QUANTIFYING THE TRAINABILITY OF PERIPHERAL NERVE FUNCTION IN

YOUNG AND OLDER ADULTS

By

JOCAROL ELIZABETH SHIELDS

Bachelor of Science in Movement Science
Delaware State University
Dover, Delaware
2010

Master of Science in Exercise Science
Texas Tech University
Lubbock, TX
2013

Submitted to the Faculty of the
Graduate College of the
Oklahoma State University
in partial fulfillment of
the requirements for
the Degree of
DOCTOR OF PHILOSOPHY
May, 2023

QUANTIFYING THE TRAINABILITY OF PERIPHERAL NERVE FUNCTION IN

YOUNG AND OLDER ADULTS

Dissertation Approved:

_____

Dr. Jason M. DeFreitas, Chair

_____

Dr. Michael A. Trevino

_____

Dr. J. Jay Dawes

_____

Dr. Alex J. Bishop

ACKNOWLEDGEMENTS

To my mentor:

I want to express my deep gratitude to my mentor, Dr. Jason DeFreitas for the guidance and support you have provided during my time at OSU. Your mentorship has been invaluable to me and I could not have completed this dissertation without your help. I am so thankful to you for taking a chance on me when most would not.

To my colleagues:

Thank you to Shawn, Claire, and Marcel for their tireless efforts in helping with my dissertation. It's not possible to achieve this without the help of you and I am truly appreciative of your support and friendship.

To my siblings, nieces, nephews and others:

I cannot thank you enough for your love and support. I know that I can always count on you, and I am grateful for the many sacrifices you made to help me achieve my goals. Thank you for being there for me, for cheering me on, and for believing in me.

To Mom:

Your unwavering love, encouragement, and belief in me have been a constant source of strength and motivation. Your sacrifices and willingness to go above and beyond to support me have not gone unnoticed, and I am truly grateful for all that you have done. Your constant reminders that I am capable and that I have what it takes to succeed have given me the strength to persevere even when the obstacles seemed insurmountable.

To Dad:

A promise is a promise. I am filled with a sense of gratitude and appreciation for all that you did for me. Your belief in me gave me the courage to pursue my dreams and follow my passion. Although you are no longer here, your spirit lives on in me, and I carry your wisdom with me always. Your love and support were instrumental in helping me to achieve this milestone, and I will always be grateful for the role you played in my life.

Name: JOCAROL ELIZABETH SHIELDS

Date of Degree: May, 2023

Title of Study: QUANTIFYING THE TRAINABILITY OF PERIPHERAL NERVE
FUNCTION IN YOUNG AND OLDER ADULTS

Major Field: Health, Leisure, & Human Performance

Abstract: It is well known that the natural progression of age can result in motor neuron degeneration. Consequently, this leads to slowing of nerve conduction, denervation, and reduced motor function. Slowing nerve speed can alter an individual's response time and could subsequently lead to increased fall risk and injury. Further exploration of potential counteractive measures to combat reduced nerve speed is warranted. **PURPOSE:** The purpose of this study is to determine if four weeks of hand resistance training can lead to positive adaptations in nerve speed in healthy untrained adults. We hypothesized that training would result in faster nerve speed in both younger and older adults, albeit the magnitude of change would be more substantial in younger participants. **METHODS:** Thirty-four subjects (18- 71 yrs) have completed this ongoing study so far (n = 27 younger, 7 older). Median nerve motor conduction velocity (NCV) was recorded before (PRE) and after (POST) four weeks of hand resistance training in both arms. Additional measures (e.g., nerve CSA, muscle CSA, MVC hand grip strength, and manual dexterity) were also obtained. Training was conducted three times per week with the use of hand grippers, grip bands and grip rings. **RESULTS:** Mixed factorial ANOVAs revealed significant increases in nerve conduction velocity for the young training and older training groups. Significant changes in nerve CSA were also discovered in both the young training and older training groups. The young training group showed significant increases in muscle CSA pre to post, however the young control was found to have decreased muscle CSA. No significant changes in muscle CSA were observed in the older training group. The young training group was found to have increased hand grip strength (MVC strength) after four weeks, while the other groups (e.g., young control and older training) did not. Finally, all groups demonstrated faster manual dexterity (both in placing and turning) speed pre to post. **CONCLUSION:** The findings of this study suggest that resistance training may be a reliable method to counteract NCV deficits in the short term. These results have the potential to improve the quality of life for our older populations

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER I

INTRODUCTION

1.1. Introduction

Aging is a multidimensional process that is accompanied by several physiological

and morphological changes which may affect one's quality of life. It is well-established

that declines in motor ability can be seen as early as the 4th decade[8,29]. However,

evidence supports the belief that functional ability especially after the age of 60 is

substantially altered via peripheral nervous system (PNS) deterioration[7,37,65]. The PNS,

located outside the brain and spinal cord plays a vital role in our understanding of the

contractile response of a muscle. It is the boundary to which nerve and skeletal muscle

interact and muscular contraction can be initiated[24]. Unfortunately, the PNS is complex

and our knowledge of counteractive measures to limit nerve deterioration is minimal.

Deterioration of the peripheral nerves is reflective of fewer functioning motor

axons or degradation of the motor axons that allow for rapid contraction and mobility.

These outcomes result in the slower transmission of a nerve impulse supplying a target

effector muscle. A slowing in nerve speed may trigger disordered movement or an

inability to control muscular activity, all of which lead to a diminished quality of life.

Additionally, older adults exhibit varying degrees of loss in strength and muscle mass as

a result of these effects and may become more susceptible to the development of sarcopenia (e.g., age-related reduction in muscle mass). Longitudinal studies of aging have verified as much in measures of power and strength[70,71].

Commonly recognized in individuals with nerve injury or disease, declining PNS function often leads to neuromuscular dysfunction. However, age-related slowing of healthy motor nerves has been found in both humans and rodents[44,68,69]. Previous research identifies a linear relationship between a slowing in nerve speed and age ($\geq$ 60 yrs.) in those who are free of neuromuscular disease[67]. While the support for an age-related slowing of nerves exists, there is much still to be understood regarding potential mechanisms that could facilitate plasticity within the PNS.

Previous studies have examined the use of therapeutic modalities as a counteractive measure to nerve speed loss in those who have neurodegenerative diseases. The technique of manual loading and unloading of the muscle has shown promising results in the transmission of nerves[23,30]. Moreover, strength training has also proven to be a counteractive modality to nerve loss in previously injured nerves[16]. However, it remains unclear if resistance training can alter nerve function in healthy non-injured adults. Previous research has shown a gradual decline in nerve speed per decade of age, though parameters to combat these declines have not been fully elucidated[59].

