2015; Carmeli E, 2011). Furthermore, a study looking at multi-finger tapping paradigm found diminished synergies in older as compared to younger adults (Olafsdottir H, 2007). Discharge rate variability was greater in the EDC motor units in older adults as compared to the younger adults. Though we did not see any age-related differences in force variability in these tasks, pervious research suggests increased discharge rate variability as a mechanism that contributes to force variability during isometric abduction and pinch tasks (Marmon et al. 2011; Moritz et al. 2005; Enoka et al. 2003; Erim et al. 1999; Keenan et al. 2007; Semmler, Kornatz, and Enoka 2003). Our data further adds to this result by seeing a similar pattern on a static index finger pressing task. Furthermore, in younger adults the FDI motor units had greater discharge rate variability than the EDC motor units. This could be attributed to the FDI being a prime mover for the pressing task, thus modulating the FDI motor units allows for precise force control.

Additionally, there was a significant association between force variability and discharge rate variability of motor units of the FDI during a hybrid task. This finding adds to the previous research that found associations between discharge rate variability and force steadiness on isometric tasks (Erim Z, 1999; Enoka RM, 2003).

Variance explained by the first principal component is greater in young than older adults, specifically on the static task. Since the first principal component represents the motor unit discharges of the motor neuron pool to the muscle, variance explained could probably identify the homogeneity of the motor neuron pool. A higher value of variance explained would indicate a more heterogenous motor neuron pool, while a smaller variance could point to a more homogeneous motor neuron pool.

The motor neurons receive inputs from the sensory systems, descending drive as well as from spinal interneurons. The alpha motor neuron transmits all this neural information to the muscle (Sherrington, 1906). Neural drive to the muscle comprises of common and independent inputs to motor neurons. The role of common inputs or the common oscillatory drive in steady force generation has been well documented (Erim Z, 1999; Negro & Farina, 2011). Also, an increased fluctuations common oscillatory drive is associated with diminished force steadiness (Enoka RM, 2003; Erim Z, 1999; Semmler, Sale, Meyer, & Nordstrom, 2004; Feeney, Mani, & Enoka, 2018). Few recent studies have alluded to the role of flexible or multiple neural drives (Tanzarella S, 2020; Marshall NJ, 2022) or functional clusters of motor neurons innervating a portion of the muscle (Hug, 2023). Our finding of a high variance explained by the first principal component in the young versus older adults could likely points to the same with age-associated differences in dexterous control.

Limitations of the study: This is one of the first studies to look at motor unit activity during a hybrid force/ motion task. Hybrid tasks pose additional constraints on movement and drive the neuromuscular system to the limit of performance which then can highlight deficits in movement with age or the neuromuscular mechanisms at play (Valero-Cuevas, 2005). The hybrid scratch task in this study was a challenging task for both young and older adults. Furthermore, EMG data was collected using a 64-channel high-density EMG array. Given the small size of the FDI muscle, the array was often bigger than the muscle, thus useable EMG was obtained from only a few channels. This, coupled with the dynamic nature of the task added to the EMG noise, thereby affecting the motor unit yield especially in the FDI muscle. Additionally, with the muscle atrophy that comes with aging, it is a challenge to palpate small hand muscles like the FDI, and get a good EMG signal. All these factors lead to the low yield of motor units, thus making interpretation of some results challenging. Future studies may use an isokinetic force matching task involving larger muscles such as the elbow or wrist joint muscles to study motor unit behavior during a hybrid force/ motion task.

Chapter 4: Dexterous performance is associated with discharge rate and discharge rate variability of motor units.

Introduction

As the baby boomer population is aging, the number of older adults aged 65 and over in the US is estimated to increase from 46.2 million in 2014 to 83.4 million in 2040 (Mather 2015). This increase in the number of older adults, paired with dexterous impairments leading to dependency (David Seidel, 2009; Williams ME, 1982) will ultimately result in increased healthcare costs. Thus, it is important to examine the mechanisms associated with poor dexterity. This will help explore preventive or rehabilitative measures to alleviate the problem.

Experimental tests examining force steadiness place several constraints on movements such as specific forces and movement trajectories. These tests require calibrated force transducers, signal processing equipment and software for analysis, all of which are costly and require specific skills and expertise to be conducted. In order to extend testing of manual dexterity beyond laboratories, tests need to be portable, cost-effective, and easy to administer. To that end, several tests of manual dexterity have been developed and employed in clinics to test dexterity.

Tests of manual dexterity such as the grooved pegboard, 9-Hole Peg Test (9-HPT), Purdue pegboard, box and block, Archimedes spiral tracing and Minnesota manual dexterity tests are reliable and sensitive in capturing dexterous impairments with age (Desrosiers et al. 1994; Desrosiers et al. 1995; Surrey et al. 2003; Marmon et al. 2011; Martin et al. 2015; Heintz and Keenan 2018). Furthermore, the National Institutes of Health (NIH) included the 9-Hole Peg Test (9-HPT) as a measure of manual dexterity in the motor battery of tests of the NIH toolbox (Wang et al. 2015). The grooved pegboard test is similar to the 9-HPT incorporated in the NIH toolbox; however, it provides a greater challenge to older adults above the age of 80 (Wang et al.

2011), and thus may be a better tool to decipher differences with age in healthy individuals. Previous research has found associations between force variability on an index finger abduction task and the grooved pegboard and the Purdue pegboard test (Kornatz et al. 2005; Marmon et al. 2011). One study reported moderate correlation ($r = 0.51$) between performance on the Purdue pegboard test and motor unit discharge rate variability (Kornatz et al. 2005). A recent study also found associations between low frequency common oscillations to the wrist extensor and performance on the grooved pegboard test in older but not young adults ($r^2 = 0.47$; Feeney et al. 2018).

The box and block test measures gross manual dexterity in healthy and impaired individuals. This test has a strong correlation with the Action Research Arm test which includes a battery of tests to assess upper extremity function (Desrosiers et al. 1994). However, associations of box and block performance to force steadiness tasks or motor unit parameters has not been studied. Both the grooved pegboard and box and block test require significant movement of the upper extremity. Recording EMG during these tasks is a challenge due to the presence of motion artifact. To identify associations between these measures and motor unit activity, we correlated the dexterity measures to motor unit activity computed index finger abduction, pinch, static index finger press and a hybrid index finger scratching task (explained in the previous chapters).

Coin rotation requires coordinated movements of the digits and is a valid measure of manual dexterity in Multiple Sclerosis and unilateral lesions (Mendoza et al. 1995; Mendoza et al. 2009; Heldner et al. 2014), but not widely used to test impairments in other populations. We will assess the use of the coin rotation task to identify age-related dexterous impairments.

The purpose of this study is to examine age-related changes in manual dexterity using the grooved pegboard, box and block and coin rotation tests. We studied associations between manual dexterity and force variability and motor unit activity measures. We hypothesize that older adults will have inferior performance on tests of manual dexterity than young adults. Force variability, and motor unit activity during isometric and hybrid tasks is associated with the measures of manual dexterity.

Methods

Ethics statement: The experiments were approved by the Institutional Review Board at the University of Wisconsin-Milwaukee. The local ethics committee approved consent for subjects ranging in age from 18–40 years and 65-90 years. All participants gave their written formal consent before participating in the study.

Participants: 26 older adults (age: 72.4±4.98 years, range: 66-86 years, 14 F, 12 M) and 28 young adults (age: 24.24±5.58 years, range: 19 – 38 years, 16F, 12M) participated in the study. All participants were right-handed as confirmed by the Edinburgh Handedness test (Oldfield 1971), with no reported neuromuscular disorders or hand pathologies volunteered for the study.

Experimental setup: Subjects were asked to perform the following functional tests of manual dexterity at self-selected speeds. For each of the tasks, participants were allowed a practice trial to get used to the task.

Grooved Pegboard test (Lafayette Instruments, Lafayette, IN): apparatus consists of 25 holes arranged in five rows and five columns. Subjects sat at a table facing the apparatus. They were required to put the metal pegs into the holes as quickly as they can. In order to place the peg into the hole, it had to be oriented correctly so that the groove on the peg matches with the groove in the hole. Subjects were instructed to fill the entire board, one row at a time from top to bottom.

Subjects completed two trials with the right hand. Time taken to finish placing all the pegs in the holes was recorded.

Box and Block test: consists of a box with a partition in the middle. Subjects sat at a table facing the box. Wooden blocks were placed on the right side of the partition. Subjects were required to pick up one block at a time with their right hand and transfer it over to the left side of the partition. They were instructed to cross the partition and not toss the blocks over the partition. The number of blocks transferred in 60 s was counted to score the subjects. Subjects completed two trials of this test.

Coin rotation test: Subjects were required to rotate a U.S. quarter through consecutive 180° turns, using the thumb, index, and middle fingers, as rapidly as possible for 30 seconds. Each subject completed three trials of this task and number of rotations completed in 30 seconds was recorded as a measure of performance. Trials where the coin is dropped were discarded.

Force variability was computed on force matching tasks: index finger abduction, precision pinch, static pressing and a hybrid scratching.

EMG and Motor Unit Decomposition: We recorded multi-channel surface EMGs with a 5 X 13 electrode grid with 4 mm interelectrode spacing (OTBioelettronica, Torino, IT) positioned on the skin overlying first dorsal interosseus (FDI), and a 5 X 13 grid with 8 mm interelectrode distance overlying the wrist extensor muscle (Extensor Digitorum Communis, EDC) during the maximal and submaximal index finger abduction, precision pinch, static pressing with the index finger and a hybrid force/ motion scratching task with the index finger. The 128 channels of EMG were recorded (2048 samples/s; 10 - 500 Hz bandpass filter) using the OT Biolab software from OTBioelettronica (Torino, IT). The surface EMG was decomposed into trains of motor unit action potentials with the convolution kernel compensation (CKC) technique (Holobar et al.

2010) and manually verified by an experienced operator. Motor unit discharge rates and discharge rate variability were computed. The resulting smoothed and detrended discharge rates from both muscles were arranged in a matrix (time samples × motor unit) and their principal components was computed using the eigenvalue decomposition of the covariance matrix. The maximum eigenvalue of the covariance matrix, which is the first principal component, was used to quantify the strength of the common low-frequency oscillations in motor unit activity. Additionally, coefficient of variance of the first principal component and variance explained by the first principal component were computed to further assess common drive.

Data Processing for tests of dexterity: For each test described above, measures of performance across three trials of each test were averaged and used for analysis. The average time for the three grooved pegboard and coin rotation trials, and average number of blocks transferred across three trials of the box and block test were computed.

Statistical Analysis: Age-related differences in performance across all tests of dexterity was assessed using an independent t test in SPSS. Associations between manual dexterity and motor unit properties was examined by running correlation analysis between the performance measures and motor unit activity such as mean discharge rate, discharge rate variability and low-frequency common oscillatory drive to motor unit discharge rates obtained during all tasks of steadiness.

Results

Age associated changes were seen in the grooved pegboard test, but not other measures of dexterity ($p < 0.001$; Figure 4.1).

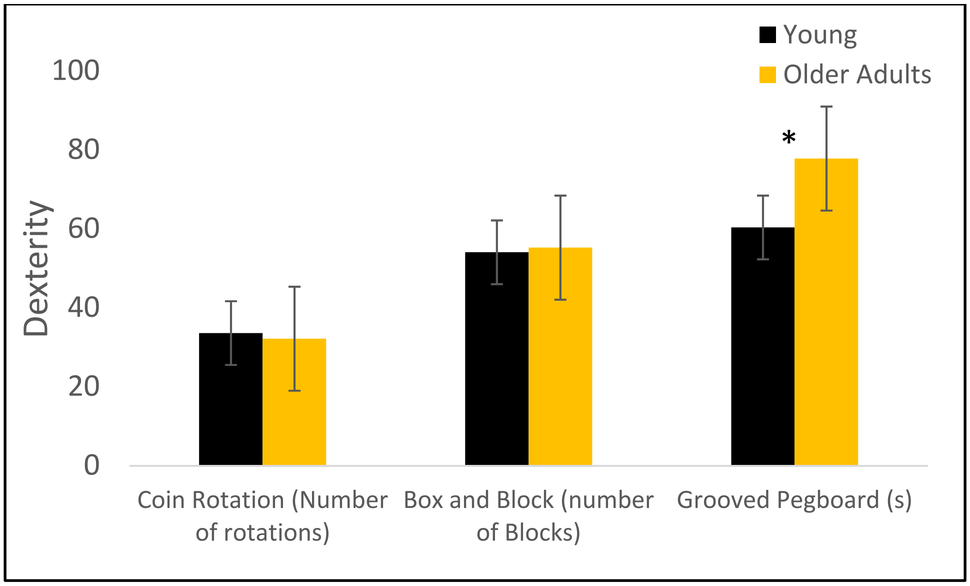


Figure 4.1: Dexterity measures in young and older adults. Older adults took significantly greater time to complete the grooved pegboard test as compared to the younger adults (*, p <0.001)

When data was combined across age groups, a significant association between performance on the coin rotation test and the grooved pegboard test (r = -0.434, p = 0.007, Figure 4.2) was observed. A quick completion time on the grooved pegboard test was associated with more coin rotations.

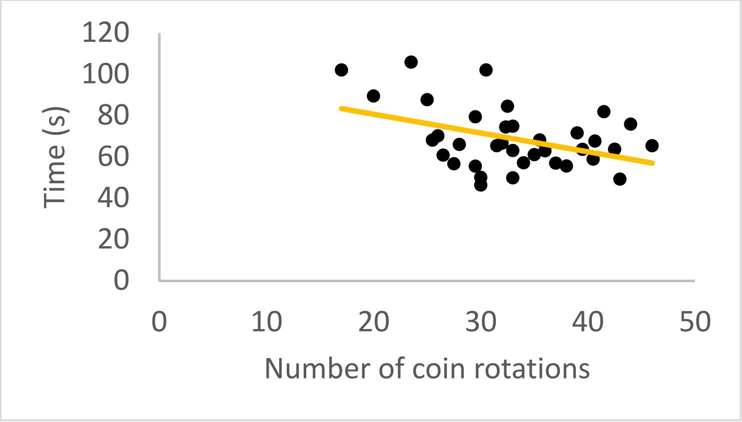


Figure 4.2: Association between performance on the grooved pegboard test and the coin rotation task across young and older adults (r = -0.434, p = 0.007).

There was a significant association between force variability on the pinch ($r = -0.6$; $p < 0.001$) and the hybrid scratching tasks ($r = -0.352$; $r = 0.003$) and the performance on the box and block test. Higher force variability was associated with fewer blocks transferred in the box and block test. Figure 4.3 shows association between force variability on the pinch task and the box and block test by age group.

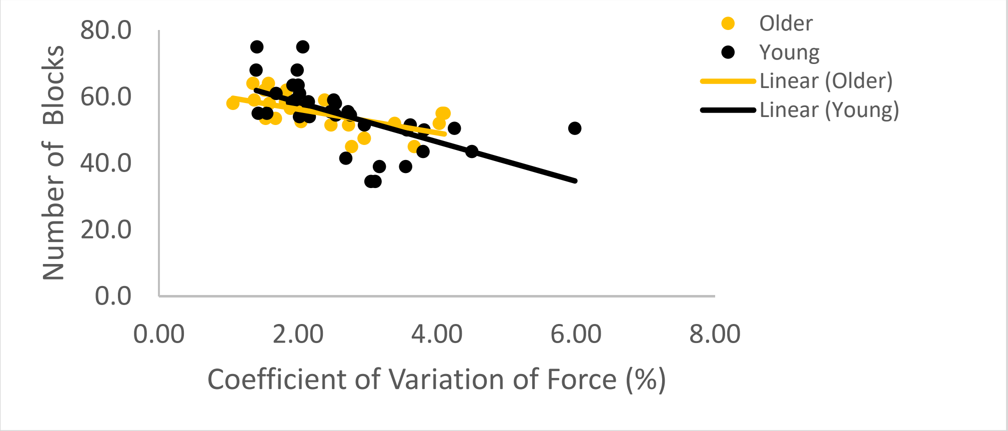


Figure 4.3: Significant association between force variability on the pinch task and box and block task score for young ($r = -0.601$; $p < 0.001$) and older adults ($r = -0.606$; $p < 0.001$)

In young adults, greater force variability on the index finger abduction task was associated with longer times to complete the grooved pegboard test ($r = 0.5$; $p = 0.049$). Also, fewer blocks transferred in 60 seconds was associated with higher force variability on the hybrid task ($r = -0.515$; $p = 0.029$).

There were also significant associations between the measures of dexterity and the motor unit parameters. These associations are highlighted in Table 1.

Task/ Parameters	**Coin Rotation**		**Box and Block Test**		**Grooved Pegboard Test**	
	Young	**Old**	**Young**	**Old**	**Young**	**Old**
Abduction						
EDC Discharge Rate Variability	**-0.337** (0.029)	0.158 (0.259)	-0.067 (0.713)	**-0.295** (0.032)	**0.492** (0.001)	-0.056 (0.716)
EDC Discharge Rate	0.031 (0.846)	0.13 (0.348)	-0.051 (0.778)	**0.42** (0.001)	0.113 (0.475)	-0.054 (0.724)
Variability of the first principal component of the FDI	-0.117 (0.531)	-0.225 (0.201)	-0.165 (0.087)	**-0.406** (0.017)	0.198 (0.892)	0.376 (0.064)
Pinch						
Variability of the first principal component of the EDC	-0.346 (0.114)	0.097 (0.683)	**-0.447** **(0.037)**	0.086 (0.719)	0.263 (0.238)	0.123 (0.662)
Static						
EDC Discharge Rate Variability	-0.266 (0.302)	-0.101 (0.710)	0.387 (0.125)	**-0.714** (0.002)	0.46 (0.063)	-0.069 (0.799)
EDC Discharge Rate	0.421 (0.092)	0.187 (0.488)	0.47 (0.057)	**0.765** (0.001)	-0.064 (0.807)	0.101 (0.709)
Variability of the first principal component of the EDC	-0.207 (0.425)	0.294 (0.308)	0.508 (0.037)	-0.384 (0.176)	**0.5** (0.042)	-0.362 (0.203)
FDI Discharge Rate Variability	-0.139 (0.651)	-0.419 (0.154)	-0.127 (0.633)	**-0.587** (0.035)	0.153 (0.617)	0.408 (0.167)
First principal component of FDI	-0.291 (0.335)	-0.324 (0.258)	-0.069 (0.823)	-0.543 (0.045)	-0.07 (0.819)	0.166 (0.571)

Table 4.1: Associations between the dexterity measure and motor unit parameters in young and older adults. Significant associations are in bold.