Resistance training has long been prescribed to older adults as a means to long-term vitality. Those who remain active throughout life have been known to have improved mobility, more independence, and greater life expectancy[17]. Moreover, resistance training has also been used in the prevention and management of sarcopenia[9,72].While little is known about the effects of resistance training and nerve speed in healthy untrained individuals, there

have been favorable findings in chronically trained athletes[55]. Due to the benefits resistance training provides, it's plausible to consider resistance training as a method to counteract losses in nerve function.

Although previous studies have investigated training and nerve speed in adults, few studies have focused interventions on the time-course of nerve speed loss and possible adaptations training may have. Additionally, our understanding of nerve function in untrained healthy individuals is still unclear. Therefore, further investigation is needed to determine the age-related changes in nerve speed function and the potential role counteractive measures may afford in resisting nerve deterioration.

1.2. Purpose of the Study

The purpose of this study was two-fold: 1) To quantify the effects of hand grip resistance training on motor conduction velocity of the nerves for the hand muscles. 2) To quantify the relationship between age and nerve plasticity of the hand grip muscles.

1.3. Research Questions/Hypotheses

This study has the potential to build upon previous information on age-related nerve speed loss and provide further insight into the effects of resistance training and motor nerve speed. The following research questions have the potential to be answered by the present study.

- **Research Question #1:** What are the effects of hand grip resistance training on motor conduction velocity of the nerves of the hand muscles?

    Hypothesis #1: Resistance training exercises will increase motor nerve conduction velocity of the median nerve in both young and older adults.

- **Research Question #2:** Will age affect nerve plasticity with training?

  Hypothesis #1: Training-induced changes in conduction velocity will be attenuated with age.

  Hypothesis #2: Resistance training will increase nerve cross-sectional area in both young and older adults.

- **Research Question #3:** What are the effects of hand grip resistance training on maximal hand grip strength?

  Hypothesis #1: Resistance training will increase maximal hand grip strength in both young and older adults.

  Hypothesis #2: The magnitude of change will be smaller for older adults.

- **Research Question #4:** What are the effects of hand grip resistance training on muscle morphology?

  Hypothesis #1: Resistance training will increase muscle size in both young and older adults.

  Hypothesis #2: The magnitude of change will be smaller for older adults.

- **Research Question #5:** What are the effects of hand grip resistance training on manual dexterity?

  Hypothesis #1: Resistance training will increase manual dexterity in both young and older adults.

1.4. Significance of the Study

This study has the potential to enhance our understanding of the adaptability of the PNS. Information obtained may further our knowledge of the time-course of changes to the PNS in healthy un-injured adults. Moreover, this project may provide insight into the plasticity of the aging PNS. To date, it remains unclear if motor nerves can be altered in healthy non-trained individuals with such an intervention. The proposed study could provide valuable information to clinicians and therapists regarding the influence of resistance training on the speed of the nerves, such as changes that may be wanted for certain functional endeavors (e.g. gripping a cup or holding a pen). If our hypotheses prove right, this study would have a high potential to improve the quality of life and generate greater independence for our older populations.

1.5. Delimitations

1. All participants will be healthy, and free of neuromuscular disease as self-reported on a questionnaire.

2. All participants will be untrained (e.g. ≤ 2 x per week), as self-reported on a questionnaire.

3. Testing will consist of both voluntary and evoked contractions.

4. Only one of the gripping muscles in the forearm will be collected (e.g. flexor digitorum superficialis).

1.6. Limitations

1. Participants responded to either a posted advertisement or informational announcement and choose to volunteer on a volunteer basis. Thus, the process of subject selection was not truly random.

2. Differences in motivation levels between participants may have produced varying levels of effort during maximal contractions.

3. Participants selected for the training group performed an at-home intervention, therefore training adherence could have been potentially hindered.

4. Assessment of motor conduction velocity has many constraints that may not be consistently controlled, including:

5. Participant height.

6. Participant weight.

7. Participant sex.

1.7. Assumptions

1. Subjects responded to the health and exercise history questionnaire accurately and honestly.

2. All subjects refrained from extensive gripping and/or upper body resistance training activities throughout the study.

3. All subjects in the training group followed the training protocol precisely and accurately for the duration of the study.

4. All subjects gave maximal effort on all strength tests.

5. The equipment used to acquire all signals was calibrated and functioning properly.

6. The samples of young and older adults were similar in terms of population and fitness levels when compared to the normative values for their respective age groups.

CHAPTER II

LITERATURE REVIEW

2.1 Age-Related Changes to the Motor Unit

Campbell et al., 1973[6]

      In this study by Campbell et al., the authors sought to better understand the physiological changes that occur in aging muscles. Assessment of the extensor hallucis brevis muscle was used to determine motor unit (MU) size and number in older individuals. Additionally, nerve stimulation of the fastest fibers of the deep peroneal nerve was performed to determine the quality of nerve conduction. Results showed that older adults had increased MU size, a lower number of functioning MUs, and slowed nerve conduction. The representative changes in MU size are due to a MU remodeling phenomenon for which older adults compensate for the physiological loss of functional MUs.

Tomlinson and Irving, 1977[63]

      In a postmortem investigation, Tomlinson and Irving identified motor neuron number in the lumbosacral spinal cord. To estimate motor neuron number, nucleoli were counted in every fifth group of ten sections from the lumbosacral cord. Results showed that individuals beyond the age of 60 possessed diminished motor neuron count. Additionally, those ≥ 60 years, were found to have counts half the amount of which were

found in younger adults. Moreover, they concluded that neuronal cell loss was uniform across all segments of the spinal cord.

Doherty and Brown, 1997[13]

The purpose of this study was to determine the impact of aging on motor units (MU) and contractile properties of the thenar muscles in younger and older adults. Thumb flexion and abduction movements of the thenar muscle were used to measure the MU properties, while the median nerve served as the simulation site to verify the contractile properties of each individual. Increased MU size and slowed contractile speed were noted in the older group. It is suggested that these findings are modifications made due to the reduction of MU numbers commonly seen in older adults.

McNeil et al., 2005[40]

McNeil and colleagues aimed to estimate motor unit (MU) number across the life span (young, old, and very old) in men. The tibialis anterior muscle was used to determine estimates of MU properties based on a percentage (25%) of maximal isometric dorsiflexion contractions. Estimates of MU number were derived from action potentials produced during the dorsiflexion contractions and compound muscle action potentials found during nerve stimulation of the peroneal nerve. Results indicated that estimates of MU's were significantly reduced in the old versus young men and further reduced in the very old group. Interestingly, a reduced number of MU's in the old group did not yield reductions in strength. These findings indicate that a period of MU remodeling occurs through the age of 65 after which probable losses in MUs and strength occur.

<u>Lauretani et al., 2006</u>[(36)]

Lauretani et al. examined the effects of axonal degeneration on muscle density in older adults. Peripheral nerve function was measured by calculating the motor nerve conduction velocity of the peroneal nerve. Muscle size and density were quantified during a lower leg peripheral tomography (pQCT) assessment. Findings from this study revealed a negative association between age and nerve conduction velocity of the lower limb. Moreover, there was no relationship between nerve conduction velocity and muscle size, and muscle density. These findings indicate that a natural consequence of aging occurs in parallel between muscular tissue and degeneration of the peripheral nerves. This is due in part to a progressive loss of motor neurons and reduction in motor axons.

<u>Kung et al., 2013</u>[(33)]

The purpose of this study was to investigate motor unit (MU) changes in extremely old sarcopenic rats. The extensor digitorum longus muscle was used to quantify MU number and stimulation of the peroneal nerve to identify a single motor axon. MU's were classified based on functional response to sag and fatigue. Results showed that the oldest rats had a significantly lower number of MU's available as compared with other rats. Additionally, the oldest rats had 60% greater slow-twitch MU's than others, indicating reinnervation of muscle fibers which leads to compensatory mechanisms (e.g., MU remodeling).

<u>Piasecki et al., 2018</u>[(48)]

In this study, Piasecki et al. investigated the effect of age on motor unit (MU) behavior (size and number) in young, non-sarcopenic old, pre-sarcopenic, and in individuals classified sarcopenic. Additionally, muscle size and muscle strength of the vastus lateralis (VL) and tibialis anterior (TA) were measured. To obtain the compound muscle action potential for contractile

responses the femoral and peroneal nerves were stimulated. Both surface and intramuscular needle recordings were used to investigate MU behavior during contractions (25% of maximal contraction). Findings showed that MU size was higher in non-sarcopenic and pre-sarcopenic men compared to young men. In estimates of MU number, the TA muscle was 63-65% lower in older men compared to younger. Using the iMUNE method, the authors calculated values proportional to the MU number after accounting for muscle size. The TA was 48% lower in all older groups, whereas the VL was 33, 47, and 50% lower in non-sarcopenic old, pre-sarcopenic, and sarcopenic, respectively compared to younger males. Muscle size was shown to progressively decrease throughout the stages of sarcopenia. Those with sarcopenia were found to have lower strength than pre and non-sarcopenic men in the knee extensors whereas findings for the ankle dorsiflexors were somewhat preserved, albeit lower in pre-sarcopenic and sarcopenic men. Conclusions from this study indicate the MU remodeling process occurs earlier in the aging process than originally thought. Moreover, sarcopenic individuals failed to show an increase in MU size, which differentiates sarcopenic from pre-sarcopenic individuals.

Gilmore et al., 2018[21]

The purpose of this study was to understand the effect of young and very old age (≥ 80 yrs) on motor unit (MU) loss and the process of compensatory MU remodeling. MU action potentials were recorded at the anconeus muscle during elbow extensions (30% and 50% maximal voluntary contraction), while compound muscle action potentials were obtained through stimulation of the radial nerve. Results showed that MU numbers were lower in very old men when compared to younger, however, the MU size was not larger as expected. These findings provide evidence that MU remodeling and the reinnervation of nerves may reach a

particular threshold, despite a loss in MU number. Additionally, the authors noted that this may

be muscle-dependent and could also be due to habitual use.

2.1.1. Summary of "Age-Related Changes to the Motor Unit"

The physiological changes that occur with aging are synonymous with the changes to the

functional unit of the neuromuscular system. This natural occurrence will greatly alter one's

voluntary movement and physical capabilities. Moreover, changes within the central nervous

system aid in the declines commonly seen with aging (e.g. deficits in gross and fine motor

skills). These differences can be distinguished by the unit responsible for coordinating the

nervous and muscular system (e.g. motor unit). For the initiation of muscular contraction to

occur, a motor neuron (MN) must transmit signals (e.g. action potentials) through a descending

pathway to which they eventually innervate the muscle fibers of a motor unit (MU). Generally,

these MUs will decline throughout the aging process[40]. It is evident that by the 7th decade older

adults have 40% fewer functioning MUs than young adults[48].

These declines in MUs are precipitated by the loss of MNs which leave the MU

disconnected from its primary communicator. Denervation results when there is a breakdown or

death of the MN at the axon resulting in a lack of neural input to the muscle fibers. The process

of denervation has been said to significantly contribute to the development of muscle weakness

and frailty in older adults[2]. Initially, this is a temporary process relieved by compensatory

mechanisms of collateral reinnervation[12,37]. Reinnervation utilizes axonal sprouting through

nerve terminals to rescue the degenerated nerve. Over a period, the resulting development

continues in a cycle of denervation-reinnervation or MU remodeling.

As a result, MU remodeling leads to increases in MU size due to surviving MNs

innervating more muscle fibers. Using electrophysiological techniques, MU size (MUNE) can be

estimated through electromyography (EMG) and evoked nerve responses (e.g. nerve stimulation). A ratio may be used to determine the MU action potential during a low-intensity contraction and compound muscle action potential (CMAP) of the nerve at a supramaximal intensity. The subsequent findings provide estimates of increases in MU size due to the remodeling process, however, there remains fewer functioning MUs in older adults. Previous studies have verified these results in MU size and number[6,13,63]. Campbell and colleagues[6] found that older adults possessed increased MU size, lower functioning MUs, and slower nerve conduction of the extensor hallucis brevis muscle. In a postmortem study, individuals ≥ 60 years had half the amount of MUs as younger adult[63].

The reinnervation process is fleeting as the added metabolic stress eventually leads to the termination of the nerve[22]. Eventually, a reinnervation threshold is reached in which maintenance of remaining MUs is no longer possible. Previous literature has indicated that reinnervation of the muscle fibers ceases in very old men around the age of 85[21]. Moreover, it was noted that MU size can be differentiated between individuals with sarcopenia (age-related loss in muscle mass) from those who were pre-sarcopenic[48].