Young adults had associations between a few motor unit parameters and performance on the coin rotation task and grooved pegboard test. Performance on the box and block test in older adults was significantly correlated with several of the motor unit parameters, across the abduction, pinch, and static scratching force steadiness tasks (Table 3.1). High values discharge rate and first principal component of motor units were associated with greater rotations on the coin rotation task, more blocks transferred in the box and block test and fast times for completing the grooved pegboard test. Higher variability in the discharge rates, or the first principle component were associated with inferior performance on dexterous tasks.

Discussion

Our results highlighted differences with age in dexterous performance were significant in the grooved pegboard test. Furthermore, dexterous performance was associated with force variability as well as motor unit

<u>Change in dexterous performance with age:</u> There were no age-associated differences in performance on the coin rotation and the box and block test. The grooved pegboard test was specifically used in the study to highlight the differences in the healthy population. Our study comprised of healthy young and older adults with no neurological impairments. The older adults in the study were active and highly functional individuals. Thus, the coin rotation and the box and block performances were very similar between the older and the younger adults. Furthermore, when looking at the normative data on the box and block test, the older adult data adhered to the normative standards (Mathiowetz, Volland, Kashman, & Weber, 1985). The scores in younger adults were lower than the normative values, making them very similar in performance to the older adults. This finding concurs with the study by Fain and Weatherford (Elizabeth Fain, 2016), that found lower normative values in grip strength in young adults between the ages of 25 -29. Few new studies have pointed to the link between increased use of smartphones and touchscreen to diminished strength and dexterity in young healthy adults (Jasraj Kaur Bhamra, 2021)

The grooved pegboard test was the only dexterous measure that showed a change in performance with age. Older adults took a significantly greater time than younger adults to complete the grooved pegboard test. The grooved pegboard test assesses fine motor control and requires additional attention to turn the peg so that the groove matches and fits into the hole. The grooved pegboard test has a higher cognitive demand, it is a more complex task, as compared to the coin rotation and Box and Block task used in this study. Thus, it highlighting the change in performance with age (Pereira, et al., 2015; Vanden Noven, et al., 2014). This could be due to the presence of greater motor redundancy in young versus the older adults. Typically aging is associated with changes in neuromuscular mechanisms, such as fewer motor units, lower firing rates and more variable motor unit firing patterns that could lead to inferior performance on dexterous tasks (De Luca and Erim 2002; Erim et al. 1999; Semmler, Kornatz, and Enoka 2003). Similar results on the grooved pegboard test were reported by other studies (Marmon, Pascoe, Schwartz, & Enoka, 2011; Feeney, Mani, & Enoka, 2018).

Our data showed a negative correlation between performance on the grooved pegboard test and the coin rotation task. Since both tasks primarily involve the use of the thumb, index finger and middle finger, similar neuromuscular mechanisms are at play in each of the tasks.

Association with force steadiness: Young adults exhibited greater associations between dexterity and force steadiness as compared to the older adults. Performance on the grooved pegboard task had a significant correlation with force steadiness during index finger abduction at 5% MVC with a high gain visual feedback condition. Both the tasks require precise control of a very low force level, thus the mechanisms responsible for both are similar, as reflected by the result. Such an association is not seen in the older adults in this study. This could be due to the complex nature of the grooved pegboard task. Since the task involves dexterous manipulation as well as cognitive control, only mechanisms responsible for force steadiness do not entirely explain performance on the grooved pegboard test in older adults. Another cognitive measure or a dual (motor + cognitive) task may help to explain performance on this task in older adults.

The pinch steadiness task was performed with the index finger and the thumb at 15% of MVC. Steadiness on the pinch task had a significant association on the box and block test in both young and older adults. Furthermore, the box and block test uses a pinch grip to grasp the block. Thus, the mechanisms responsible for pinch force variability and the box and block test may be similar. The young adults' data also had a significant association between the box and block test and force steadiness on a hybrid task at 15% MVC. Both tasks reflect pressing and moving, thus involve similar mechanisms that may explain this association.

Associations with motor unit parameters: Our results showed that older adults' data on the box and block test was significantly associated with several motor unit parameters across the abduction, pinch and static pressing tasks. The variability of motor unit discharge rate was measured as discharge rate variability and the variability of the first principal component. Similarly, the mean discharge rate of motor units was measured as an average discharge rate of the motor units that were identified and also, as the value of the first principal component. Higher discharge rate variability of the motor units, and lower motor unit discharge rates, were associated with fewer blocks being transferred on the box and block test. The box and block test is commonly used by occupational therapists to test for dexterity in clinical populations. However, the neuromechanical mechanisms that are associated with performance on the test have not been studied to our knowledge. This is the first study to demonstrate an association between motor unit parameters and dexterous performance on the box and block test in neurologically intact individuals.

Our data also showed 2 anomalies, where greater discharge rate variability of motor units during the static task was associated with better performance on box and block test and grooved pegboard test. There has been research done on associations between discharge rate variability of motor units and performance on the grooved pegboard test (Feeney, Mani, & Enoka, 2018), where increased discharge rate variability was associated with an inferior performance on the grooved pegboard test. In our study, the static task was done on a low-friction surface, and therefore required very precise force control. The grooved pegboard and box and block tests, while dexterous tasks, do not require the precise of force as the static pressing task on a low-friction surface, hence the discrepancies in the results. Future work examining associations between motor unit parameters and dexterous tasks could look at additional wrist muscles as well as the thenar muscle.

Conclusion: Our study shows age associated differences on the grooved pegboard test, thereby agreeing with previous research results. This test highlights dexterity differences with age in a healthy population, which the other tests did not show. Furthermore, since the grooved pegboard test involves motor as well as cognitive processes, it is important to explore associations between cognitive measures and performance on the task, especially in older adults. Lastly, our data was able to suggest possible mechanisms responsible for manual dexterity with age, as measured by the box and block test. Since changes in dexterous manipulation are associated with muscle atrophy and changes in motor unit properties, the redundancy afforded by these mechanisms may be limited in older adults. Thus, the significant associations from Table 4.1 were more evident in older compared with younger adults.

Chapter 5: Summary and Conclusions

Objectives: Aging is associated with a decreased ability to manipulate objects with the hand. Tasks requiring the use of smaller forces and precise force control are the ones that are often most challenging (Kern, Semmler, & Enoka, 2001). These changes are in dexterity are associated with changes in discharge rate properties of motor neurons (De Luca & Erim, Common drive of motor units in regulation of muscle force., 1994; Galganski, Fuglevand, & Enoka, 1993). Motor unit recordings were traditionally obtained from intramuscular EMG. However, the development of high-density surface EMG arrays enables recording activity over a larger muscle area and using algorithms to extract motor unit data from surface EMGs (Merletti, Holobar, & Farina, 2008).While a number of studies have examined motor unit properties using this technology, fewer studies have examined age-associated changes in dexterity using this technology (Feeney, Mani, & Enoka, 2018). The objective of this dissertation was to examine age-associated differences in dexterous performance and examine associations between the force steadiness and measures of dexterity and motor unit parameters such as discharge rate, discharge rate variability and low-frequency common oscillatory drive using the multichannel HD EMG arrays

Summary of Methods: 26 older adults (66-86 years) and 28 young adults (19 – 38 years) participated in the study. Research participants performed force matching tasks during index finger abduction, precision pinch (Chapter 2), static pressing and hybrid force/ motion tasks (Chapter 3). They also performed tests of manual dexterity, coin rotation, box and block test and grooved pegboard test (Chapter 4). The coefficient of variation (CV) during the force-matching task was computed. Multichannel high-density EMG was measured from the First Dorsal Interosseus (FDI) and extensor Digitorum Communis (EDC). The EMG signals were decomposed to obtain motor unit discharge rate parameters such as discharge rate and discharge rate variability of the motor neurons was computed. Low-frequency common oscillatory drive to the motor neurons was computed using Principal Component Analysis (PCA) on the motor unit discharge rates. Associations between the force variability, dexterity scores and motor unit parameters were analyzed for group differences and associations.

General Conclusions: This dissertation examined force control and motor unit activity across isometric force tasks and hybrid force/ motion tasks in addition to common tests of dexterity. Age-associated differences in dexterity were reflected in higher force variability on the index finger abduction tasks and a higher time to complete the grooved pegboard test. The younger adults had a higher mean discharge rate and higher value of the first principal component which represented the common oscillatory drive to the motor units. These motor unit parameters were associated with force variability as well as measures of dexterity. A high discharge rate and first principal component was associated with low force variability and superior dexterous measures such as more coin rotations in 30 s, more blocks transferred on the Box and Block test in 60s and quicker completion times for the grooved pegboard test. A higher discharge rate variability was associated with inferior performance on these tests of dexterous motor control.

Age associated deficits in motor unit activity were assessed using the high-intensity EMG array, across tasks, traditionally used in dexterity analysis as well as novel tasks. Furthermore, the study looked at control on a static task on a low friction surface, which can be extremely challenging for older adults. While force control on such tasks have been studied, this was the first motor unit activity has been examined to study the age-associated differences. The hybrid force motion task in our study is different from the isometric tasks commonly used to study dexterous control with aging. This task presented a challenge to motor control across young and older adults since it required simultaneous control of force and motion. Recording useable EMG during this task posed challenges and limited the motor unit yield during this task. Our conclusions from this task are based off of the small motor unit data especially in the FDI muscle, which is confounding. Future research may look at an isokinetic force matching task in order to move while controlling a force.