The aforementioned loss in MUs has been purported to associate with losses in muscle strength and muscle mass. McNeil et al.[40] indicated that reductions in strength were not associated with losses in MUs in the ankle dorsiflexors until the age of 65. Whereas, Piasecki et al.[48] found that knee extensor and ankle dorsiflexion strength was diminished in sarcopenic men. With consideration of muscle mass and muscle density, Lauretani et al.[36] did not report a relationship with axonal degeneration. These studies provide an understanding of the physiological and morphological alterations that occur to the MU throughout the aging process and the subsequent consequences to the neuromuscular system.

2.2. Age-Related Changes in Motor Nerve Conduction Velocity

Wagman and Lesse, 1951[67]

In this early study of human nerve transmission, Wagman and Lesse investigated the conduction velocity of the ulnar nerve across the lifespan. Subjects ranged in age from 3 to 83 years old and were free of neurological disease. Supramaximal percutaneous stimulation was applied to the ulnar nerve supplying the hypothenar muscles. Findings suggested that conduction velocity may decrease from the age of 60 on but could be seen as early as 50 years old. Moreover, a statistical difference in velocities was found when compared to younger adults. Of importance, this study reported that maximum conduction velocity of the ulnar nerves was found before the age of 10. The author's stated that the association between a slowing in conduction velocity and age could be due in part to a variety of factors such as selective degeneration of the largest fibers supplying the hypothenar muscles, lowered oxygen supply, or low temperature of the nerves.

Norris et al., 1953[44]

Norris et al. expanded on previous findings by Wagman and Lesse[67] looking at changes in conduction velocity in adults. 175 male participants were included in this study comprising 25 subjects per decade (3rd – 9th decade). Electrical stimulation was applied to the ulnar nerve of the left arm in three segments (axilla to wrist; elbow to wrist; and axilla to elbow). Determination of conduction velocity was taken on two separate visits with the mean conduction velocity being reported. The author's concluded that conduction velocity decreases with increasing age in all three segments of the ulnar nerve. Further, there were no significant differences between the conduction velocities of the upper and lower arm segments. A 0.18 m/s slowing in conduction velocity in the ulnar nerve per year of age was reported.

<u>Mayer, 1963</u>[39]

Mayer examined conduction velocity in subjects across the life span. Additionally, this report included findings on individuals with diabetes without evidence of peripheral neuropathy and in those who had diabetes and clinical peripheral neuropathy. Using a supramaximal stimulus, the median, ulnar, peroneal, and tibial nerves were examined. To understand conduction velocity across the lifespan, subjects were classified into three different groups (10 to 35 yrs, 36 to 50 yrs, and 51 to 80 yrs) and by health status. A significant change in conduction velocity wasn't present until after the age of 50 in subjects who were classified as healthy. Moreover, this change was more prominent in the distal portions stimulated. A slowing in velocity was confirmed between the 36 to 50 yrs group and the 51 to 80 yrs group, however, it was not significant. Diabetic subjects without peripheral neuropathy showed a greater affected conduction velocity in the 10 to 35 yrs old groups than the other groups. The conduction velocities of the other groups did not differ significantly from those of the healthy subjects. In those with diabetes and peripheral neuropathy, there was a slowing at each age group and nerve and to a greater degree than in those with diabetes and no peripheral neuropathy. The results of this study showed that nerves of the upper body were more affected than the lower body with age, however, obtaining a supramaximal response in the lower limb was more difficult with age.

<u>Dorfman and Bosley, 1979</u>[14]

In this study, Dorfman and Bosley examined age-related changes in the conduction velocity of the median nerve in older and younger adults. Median motor nerves were stimulated at a supramaximal intensity with an isolation transformer. A significant association between age and conduction velocity of the median nerve was found and resulted in an 0.15 m/s slowing per year for the motor fibers. These findings were similar to those found by Norris et al.[44].

<u>Stetson et al., 1992[59]</u>

Stetson et al. sought to determine if there was an association between age and nerve conduction velocity in the median nerve of 105 participants who did not regularly patriciate in high force or repetitive hand exertions. Sex was also considered (see *2.3.2 Sex and Conduction Velocity*). A supramaximal stimulus was applied to the dominant forearm. Results indicated that age was significantly associated with median nerve conduction velocity. Importantly, the author's noted a 0.8 m/s decrease in motor conduction velocity per decade of aging, however, this study included only subjects aged 20-66. The authors concluded similarly to others that decreased conduction velocity may be attributed to a reduction in nerve fibers or nerve diameter.

<u>Bouche et al., 1993[3]</u>

Bouche and colleagues studied the effect of age on the peripheral nervous system in those with and without risk factors. Individuals thought to have a risk factor were considered as those either having clinical factors as noticed by a neurologist, peripheral vascular issues, alcohol abuse, or abnormal biological results. Subjects were categorized into one of five groups based on age and risk factors (Group 1: young subjects, Group 2: subjects ≤ 80 without risk factors, Group 3: subjects > 80 without risk factors, Group 4: subjects ≤ 80 with risk factors, and Group 5: subjects > 80 with risk factors). An evaluation of the motor and sensory nerves was conducted to assess conduction velocities. The median and peroneal nerves were stimulated and measured for conduction velocity parameters. Findings from this study showed that median conduction velocity was the only motor parameter that statistically decreased in patients under 80. Additionally, significant changes occurred in subjects >80 in all conduction parameters. Between-group comparisons indicated that peroneal conduction velocity was significantly

different between groups 2 and 3. Moreover, older age (≤ 80 vs. >80) regardless of risk factors did show a decreased peroneal conduction velocity. With consideration of risk factors, significant differences were observed in the peroneal nerve. These results indicate that age and risk factors play a significant role in peripheral nervous system function.

Palve and Palve, 2019[47]

This study aimed to determine at which specific age significant changes in motor nerve conduction velocity occurred. Using a supramaximal stimulus, the median, peroneal, and tibial motor nerves were assessed across three age groups (group 1: 18-30 yrs, group 2: 31-45 yrs, and group 3: 46-60 yrs). Findings showed a linear slowing in conduction velocity with increasing age in all three motor nerves. Additionally, this slowing in conduction velocity was more pronounced in the nerves of the lower limbs (peroneal and tibial) than upper (median). The authors concluded that conduction velocity showed a prominent decreasing trend around ≥ 46 years of age. This may be due in part to a reduction in nerve fibers, nerve diameter, or a change in fiber membrane due to aging.

2.2.1 Summary of "Age-Related Changes in Motor Nerve Conduction Velocity"

Deterioration of the peripheral nervous system (PNS) is commonly associated with the natural progression of age. Previous research has investigated these changes to improve our understanding of the mechanisms causing contractile disturbances. The exploration of these mechanisms is typically utilized to detect peripheral dysfunction and is useful in identifying an association in slowed movement response. Outcomes of diminished muscular contraction are due in part to physiological alterations occurring in the transmission of a nerve impulse supplying a target muscle. Thus, examining the changes occurring in the PNS has an important role in our comprehension of the neuromuscular contractile response.

To understand physiological changes occurring in the transmission of a nerve impulse (e.g. action potential) a stimulus must be strong enough to reach a threshold value. This threshold value can be induced through transcutaneous electrical stimulation of a nerve. As a result, conduction velocity measures (NCV) can be calculated from the transmission of thousands of action potentials that fire along axons. Decreases in conduction velocity have been attributed to the degeneration of the largest fibers supplying the muscle. Moreover, the speed of this transmission can depend upon the size of the axon and the degree of its myelination (insulation surrounding the axon).

Early findings of motor conduction studies showed that conduction velocity decreases can be seen as early as the fifth decade[67]. These findings were further substantiated by Mayer [39]. Although, Palve and Palve[47] reported decreasing trends in motor conduction velocity around 46 years of age. The abundance of conduction velocity studies of the motor nerves supports a linear association with increasing age and a slowing in transmission speed. Changes per year of age are as much as 0.15 m/s to 0.18 m/s per year[14,44]. Additionally, Stetson et al.[59] reported a 0.8 m/s slowing per decade in individuals aged 20-66. Moreover, variations among the different nerve segments have been reported[39,44]. A study by Norris et al.[44] found that conduction velocity decreases with age at all three segments of the ulnar nerve. Specifically, the distal portions of the nerve have been found to have greater slowing than proximal sites[39].

Results of these studies substantiate the underlying physiological alterations occurring throughout the aging process. Measures of conduction velocity are indicative of ongoing axonal impairment to the neuromuscular system, though this disruption is not complete. Studies have shown that repair and regeneration of nerves can occur with damage so it is reasonable to consider plasticity changes in healthy older adults[16,20,23,30]. It is proposed that the slowing in

conduction velocity may be counteracted through preventative measures, however, it has not been fully elucidated in older adults.

2.3. Variables Influencing Conduction Velocity

2.3.1. Height and Conduction Velocity

<u>Campbell et al., 1981[5]</u>

Campbell and colleagues investigated height and its relationship with conduction velocity. Peroneal nerve conduction velocity was obtained through stimulation of the fibular head and ankle and recorded at the extensor digitorum brevis muscle. Findings showed that peroneal conduction velocity was highly correlated inversely with body height. Moreover, they concluded that height explained almost 50% of the inter-subject variability in conduction velocity. It is noted that abrupt axonal tapering may occur in taller subjects which causes a greater amount of the distal nerve to comprise of smaller axons resulting in a lower average conduction velocity.

<u>Soudmand et al., 1982[58]</u>

Soudmand et al. sought to determine if differences between lower and upper limb conduction velocity exist with consideration of height. Forty-one subjects were stimulated bilaterally at the median and peroneal nerves. Peroneal conduction velocity was proven to be significantly inversely correlated to height, however median conduction velocity was not. In determining intrasubject variability when comparing side to side there were favorable correlations in the upper limbs (median nerve), although the lower limbs (peroneal nerve) showed less correlation. This information supports previous findings that reported a slowing in conduction velocity of the lower limbs and distal segments. Moreover, this study identified conduction velocity differences in the comparison of the upper and lower limbs. This indicates

that the distance an axon travels (or axonal tampering) plays a key part in the transmission of a signal to the muscle.

<u>Rivner et al., 1990[51]</u>

Rivner et al. investigated how height and nerve conduction velocity measures correlate in adults. Conduction velocities were measured in the peroneal, tibial, and median nerves. Additionally, the distal lower axonal length and upper axonal length were measured. Participants were asked to confirm their height and age verbally. Height was found to be inversely correlated with both peroneal and tibial conduction velocity, but not with median conduction velocity. Moreover, distal lower axonal length was also correlated with peroneal and tibial conduction velocity. Further discussion of the variation of axonal diameter and the distance an impulse must travel due to height was alluded to. Similar to other studies the concept of a tapered segment hypothesis in which the larger proportion of the distal segment consists of slower conducting axons could explain this inverse relationship to height, particularly in the lower limbs[5,58].

<u>Rivner et al., 2001[52]</u>

A second study by Rivner et al. studied the influence of age and height on nerve conduction velocity. Stimulation was conducted along two different motor nerves (peroneal nerve and ulnar nerve) to calculate conduction velocity. The peroneal nerve was stimulated at the fibular head and the dorsum with recording done at the extensor digitorum brevis muscle. The ulnar nerve was stimulated above the ulnar groove and 7 cm from the recording site of the hypothenar eminence. Results were indicative of a negative correlation between age and conduction velocity of the peroneal and ulnar nerves. Similarly, a negative correlation was found between conduction velocity and height and proved to be more responsible for the variability in

conduction velocity. With measures combined, both age and height accounted for over 10% of the variance in conduction velocity in the ulnar nerve and over 15% in the peroneal nerve. These findings support the consideration of both the measures of age and height when studying nerve conduction velocity measures.

Thakur et al., 2011[62]

Thakur et al. sought to understand the association of height with nerve conduction parameters in the upper and lower limbs. The median, ulnar, radial, peroneal, and tibial nerves were stimulated bilaterally. Results from this study found that the median and ulnar nerve conduction velocity were significantly correlated with height. This was true of both the right and left limbs tested. Further, this study found that median conduction velocity was associated with height which had not been previously verified. Additionally, none of the lower limb nerves examined showed correlations with height, which is contradictory to previous reports. The authors contribute this result to a poor sample size (n= 34).

Naseem et al., 2016[66]

In this study, Naseem et al. explored upper limb motor conduction velocity as it pertains to height. Stimulation was conducted on the median and ulnar nerves bilaterally to obtain conduction velocity. Recording electrodes were placed on the abductor pollicis brevis and abductor digiti minimi, respectively. Statistics were arranged into two sex groups (male and female) on each arm. A significant negative correlation with height was found for all nerves and all sexes in the study. The findings from this study indicated an association between height and median and ulnar nerve velocity which had been previously verified.