A data collection that spanned several different but related tasks allowed us to examine associations between motor unit parameters on the steadiness tasks and performance on the dexterous tasks. Future work should continue to examine dexterous control and motor unit activity across tasks requiring force control over a range of forces. Furthermore, testing pairs of agonist-antagonist muscles during a task will help highlight the deficits in motor control.

Our results showed a change in motor unit properties with age. However, of all the tasks, only two showed an age-associated change in dexterous performance. We believe this could have a likely association with differences in dexterous experience between the two groups. While majority of the older in the study engaged in dexterous activities such as writing, knitting, quilting, playing an instrument, bowling etc., a large number of the younger adults listed texting or playing video games as their dexterous activity. Although all these activities use hands the former activities require precise force and position control using fingers, which is not the demand of a typing task used in texting. Thus, the key to preserving dexterous control with increasing age may lie in including more dexterous activities involving individual fingers and small forces such as writing, cutting vegetables, knitting, etc. in everyday life.

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APPENDIX A: Review of Literature

Aging and Changes in Motor Control

I. Aging in numbers

Longevity is a direct outcome of the advances in modern medicine. The number of individuals aged 65 and over has been increasing across the world. Currently, there are about 49.2 million older adults residing in the US. This number is projected to increase to 94.7 million by 2060 (Vespa 2018). As life expectancy increases, maintaining health of the elderly is critical to good quality of life. Healthy aging research is concentrated around biomarkers of physiological functions, endocrine function, physical capability, cognitive function and immune function (Lara et al. 2015). Of these, physical capability which includes strength, mobility, balance and dexterity is a key factor in assessing the level of care a person needs. Our research will focus on changes in dexterity caused by age.

Hand movements are controlled by a relatively large area of the central nervous system. The hand is responsible for a large range of actions from small and precise movements to those requiring strength. Most tasks of daily living, work-related, household chores or recreational depend on proper hand function. Advanced age and poor manual dexterity are associated with dependence and residential living site (Ostwald et al. 1989; Incel et al. 2009).The ability to perform all ADLs helps maintain independence of a person and prevents them from needing care or being institutionalized. The monthly cost of senior care varies from $3000 to $7500 (Aging 2017), depending on the type of care sought. Thus, focusing research efforts toward interventions to preserve manual dexterity with age and maintain independence is important to keep healthcare spending to a minimum and maintain quality of life.

II: Physiological changes with age

Cortical changes: Aging causes changes at the cortical level that can affect motor control. The primary motor cortex is involved in the planning, control and execution of movement. The cerebellum is responsible for coordination and fine motor control. Together, these areas are critical to successful completion of any motor task. Research shows that aging causes atrophy in both the frontal cortex and the cerebellum. This result has been confirmed in individuals with no history of dementia using cadaveric specimens as well as in MRI studies (Salat et al. 2004; Clark and Taylor 2011). Larger cerebral volume is related to better performance on a dexterous manipulation task like Archimedes spiral tracing (Hoogendam et al. 2014). Thus, atrophy in cortical structures may influence dexterity.

Additionally, decreases in gray and white matter volumes have also been observed. The prefrontal cortex in particular is affected by the gray matter atrophy (Seidler et al. 2010). All these changes together impair motor performance with advanced age.

Motor neuron: A motor neuron is the final common pathway that transmits all neural information to the muscle. The motor unit is the basic functional unit of the neuromuscular system. It consists of the alpha motor neuron, its dendrites, axons and the muscle fibers it innervates. Sensory and descending inputs aggregate onto a single motor neuron and cause it to discharge thereby transmitting signal to the muscle fibers it innervates. A motor neuron encodes information using either recruitment or rate coding. Recruitment is the activation of more motor neurons in order to generate force. Rate coding refers to changing the firing frequency of the motor neuron to alter force. Whether recruitment or rate coding is the mechanism that contributes to force generation at any given point in time depends on the function performed by the muscle (Fuglevand et al. 1993). All the motor neurons that innervate a single muscle make up the motor neuron pool. The number of muscle fibers innervated by a single motor neuron is known as the innervation ratio. The innervation number depends on size of the muscle. For example, a large leg muscles like the tibialis anterior has 520 motor neurons, hand muscles like the extensor digitorum communis and the first dorsal interosseous have 273 and 172 respectively and rectus lateralis, a small eye muscle that has 5 motor neurons (Heckman 2004).

Apoptosis is a process of neuronal death and typically starts in the fifth decade of life. Death of cortical and spinal neurons leads to altered signals from the spinal and supraspinal pathways to the motor neurons. Furthermore, decrease in the number of motor neurons results in reorganization of the motor system. With fewer motor neurons available, there is an increase in the innervation ratio and number of muscle fibers innervated by a single motor neuron increases. For example, the innervation number for TA changed from 150 in young to 59 in older adults (Campbell et al. 1973; Tomlinson and Irving 1977; Enoka 2015). There are also modifications in the recruitment and rate coding patterns. During voluntary contractions, motor neurons follow orderly recruitment whereby smaller motor neurons are recruited before the larger ones (Henneman 1957). In addition, typically the motor units recruited first are de-recruited last and vice versa. As individuals age, though recruitment order is maintained, derecruitment patterns are disrupted (Erim et al. 1999). Several reports of decreased discharge rate and increased discharge rate variability have been documented (Laidlaw et al. 2000; Enoka et al. 2003; Taylor and Enoka 2004; Moritz et al. 2005; Christou 2011) For example, discharge rates during an MVC task were found to be 22.3pps in older adults compared to 28.1 pps in the tibilais anterior muscle in younger adults (Rubinstein and Kamen 2005). Similarly, in the FDI, average discharge rates were 7.1 pps in older adults compared to 12.1 in the younger adults (Barry et al. 2007).

Motor neurons receive inputs from a number of different sources, both independent and shared. The common inputs modulate discharge rates of motor neurons, which affects force exerted by the muscle (Farmer et al. 1993; Negro and Farina 2011). The common inputs are oscillatory in nature, and only the low-frequency components of these shared signals are reflected in the neural drive to the muscle, which in turn is responsible for force production (Farina et al. 2016). Previous research has shown that modulation in the low frequency common oscillatory inputs across the motor neuron pool is another factor contributing to age-related dexterous impairments (Erim et al. 1999; Enoka et al. 2003; Negro and Farina 2011). The strength of the common oscillatory inputs to the motor neurons has been typically examined using coherence measures (Farmer et al. 1993; Conway et al. 1995; Halliday et al. 1998; Semmler et al. 2003; Marmon et al. 2011). Coherence is similar correlation analysis performed in the frequency domain and helps identify the specific frequencies at which motor output is affected by the common oscillatory input. Previous research has reported increase in coherence between pairs of motor units (Semmler et al. 2003) and, EEG_EMG, MEG-EMG coherence (Johnson and Shinohara 2012; Kamp et al. 2013) between older and young adults. This increase in coherence indicates the inability of older adults to appropriately regulate the common oscillatory inputs to the motor neurons and explains some of the motor impairments with age. Recent advances in technology and the use of multi-channel EMG arrays has allowed for development of novel metrics to assess common oscillatory inputs (Negro et al. 2009; Feeney et al. 2018). These metrics of measurement are discussed in subsequent sections.

Muscle: The loss of motor neurons discussed above, leads to deinnervation of muscle fibers. These muscle fibers then degenerate causing an overall decrease in muscle mass and decline in strength. This phenomenon is known as sarcopenia (Clark and Taylor 2011; Martin et al. 2015). Additionally, loss of muscle mass causes limitations and slowing of movements.

The muscle comprises of two types of fibers, type I and type II. Type I fibers are slow twitch muscle fibers that enable endurance tasks, whereas type II muscle fibers are fast-twitch muscle fibers and participate in activities requiring rapid generation of power. As people age, the type II muscle fibers go through a greater amount of atrophy, and thus represent a smaller part of the muscle volume. The proportion of type I fibers increases, thus causing the muscle to have overall slow contraction properties and decreased ability to perform activities requiring greater force. These changes in muscle composition affect smaller muscles more than the larger muscles, thus resulting in greater changes in hand function and fine motor control as compared to the gross motor skills (Enoka et al. 1999; Enoka et al. 2003; Christou 2011).