2.3.1.1 Summary of "Height and Conduction Velocity"

Many various physical characteristics are said to aid in the variability of conduction velocity. The length dependency of the transmission of a nerve has been much discussed in the literature. Most studies have identified the nerves of the lower limbs to be more affected due to axon size and the distance gradient necessary for a nerve to propagate. These findings have resulted in inverse relationships between conduction velocity and height[5,51,52,58]. In particular, Rivner et al.[51] found that both peroneal and tibial conduction velocity was inversely correlated to height as well as measures of distal lower leg axonal length. Moreover, Campbell et al.[5] found that 50% of the inter-subject variability in conduction velocity was explained by height. Additionally, Rivner et al.[52] reported that both age and height accounted for over 15% of the variance in the conduction velocity of the peroneal nerve. Studies of the lower limb have noted that these associations may be due to the concept of abrupt axonal tapering. Axonal tapering occurs in taller subjects due to a greater amount of the distal nerve composing of smaller axons, resulting in a slower average conduction velocity.

Previous studies assessing height and upper limb conduction velocity found no associations[58]. However, Rivner et al.[52] reported that both age and height accounted for over 10% of the variance in a study of the ulnar nerves. Further, other studies have shown significant associations between height and conduction velocity of the median and ulnar nerves [62,66]. Due to the inverse correlation height has on conduction velocity measures it would be appropriate to consider this measure when studying nerve conduction.

2.3.2 Sex and Conduction Velocity

LaFratta and Smith, 1963[34]

This early study by LaFratta and Smith first categorized sex differences in conduction velocity. Stimulation of the ulnar nerve was conducted on 128 males and 21 females with the recording electrodes placed over the abductor digiti minimi muscle. The ulnar groove was stimulated at the elbow and the wrist on the left arm. For comparison of sex differences, 20 female participants and 20 male participants' data were randomly selected for consideration. It was reported that women had a significantly greater mean conduction velocity as compared to males. The author's postulated that these results could have occasional application in clinical evaluations of patients.

Stetson et al., 1992[59]

Stetson et al. sought to determine if there was an association between sex and nerve conduction velocity in the median motor nerve. A supramaximal stimulus was applied to the dominant forearm of each participant. Results showed that sex was not significantly associated with median nerve conduction velocity. Sex and height were highly correlated although this did not change associations with conduction velocity. The authors concluded sex is not the most important factor in the prediction of motor conduction velocity.

Robinson et al., 1993[53]

Robinson et al. investigated the influence of height and sex on conduction velocity. The median, ulnar, peroneal, and tibial nerves of 54 men and 62 women were observed. Initial raw data revelated significantly faster conduction velocities in all nerves except the median nerve in female participants. However, when correcting for height, conduction velocity differences between sexes disappeared. These findings indicate that motor nerve sex differences can be

found. Additionally, height which is known to have great variability between sexes is an important variable in the consideration of nerve conduction parameters.

Hennessey et al., 1994[27]

Hennessey and colleagues studied the effects of sex and arm length on nerve conduction velocity of the upper limb. Forty-four subjects (male: n=23, female: n=21) participated in this study. The median and ulnar motor nerves were stimulated with recording electrodes placed over the abductor pollicis brevis and abductor digiti minimi, respectively. No differences between sex were found regarding conduction velocity. Moreover, no correlations were found in the comparison of arm length to conduction velocity.

Gakhar et al., 2014[18]

Gakhar et al. examined the nerve conduction properties in males and females between the ages of 20-30 years old (males: n=35, females: n=35). The median and ulnar nerves were stimulated with the abductor pollicis brevis and abductor digiti minimi, respectively. Findings revealed that females had a significantly greater median conduction velocity than their male counterparts. Similar results were reported for the ulnar nerves; however, they were not significant. These results correspond to previous findings and help to identify sex differences across the age span.

Kumar and Prasad, 2016[32]

In this study, Kumar and Prasad investigated the conduction velocity of the median and tibial nerves between the sexes. Participants aged from 20-60 years old (male: n=80, female: n=38) and were free of any neurological disorders. The median nerve was stimulated at a point slightly ulnar to the tendon of the flexor carpi radialis and at the antecubital region with the recording electrode placed halfway between the midpoint and distal wrist crease and the 1st

metacarpophalangeal joint. The tibial nerve was stimulated slightly posterior to the medial malleolus and at the mid popliteal fossa with the recording electrode placed over the medial foot. The authors reported men had a higher and more significant median and tibial conduction velocity than their counterparts. They concluded that while their findings have similarities with previous studies, height was not considered as a covariate along with sex.

2.3.2.1 Summary of "Sex and Conduction Velocity"

The influence of sex on conduction velocity is an additional measure often assessed in nerve conduction measures. Many studies have reported significant differences in conduction velocity between sexes in the ulnar nerves[18,34]. In a study of young adults, Gakhar et al.[18] indicated females had a greater mean conduction velocity of the median nerve than males. These findings provide the support that females possess a greater capacity to generate faster conduction velocities of the upper limbs.

However, sex differences can be linked to differences in height. Previous studies have shown the importance of considering height when deciphering conduction velocity between sexes. Robinson et al.[53] observed sex differences in conduction velocity in several nerves without respect to height. Upon correction, the authors found no significant differences between males and females. Further, Kumar and Prasad [32] reported faster conduction velocities of the median and tibial nerves in males, however, they noted height was not considered a covariate. Moreover, Stetson et al.[59] found no differences in conduction velocity with consideration of sex and height. Arm length which is related to height was also found to not correlate with conduction velocity between sexes[27]. Although few studies have shown that independent of height, sex differences in conduction velocity occur there is more evidence to support a correction for height when measuring conduction velocity.

2.3.3 Body Mass and Conduction Velocity

Elam, 1987[15]

Elam investigated the relationship between body fat and tibial nerve conduction velocity in college athletes. The body fat of eighteen male athletes was measured using hydrostatic weighting. Moreover, relative body fat was calculated from residual long volume and body density. Tibial nerve conduction velocity was measured on each participant utilizing their right leg. A significant relationship between lower body fat and faster tibial nerve conduction velocity was found in this study. These results indicate that athletes with greater body mass could be affected in athletic performance due to slower nerve transmission targeting the lower limbs. It is suggested that more thorough investigations are needed to assess body mass and conduction velocity parameters in other specific populations.

Simmons et al., 1997[56]

In this letter to the editor, Simmons et al. discussed their findings on ulnar nerve conduction velocity and overweight individuals. Stimulation of the ulnar nerves was performed and recorded from the hypothenar muscles. Subjects were classified as normal weight, overweight, and severely overweight according to BMI. Findings showed that conduction velocity across the elbow was significantly faster in overweight individuals than in the normal group. The authors postulated that their results were due to technical issues involving the overestimation of nerve length as a result of adipose tissue around the elbow.