III: Challenges in dexterity with age

Aging is accompanied by a decline in physical function. The number of functioning units and the interaction between them is compromised (Morrison and Newell 2012). The hand comprises of an intricate network of several muscles and tendons. Performing fine motor movements can require either co-contraction of several of these muscles or precise activation of a few muscles. Thus, hand function is very susceptible to injury, weakness or age. Hand function starts to decrease after the age of 65 (Shiffman 1992; Desrosiers et al. 1994; Desrosiers et al. 1995; Cole et al. 1999; Ranganathan et al. 2001; Christou 2011; Clark and Taylor 2011; Marmon et al. 2011; Keenan and Massey 2012; Soer et al. 2012; Holt et al. 2013; Martin et al. 2015; Heintz and Keenan 2018; Joshi 2018). This change is associated with age and is independent of gender and lifestyle (Martin et al. 2015). Several tests are used in clinics and laboratories to measures manual dexterity and are sensitive to aging. These include the Purdue pegboard test, box-and-block test, Archimedes spiral tracing task, and Minnesota manual dexterity (Desrosiers et al. 1994; Desrosiers et al. 1995; Surrey et al. 2003; Martin et al. 2015). Research looking at a battery of tests to assess hand function observed a decrease in individuals starting by the age of 65 (Shiffman 1992) and a significant deterioration over 75 years of age (Ranganathan et al. 2001). In addition, a coin rotation task is a dexterity test that requires the coordinated action of the index finger, thumb and the middle finger. This task has been typically used to study dexterous impairments in MS (Heldner et al. 2014). It has also been used to differentiate impairments in individuals with brain injury from healthy controls (Mendoza et al. 2009). Furthermore, a 20 – 25% decrease in grip strength has been seen after 60 years of age and is associated with disability and mortality (Gale et al. 2007; Chaturvedi 2015). Reduction in strength, coordination, slowness and tremor are all responsible for poor dexterity with age. The following sections will elaborate on changes in force control that lead to dexterous impairments and the influence of friction and visual gain on these impairments.

Force Control

A population of motor units controls the force produced by an individual muscle. Force is controlled by recruitment and rate coding of the motor units. Changes to muscle composition, motor neuron and cortical changes with age have a direct effect on control of force.

Motor deficits with age can be divided into strength, sensorimotor control and coordination (Lawrence et al. 2015). Experimentally, strength is measured as the maximum force produced during a contraction, also known as the maximal voluntary contraction (MVC). Dexterity research typically examines grip, pinch and index finger abduction strength. Though deficits in strength with age are predominant in larger muscles such as those in the lower limb, decreased grip strength has been found with age (Ranganathan et al. 2001) and is associated to measures of mortality (Gale et al. 2007). Strength, in spite of being most susceptible to age, plays a smaller role in ADLs, thus additional factors affecting motor control need to be examined (Lawrence et al. 2015).

Control of submaximal forces is critical to performing several everyday tasks. For example, gradually increasing or decreasing force on the gas pedal while driving or applying a steady force while peeling fruit are critical to perform action and successfully complete the task. Force control is measured as the ability of an individual to maintain a steady acceleration while performing concentric and eccentric contractions or measuring force steadiness during an isometric task. Force steadiness is estimated by the computing the standard deviation of force about a mean. While comparing between young and older adults, since the amplitude of MVC force differs, force steadiness is measured by normalizing the standard deviation to the individual's mean force. Thus, the normalized measure of steadiness, the coefficient of variability (CV) is typically used while comparing between groups. Previous research has shown that older adults have greater force variability than younger adults (Enoka et al. 1999; Christou 2011; Marmon et al. 2011). This difference is amplified at lower force levels, typically below 20 N (Galganski et al. 1993). Since most ADLs use a small force, steadiness deficits adversely affect performance on the fine motor tasks performed daily. Research studies have found that variability during a force steadiness was associated with performance on the grooved pegboard test (Marmon et al. 2011; Feeney et al. 2018).

Impairment in coordination across muscles is another factor causing movement limitations with age. Typically, multi-joint movements are challenging. Some muscles atrophy more than others causing unequal strength deficits that affect coordination (Clark and Taylor 2011). Additionally, changes to muscle fiber constitution, influence relative timing of muscle activation resulting in poor coordination (Clark and Taylor 2011). Studies looking at force steadiness during a multi-digit contraction versus a grip task show greater force variability in older adults during the multi-digit grasping (Sosnoff and Newell 2006; Parikh and Cole 2012). In addition to strength and steadiness deficits, difficulties aligning forces and moments correctly to achieve a multi-joint task are present in older adults, which limit performance of coordinated tasks (Cole et al. 1999; Diermayr et al. 2011; Parikh and Cole 2012).

Everyday tasks are performed automatically, without particular attention to the task. As people age, these tasks become less automatic and involve more attention (Seidler et al. 2010). Several studies have looked at the effect of a dual task on performance. A dual task has more than one task constraint. Driving a vehicle, which involves control of the steering wheel, brake and gas pedals all while attending to the pedestrians and traffic is an example of a dual task. These duals tasks are mimicked in a research setting by having participants perform a motor task concurrently with a cognitive task or another motor task. Example, holding a steady isometric elbow extension while doing mental mathematics and attending to a visual feedback (Pereira et al. 2015) or maintaining a steady posture and attending to a visual stimulus (Peterson and Keenan 2018). Studies looking at the effect age has on performance of a dual task have found that while these tasks pose a challenge to motor control across age groups, impairments in older adults are significantly greater than the younger adults (Pereira et al. 2015; Peterson and Keenan 2018). This is frequently attributed to increased attentional demands of the task (Woollacott and Shumway-Cook 2002; Keenan et al. 2017). Reallocation of neural resources to perform optimally on both the tasks affects performance on the motor task. It has been suggested that in older adults, greater activation of the prefrontal cortex during a motor task affects performance on a dual task, since resources are shared (Parikh and Cole 2016).

Among other tasks studied to explore force control and dexterity are the strength-dexterity (S-D) task and hybrid force/motion tasks. Valero-Cuevas and colleagues have designed the S-D test that measures fingertip forces during compression of a spring. The task involves pressing the spring without buckling it and requires precise manipulation of low forces, typically under 3N. A study looking at performance on the S-D test across age-groups found that the decline in dexterity starts in middle-age with rapid decline after the age of 65 (Dayanidhi and Valero-Cuevas 2014). Furthermore, performance on hybrid force/ motion tasks has also been studied to assess motor control. These tasks require concurrent control of force while producing motion and are thus challenging to motor control. Increased tasks constraints reduce motor redundancy, thus restricting performance of the task to certain boundary conditions. Maximal downward force was decreased in young adults on a scratch task versus a static force pressing task (Keenan et al. 2009). Speed of movement did not affect performance of the task; however, adding movement to the static force task affected maximal downward force generation (Keenan et al. 2009). Similar to this, another study looking at force steadiness while holding a 2N force during a static and hybrid task force variability increased by 277% in young and 335% in older adults on the hybrid versus static task (Joshi and Keenan 2016; Joshi 2017). Thus, more complex tasks that require control of more than just one variable exacerbate motor control deficits in older adults. Moreover, these tasks mimic ADLs and need to be studied in order to understand the motor deficits that take place with increasing age.

Frictional Properties of the Surface

Everyday tasks require interacting with the environment in addition to controlling forces and moments. These interactions introduce additional challenges to motor control. Frictional properties of the surface affect force steadiness and dexterous manipulation (Cole and Johansson 1993; Seo et al. 2011; Keenan and Massey 2012; Joshi and Keenan 2016; Heintz and Keenan 2018). Greater force variability was observed while pressing on low- versus high friction surfaces (Seo et al. 2011; Keenan and Massey 2012). Furthermore, cutaneous changes with age can alter interactions between surfaces with varied frictional properties (Cole et al. 1999). In the elderly, the skin becomes more slippery (Johansson 1996; Cole et al. 1999), thus potentially making dexterous manipulation difficult. Additional challenges are imposed while interacting with low-friction surfaces. For example middle-aged and older adults were found to have significantly higher grip forces while grasping a low- vs-high friction surface (Cole et al. 1999). Increasing contact force while manipulating low-friction surfaces may be a strategy used by the aging motor system to compensate for cutaneous changes. Another study found that older adults had greater RMS error while tracing a spiral with their finger as compared to younger adults (Heintz and Keenan 2018). However, an age-related difference was not seen across friction conditions (Heintz and Keenan 2018). Impairments in force control while manipulating low-friction surfaces are documented in older adults even in absence of sensory feedback. For example, increased force variability was seen as participants performed an isometric pressing task on a Teflon surface with a custom-molded splint attached to the finger. This impairment was greater in older versus young adults (Keenan and Massey 2012).

Frictional properties of the surface affect performance on hybrid tasks differently. Hybrid force/motion tasks require simultaneous control of normal and shear forces, which makes them challenging for motor control. Frictional properties of the surface have an effect on the shear force, since individuals need to generate enough shear force to overcome friction and move across the surface. When individuals were asked to perform a hybrid task of pressing and moving, both the young and older adults optimized performance on the low-friction surface as compared to the high friction surface, though younger adults exhibited significantly lower force variability than the older adults (Joshi and Keenan 2016; Joshi 2017). Older adults had lower mean shear forces and shear force variability than young adults (Joshi 2017) which may indicate that older adults had trouble generating appropriate shear force to manipulate the surfaces. This could be related to impaired sensory control in older adults (Johansson 1996) or the inability to appropriately explore the uncontrolled manifold (Scholz and Schoner 1999). The forces or force direction, whereby variability does not influence performance variable needs to be studied. Further research is required to investigate the mechanisms causing these changes in dexterity.

Visual Information

Experimental paradigms examining force steadiness rely on a visual feedback for participants to alter performance in real time. Visual gain represents the amount of visual feedback provided and can be changed by altering the ordinate scale on the feedback or visual angle. Research has shown that increasing visual gain leads to increased force variability on isometric force and position-holding tasks in older adults (Kennedy and Christou 2011; Sosnoff and Newell 2011; Baweja et al. 2012). For example, when the ordinate scale was changed from 2 – 512 pixels/N, older adults exhibited greater force variability on an index finger abduction task as compared to the young adults (Sosnoff and Newell 2006). Greater visual feedback essentially provides more information to the participant. Small variations in force are amplified, thus prompting participants to try to correct them. In another study, an increase in the visual angle from 0.05˚ to 0.5˚ led to a 43% increase in force variability in older but not young adults (Kennedy and Christou 2011). Additionally, positional variability on concentric index finger abduction and ankle dorsiflexion was also found to increase in the elderly with greater visual angle (Baweja et al. 2012). This increase in force and position variability in older adults is due to limitations in visuomotor processing or the increased attention demands imposed by high visual gain (Kennedy and Christou 2011) and has been attributed to altered modulation of muscle activity (Baweja et al. 2012; Park et al. 2017). However, specifics about neural changes with age causing these limitations are unknown.

IV: Electromyography and Motor Unit Decomposition:

Electromyography (EMG) is a technique used to measure the electrical activity of a muscle. As discussed previously, the muscle fibers are activated by motor neurons. These motor neurons use electric impulses known as action potentials to signal the muscle fibers to contract. An action potential in the motor neuron generates action potentials in all the fibers it innervates. The neuromuscular junction is the point at which the motor neuron transmits signal to the muscle fiber and is located at the center of the muscle fibers. The action potential propagates from the neuromuscular junction across the fibers both directions. The area comprising of all the neuromuscular junctions is known as the innervation zone.

Electrical activity generated by a muscle depends on the recruitment and rate coding properties of the motor neurons. Thus, EMG is an aggregation of action potentials of the motor neuron pool and is used as a tool to peek into the neuromuscular system and identify changes occurring with impairment or injury. The mechanism of EMG detection, problems in detection, motor unit decomposition and the relationship of EMG to force are discussed in this section.

Recording Electrodes: Muscle activity can be either measured by intramuscular electrodes or placing electrodes on the skin overlying the muscle, known as surface EMG. Intramuscular EMGs require inserting fine wire electrodes into the muscle. Due to proximity to the muscle fibers, these electrodes record activity from only a few muscle fibers and motor neurons activating them. Surface electrodes in contrast provide a measure of activity from all the muscle fibers underlying it, thus provide a more global measure of muscle activity. Since we propose to use surface EMG for our research, we will discuss that in detail here.

A typical surface EMG system uses silver-silver chloride (Ag-AgCl) electrodes. This electrode measures action potentials in the muscle fibers beneath it and is recorded as voltage with respect to a ground electrode. There are two modes of EMG detection; the monopolar mode has a single electrode placed on the muscle and its activity is recorded with respect to a ground electrode and a bipolar recording has two electrodes placed on the skin overlying the muscle. The monopolar mode is more susceptible to unwanted electrical noise. The bipolar is less susceptible to noise than the monopolar mode; detection and signal processing techniques can be used to minimize this noise. Signals from electrodes are transmitted to a signal-processing device. Here a difference between the voltages measured by the electrodes is calculated, amplified and filtered in order to get the final EMG signal. The quality of the EMG signal depends on several factors, discussed below.

Though surface electrodes provide an aggregate measure of activity from several muscle fibers, distance from the actual muscle increases their susceptibility to noise. Layers of subcutaneous tissue and skin lie between the muscle and the recording electrode. The subcutaneous tissue acts as a low-pass filter and skin provides higher impedance that diminishes the signal (Merletti and Lo Conte 1997; Merletti et al. 2001). Skin impedance can be reduced by cleaning the skin with alcohol before placing electrodes on it. Furthermore, activity from surrounding muscles is also a source of noise when getting EMG measurements (De Luca and Merletti 1988). This noise is called crosstalk and gives an incorrect measure of intended muscle activity (De Luca and Merletti 1988). Using a bipolar electrode configuration comprising of two detection electrodes, with ground electrodes along with a double differential amplifies helps reduce crosstalk and any other source of noise common to both the electrodes used and obtain a clean EMG signal.

Electrode placement on the skin over the muscle is critical to getting true measure of muscle activation. For a bipolar configuration, the electrodes need to be places 10 – 20 mm apart in the direction of the muscle fibers. Since action potentials travel along the muscle fibers, electrodes that do not align with the fiber direction are unable to detect the action potentials, thus misrepresenting muscle activity. Furthermore, as discussed above, the action potential travels in opposite directions from the innervation zone, thus electrodes placed across the innervation zone, will record very low amplitude EMG measurement due to signal cancellation (Merletti et al. 2001; Keenan et al. 2006). Correct measure of muscle activity can be obtained by placing the detecting electrodes on the same side of the innervation zone (Merletti et al. 2001; Keenan et al. 2011). Multichannel EMG systems record muscle activity across the length of the muscle and can be used to detect the presence of innervation zones (Gerdle 1999; Farina et al. 2008). These electrodes are either one- or two-dimensional and can be used for several purposes such as calculating conduction velocity and obtain motor unit recordings (Merletti et al. 2001).

EMG Quantification: A surface EMG signal comprises the superimposition of action potentials from several motor units and thus appears random in nature. This raw EMG is known as the interference EMG (Merletti et al. 2001). Extracting information from the EMG requires signal processing. The interference EMG has both positive and negative values. Thus, EMG has an average value close to zero due to positive and negative values. The process of rectification is used to convert the signal to a single polarity. Half-wave rectification involves getting rid of the negative values and just using the positive values. However, data is lost in this process. Fullwave rectification is most commonly used and requires taking the absolute values of the instantaneous signal, thus making all values positive. The rectified EMG is then smoothed or low-pass filtered using a digital filter or a moving window average.

Amplitude of the EMG signal is quantified as average EMG or area under the rectified smoothed EMG. Root mean square (RMS) value of the EMG is also computed as it gives a measure of power of the signal. Since EMG measure is affected by several factor as discussed above, absolute EMG amplitude is not a reliable measure. For example, the absolute EMG amplitude was lower in older than young adults (Moritani et al. 1985). This could be due to the change in motor neuron activation properties and muscle fiber reorganization that takes place with age. However, increased adipose tissue in older adults could also lead to a lower absolute EMG value. To overcome this measurement shortcoming and EMG amplitude effectively, EMG is normalized to a standard more reliable value, typically the EMG at MVC. The normalized value is expressed as percentage of MVC and is used to denote level of muscle activity.

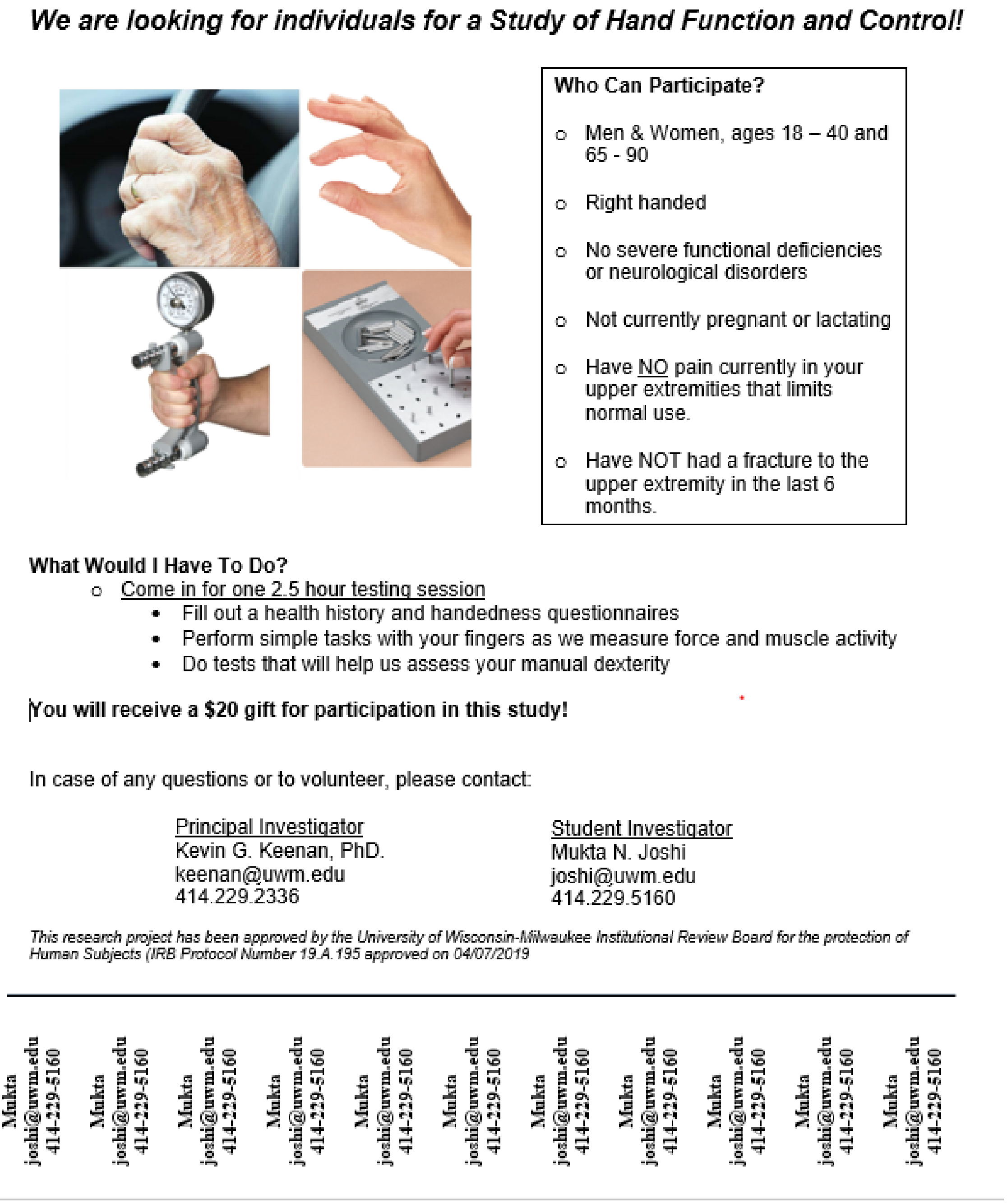
Since EMG measures activation of the alpha motor neuron pool, which is also responsible for force generation, there is a relationship between EMG and force. EMG amplitude during an isometric contraction has a near linear relationship to force, especially in small hand muscle (Woods and Bigland-Ritchie 1983). Larger muscles though may not have the same linear relationship to force due to different recruitment and rate coding patterns. More recent research looking at EMG and force relationships found a higher association between low-pass filtered EMG amplitude and rate of change of force (Yoshitake and Shinohara 2013a).