Buschbacher, 1998[4]

In this study, Buschbacher aimed to understand the effect of body mass on nerve conduction measures. The median, ulnar, peroneal, and tibial motor nerves were stimulated. Additionally, sensory and mixed nerves were also measured. To quantify body mass, body mass

index (BMI) was measured by dividing weight (kg) by height (m). Nerve conduction velocity was found to not be affected by body mass in any nerve type. These findings differ from those of Elam[15] in which a relationship was found in athletes. However, this study provides a more comprehensive assessment of motor and sensory nerve transmission as it pertains to body mass.

Landau et al., 2005[35]

In this short report, Landau and colleagues investigated the impact of body mass index on ulnar nerve conduction velocity in patients with ulnar neuropathy at the elbow, in those with carpal tunnel syndrome, and healthy controls. However, only data for healthy controls were provided. BMI was calculated as stated by the subject's height and weight. The ulnar nerves were stimulated with recording electrodes placed over the belly of the abductor digiti minimi. Similar to Simmons et al.[56] this study found that controls demonstrated positive correlations between increasing BMI and faster ulnar conduction velocity above the elbow. Moreover, the authors also noted that above the elbow conduction velocity was slower in those with low BMI. This study did not consider the effect of temperature which may be increased in heavier individuals due in part to added insulation.

Awang et al., 2006[1]

Awang et al. studied the influence of body mass on the motor conduction velocity measures in Malays. Participants were placed into four different categories based on their BMI and supramaximal stimulation of the median, ulnar, and peroneal nerves was conducted to assess measures of conduction velocity. A slowing in conduction velocity was observed with increasing BMI in the three motor nerves measured. These findings contradict previous results by Buschbacher[4] in which no effect occurred in conduction velocity with consideration to BMI.

<u>Rami et al., 2012[49]</u>

Rami et al. sought to determine the effect of body mass on nerve conduction parameters in Indian populations. Additionally, age was considered a covariate (young: 18-45 yrs; older: 46-66 yrs). Conduction velocity of the median and ulnar nerves of the upper body and the peroneal and tibial nerves of the lower body was measured. Recordings were made bilaterally, however, only the data from the right side was presented. BMI was obtained using the previous aforementioned method[4]. Results showed no significance between body mass and a slowing in nerve conduction velocity in the younger age group. However, there was a consensus that the older group showed a more significant slowing in conduction velocity with increasing BMI in the ulnar nerve. Although significant, the authors dismissed this finding as no observable trend in slowing was observed in any other nerve studied.

2.3.3.1. Summary of "Body Mass and Conduction Velocity"

Body mass parameters are of interest in conduction velocity studies as additional adipose tissue may alter nerve transmission to varying degrees. In a study of athlete's Elam[15] observed a significant relationship between lower body fat and faster conduction velocity in the lower limb. Further, Awang et al.[1] reported a slowing in conduction velocity with increases in body mass in both the upper and lower limbs. Conversely, some studies have suggested that increased body weight is associated with faster conduction velocities[35,56]. Landau and colleagues[35] reported positive correlations between increased body mass and faster ulnar conduction velocity. Moreover, they noted conduction velocity was slower in those with low body mass. It has been suggested that an overestimation of nerve length as a result of additional adipose tissue surrounding the nerve may result in differing viewpoints on body mass and conduction velocity.

Moreover, temperature variability in heavier individuals was not considered in these studies and may contribute to these findings.

2.3.4. Temperature and Conduction Velocity

Henrickson, 1956[28]

      Henrickson was the first to investigate the relationship between skin temperature and nerve conduction velocity. His thesis concluded that skin temperatures between 29°C to 38°C produced decreased nerve conduction velocity by 2.4 m/s for each 1°C in response to reduced intramuscular temperature surrounding the muscles near the median and ulnar nerves. This seminal work highlighted the importance that many physiological factors such as skin temperature may induce in nerve conduction velocity studies.

De Jesus et al., 1973[10]

      De Jesus et al. sought to further understand the effect of cold on nerve conduction of the fastest and slowest nerve fibers. Electrical stimulation was applied to the median nerve at the elbow and wrist. During this study, the arm was cooled at 20°C until the desired hand temperature was maintained for 10 minutes without direct cooling. Upon the initial stimulations, the arm was gradually warmed and stimulations were repeated at increments of 5°C to 35°C to 38°C. Surface temperature and near nerve temperatures were recorded multiple times at different surface temperature sites. A linear relationship was reported between skin temperature and conduction velocity of the median nerve.

Halar et al., 1980[26]

      The purpose of this study was to decipher whether correlations between skin temperature and tibial motor nerve conduction velocity exist. Additionally, this study aimed to determine the relationship between skin surface temperature and subcutaneous and intramuscular skin

temperatures. Initially, all measures (conduction velocity, skin surface temperature, and subcutaneous and intramuscular temperatures) were taken at ambient room temperature (25°C). This was followed by recording all measures after the calf muscle was cooled (26°, 28°, and 30°C). Tibial conduction velocity was found to significantly correlate with corresponding changes in all temperature variables. These were reported as 1.4 m/sec/1°C of change in skin surface temperature, 1.7 m/sec/1°C of change in subcutaneous temperature, and 1.1 m/sec/1°C of change in intramuscular temperature. The secondary question in determining the relationships between various temperature variables found that all methods significantly correlated to one another. While the results of this study did not find correlations between ambient temperature and conduction velocity, the authors recommend skin temperature measures to ensure consistency in nerve conduction parameters.

Halar et al., 1983[25]

Halar et al. investigated nerve conduction velocity and temperature corrections of the upper extremities. Median and ulnar conduction velocities were obtained using a supramaximal stimulus. Investigators measured skin temperature and near nerve temperature at each site at ambient room temperature (baseline) and after cooling on the forearm (26°, 29°, and 30°C). Skin temperature was measured at the volar surface of the forearm, wrist, palm, and fingers. Near nerve temperature was measured at the forearm, mid palm, thenar, and hypothenar eminence. After cooling, significant decreases were found in the conduction velocity of the median and ulnar nerves. Further, a higher correlation between skin and nerve temperature after cooling than at ambient temperature was also reported. The skin temperature of both nerves was significantly correlated to nerve conduction velocity. The median nerve was altered by 1.5 m/sec/1°C in change of the wrist skin temperature, while the ulnar nerve was altered by 2.1 m/sec/1°C in

change. The findings from this study suggest that temperature corrections be made when the wrist skin temperature is outside the range of 29.6 – 36.4°C when considering these nerves.