Frequency content of the EMG signal is another measure of activity. This is affected by the discharge characteristics of the motor neuron and the oscillatory inputs that drive motor neuron activity. Frequency content of the EMG signal is measured using the fast Fourier transform (Gerdle 1999). The power spectral density of the EMG represents power in each frequency of the signal. Power in different frequency bands is used to measure corticomuscular coherence (Conway et al. 1995; Baker et al. 1999), which is a measure of transmission of signal from the cortex to the muscle.

Motor Unit Recordings: Identification of individual motor units allows determining motor neuron properties such as discharge rate, and provides information about inputs to motor neurons. Individual motor units have been detected using intramuscular EMGs for many years (Adrian and Bronk 1929). However, this technique enables detection of only a few motor units and majority of the motor units during a muscle contraction are not accounted for. In recent years, extracting motor neuron information from surface EMGs has become more popular, though it is still not commonly done. Surface recording are non-invasive and thus more desirable. A conventional bipolar surface EMG recording record overlapping potentials that are similar in shape, thus making separation of action potentials extremely challenging (Farina et al. 2016). High-density multichannel EMG electrodes enable recording muscle activity across the length of the muscle, thus providing several recording sites over the muscle. This allows for detecting action potential transmission temporally along the length of the muscle, thus making identification of individual motor units feasible. Blind source separation methods are used to identify individual motor units with high accuracy (Holobar et al. 2009). The Convolution Kernel Composition (CKC) method has been used to identify discharge patterns of individual motor units during a low-force contraction (Holobar et al. 2009). An average of 15 in the abductor pollicis, 13 in the biceps brachii, and 8 motor units in the vastus lateralis were identified.

Common drive represents oscillatory inputs to the motor neuron pool from all sources, spinal, cortical and peripheral. Coherence is a measure that represents presence of common inputs to motor neurons (Conway et al. 1995; Baker et al. 1999). It is the equivalent of correlation in the time domain, but is used in the frequency domain and has been used to examine oscillatory drive to the motor neurons or muscle. EEG-EMG, EMG-EMG, or coherence between pairs of motor units have been studies to assess the role of oscillatory drive in motor control. Studies have found coherence in the 1-12 Hz and 15 - 30 Hz bands (Baker et al. 1999; Halliday et al. 2000; Semmler et al. 2003). Changes in coherence have been reported with age and presence of tremor, especially in the low frequencies (Semmler et al. 2003). However, sensitivity of EMG measures to electrode placement over the innervation zone and a multitude of other factors, make EMG-EMG, or EMG-EEG coherence less reliable. Furthermore, coherence between pairs of motor units underestimates oscillatory drive to the entire motor neuron pool. A more reliable measure is common oscillatory drive as developed by Negro and colleagues (2009) computes the first common component (FCC) by performing a principal component analysis on smoothed discharge rates of individual motor units. FCC was found to explain approximately 72% of the variability in force and thus is a measure that captures the most underlying variability in motor fluctuations. Moreover, a reliable measure of common oscillatory drive requires over 4 individual motor units to compute the FCC (Negro et al. 2009; Negro and Farina 2011). This measure has been tested in healthy young adults. However, its use to study motor control in older adults needs to be explored.

Appendix B: Recruitment Flyer



We are looking for individuals for a Study of Hand Function and Control!

Who Can Participate?

- Men & Women, ages 18 – 40 and 65 - 90
- Right handed
- No severe functional deficiencies or neurological disorders
- Not currently pregnant or lactating
- Have NO pain currently in your upper extremities that limits normal use.
- Have NOT had a fracture to the upper extremity in the last 6 months.

What Would I Have To Do?

- Come in for one 2.5 hour testing session
  - Fill out a health history and handedness questionnaires
  - Perform simple tasks with your fingers as we measure force and muscle activity
  - Do tests that will help us assess your manual dexterity

You will receive a $20 gift for participation in this study!

In case of any questions or to volunteer, please contact:

Principal Investigator	Student Investigator
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This research project has been approved by the University of Wisconsin-Milwaukee Institutional Review Board for the protection of Human Subjects (IRB Protocol Number 19.A.195 approved on 04/07/2019

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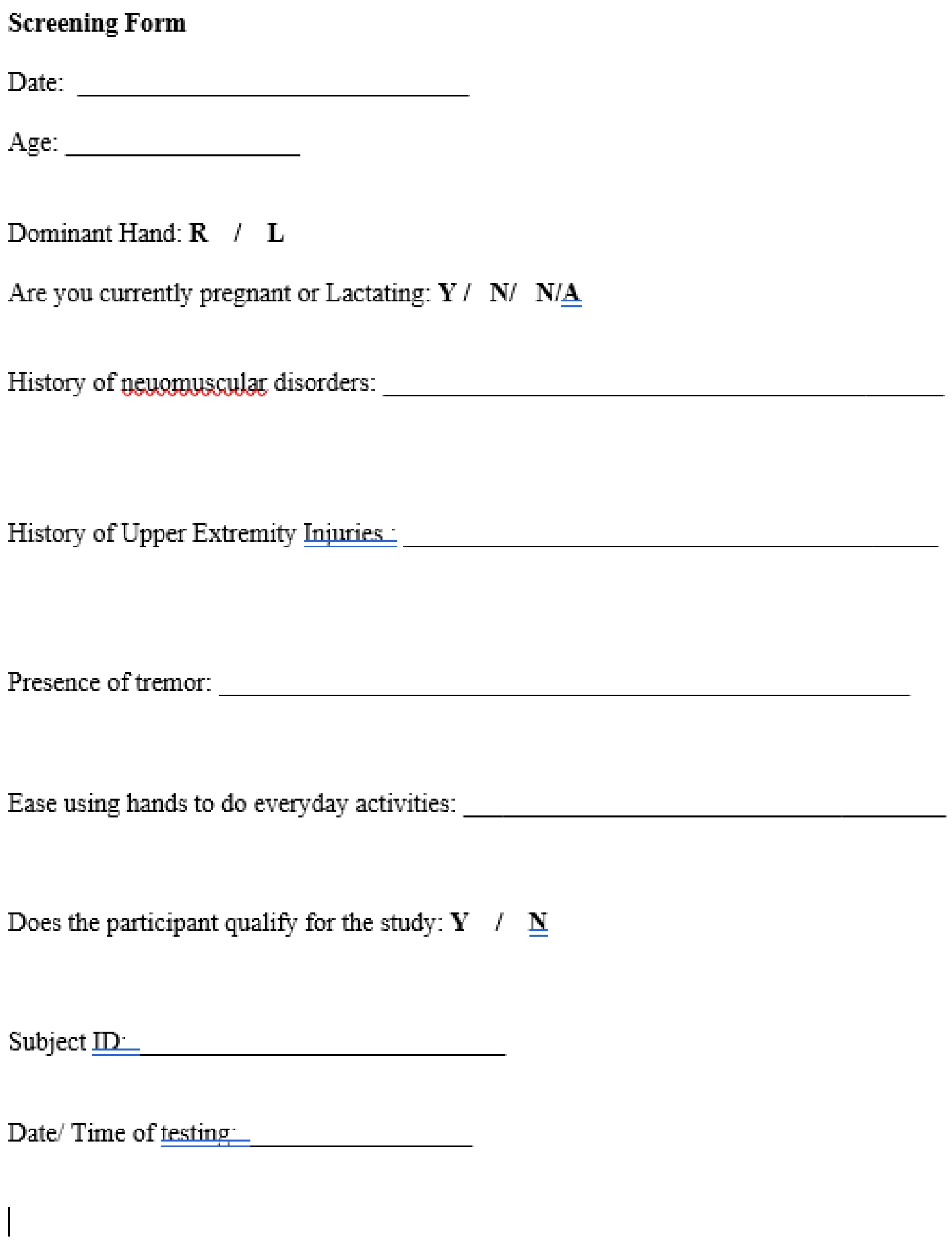
Appendix C: Screening Form



Screening Form

Date: ______________________________

Age: __________________

Dominant Hand: **R / L**

Are you currently pregnant or Lactating: **Y / N/ N/A**

History of neuomuscular disorders: ____

History of Upper Extremity Injuries : ____

Presence of tremor: ____

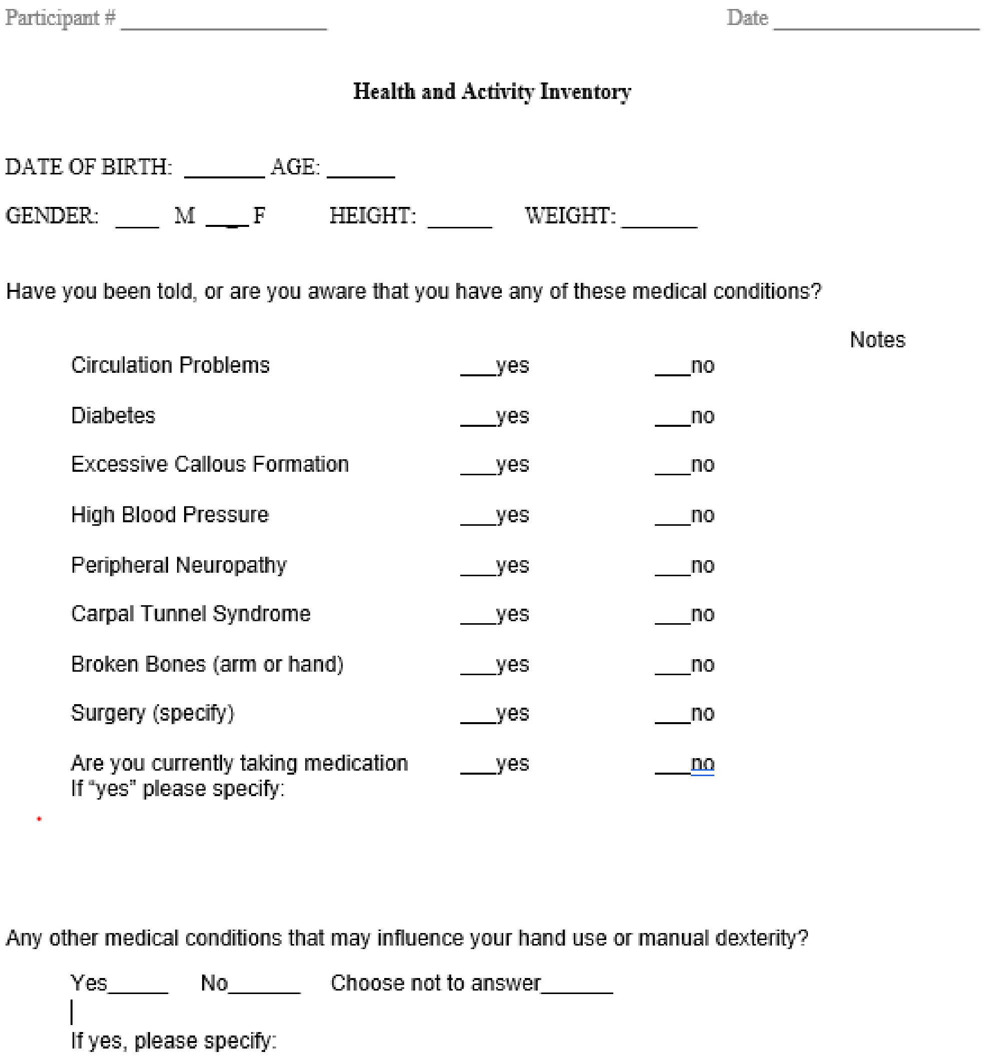
Ease using hands to do everyday activities: _____________________________________

Does the participant qualify for the study: **Y / N**

Subject ID: ______________________________

Date/ Time of testing: __________________

Appendix D: Health History Questionnaire



Participant # ____________________   Date ____________________

Health and Activity Inventory

DATE OF BIRTH: _______ AGE: ______

GENDER: ____ M ___ F   HEIGHT: ______   WEIGHT: _______

Have you been told, or are you aware that you have any of these medical conditions?

			Notes
Circulation Problems	___yes	___no	
Diabetes	___yes	___no	
Excessive Callous Formation	___yes	___no	
High Blood Pressure	___yes	___no	
Peripheral Neuropathy	___yes	___no	
Carpal Tunnel Syndrome	___yes	___no	
Broken Bones (arm or hand)	___yes	___no	
Surgery (specify)	___yes	___no	
Are you currently taking medication If "yes" please specify:	___yes	___no	

Any other medical conditions that may influence your hand use or manual dexterity?

Yes_____   No______   Choose not to answer______

If yes, please specify:

Participant # ____________________ Date ____________________

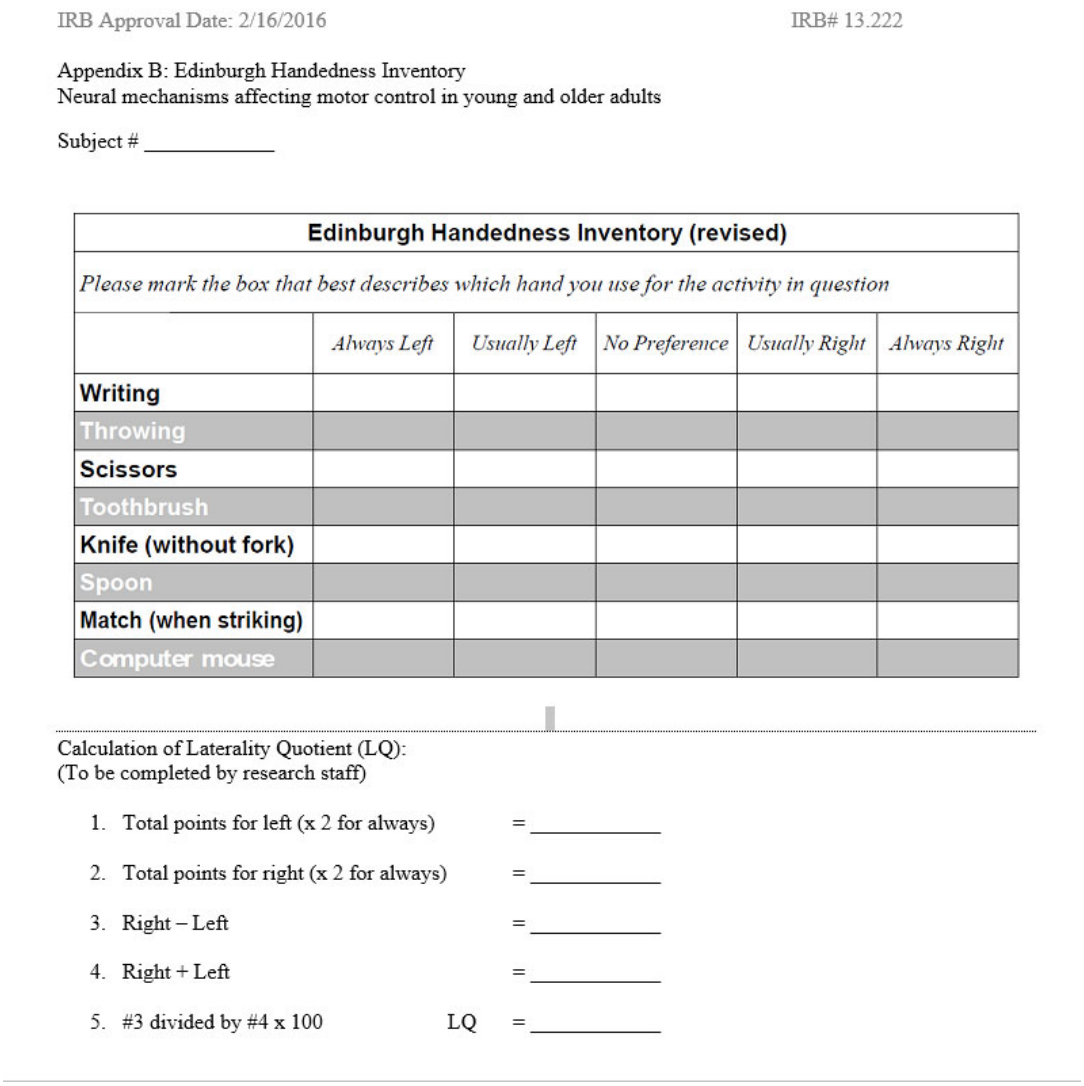
Please list all <u>athletic activities</u> you have participated in during the last five years and indicate the skill level and duration of these activities (i.e. recreational, collegiate, master's level, etc.)**:**

Activity	Skill Level	Duration

Please list all <u>manual dexterity skills</u> (e.g., playing the piano or guitar, knitting, video gaming with a joystick, etc) that you have participated in during your life (and you had to perform the skill for over 6 months) and indicate the skill level and duration of these activities:

Activity	Skill Level	Duration

Appendix E: Edinburgh Handedness Test



IRB Approval Date: 2/16/2016 IRB# 13.222

Appendix B: Edinburgh Handedness Inventory
Neural mechanisms affecting motor control in young and older adults

Subject # ____________

Edinburgh Handedness Inventory (revised)

Please mark the box that best describes which hand you use for the activity in question

	Always Left	*Usually Left*	*No Preference*	*Usually Right*	*Always Right*
Writing					
Throwing					
Scissors					
Toothbrush					
Knife (without fork)					
Spoon					
Match (when striking)					
Computer mouse					

Calculation of Laterality Quotient (LQ):
(To be completed by research staff)

1. Total points for left (x 2 for always) = ____________
2. Total points for right (x 2 for always) = ____________
3. Right – Left = ____________
4. Right + Left = ____________
5. #3 divided by #4 x 100 LQ = ____________