Geerlings and Mechelse, 1985[19]

In this study, Geerlings and Mechelse aimed to discover the minimal warm-up time to calculate the change in conduction velocity as it pertains to tissue temperature. Conduction velocity was measured at the median nerve while recording from the abductor pollicis brevis muscle. To account for skin temperature, measures were taken at the volar surface of the wrist and mid part of the forearm. In the first experiment, the participant's arms were cooled to 20°C using a water immersion technique, then warmed and maintained at 34°C with infrared radiation. A second experiment was conducted by placing the arm warm in running water until it reached 34°C. A gradual change in conduction velocity and skin temperature was identified in both experiments.

Moses et al., 2007[43]

Moses et al. investigated the relationship between skin temperature and the neuronal characteristics of the motor nerves of the upper limbs. The goal of this study was to determine the potential relationship between temperature and nerve conduction velocity when skin temperature is not altered (cooled or warmed) as was previously done in most studies. The median, ulnar nerves were stimulated, while a thermometer probe measured skin temperature at the medial distal crease of the wrist throughout testing. The room temperature was kept consistent between 17.6° and 26°C. Results showed that skin temperature and nerve conduction velocities of the upper limbs were linear but no correlation was sufficient enough to produce a regression analysis. This was due to a wide variety of values and narrow temperature differences. However, each nerve was found to correlate well with previous studies that manipulated skin

temperature[19,25]. It was concluded that monitoring and understanding normative values in skin temperature and deciphering which measures are of importance are vital to diagnosing clinical neuropathies.

<u>Richards et al., 2021[50]</u>

Richards and colleagues investigated the effect of local cooling on nerve conduction velocity and motor unit (MU) behavior. The primary purpose of the study was to determine if MU firing rates change similarly after cooling to those of nerve conduction velocity measures. The ulnar joint was cooled for 20 minutes with ice. Supramaximal stimulation of the ulnar nerve was conducted and recorded from the first dorsal interosseous (FDI) muscle. To obtain MU firing rates surface electrodes were placed over the FDI muscle and subjects performed repetitions at 30% of their maximal effort for decomposition of the MU action potentials. All measures (nerve stimulation and MU recordings) were performed pre-cooling, post-cooling, and 15 minutes after rewarming in ambient temperature. Ulnar nerve conduction velocity showed a significant difference between time points (pre-cooling and post-cooling, and pre-cooling and 15 minutes rewarming) when measured across the elbow joint. Significant differences in MU firing rates were observed between pre and post-cooling and pre-cooling and 15 minutes of rewarming. This indicates that an association between ulnar nerve conduction velocity and MU firing rates in the FDI muscle occurs. The authors acknowledge that cooling may subsequently increase the axonal refractory period which has been linked to axonal demyelination, a consequence of impaired conduction velocity.

2.3.4.1. Summary of "Temperature and Conduction Velocity"

Consistent skin temperature is considered one of the greatest sources of error in the assessment of nerve conduction velocity[45]. The variability in the temperature surrounding a

nerve, particularly in the distal regions has been shown to greatly influence conduction latency. Henrickson[28] was the first to report this relationship and found that nerve conduction velocity decreased by 2.4 m/s for each 1°C in response to decreases in muscle temperature for the median and ulnar nerves. More recently, Halar[25] found similar alterations in the ulnar nerve (2.1 m/sec/1°C in change). Other examinations of the influence of temperature have been observed through various cooling and warming methods as well as different measuring techniques. Halar et al.[26] found significant correlations with multiple measuring variables (skin temperature, subcutaneous temperature, and intramuscular temperature) and conduction velocity in the tibial nerve. Moreover, positive linear relationships have been reported in several studies[10,19,25,43]. Recently, Richards et al.[50] studied the effect of local cooling on nerve conduction velocity and motor unit (MU) behavior and found an association between ulnar nerve conduction velocity and MU firing rates pre to post-cooling in the first dorsal interosseus muscle. This is believed to be due to an increased axonal refractory period known to be associated with axonal demyelination, commonly seen in impaired conduction velocity. It is suggested that skin temperatures be kept consistent (29.6 – 36.4°C) when investigating the nerves up the upper limbs.

2.4. Age-Related Strength Parameters and Conduction Velocity

Metter et al., 1998[41]

Metter et al. sought to understand the relationship between peripheral motor nerve conduction velocity and the age-associated loss of grip strength. The measures obtained in this study were conducted as a part of the Baltimore Longitudinal Study of Aging from 1967-1970. Males who were free of neuropathic or myopathic disorders and could be examined every 1 to 2 years were included. To assess conduction velocity, electrical stimulation was applied to the median nerve of the right arm with recording electrodes placed on the abductor pollicis brevis.

Hand grip strength was measured using a hand grip dynamometer with the highest of the three trials being considered their best. As previously understood, an age-related linear decline in median conduction velocity was found. Importantly, median nerve conduction velocity significantly contributed to grip strength. The results of this study highlight the importance of preserving muscular strength and peripheral nerve function over time.

Strotmeyer et al., 2009[60]

Strotmeyer et al. examined the effects of sensory and motor function on quadriceps strength in older adults. Participants were a part of an ongoing cohort across various testing sites. Motor nerve conduction velocity was measured from the peroneal nerve of the right leg. To quantify lower extremity strength, knee extensions and ankle dorsiflexions were performed. For knee extensions, three trials were performed and the best of three was calculated as maximal torque (Nm). One year following peripheral nerve measures, ankle dorsiflexions were measured with the best of three trials calculated as maximal torque (Nm) produced. Poor motor conduction velocity was not associated with weaker quadriceps strength; however, the motor amplitude was. It is unclear as to why conduction velocity showed weaker associations with strength, however, the correlation may be indicative of more axonal damage occurring rather than demyelination of the nerve which is known to be a factor with conduction velocity.

Ward et al., 2014[71]

In a longitudinal study of older adults, Ward et al. investigated whether sensorimotor nerve function predicts quadriceps strength. Beginning in year 4 of the study, nerve function and strength measures were measured semiannually over six years. Peroneal conduction velocity was measured at the extensor digitorum brevis muscle. To measure isokinetic strength, three to six maximum knee extensions were performed and the best three were averaged. Findings showed

that motor conduction velocity was not related to strength longitudinally, however, the motor amplitude was. The results of this study found that motor amplitude and sensory measures were more predictive of strength deficits commonly seen in older adults.

2.4.1. Summary of "Age-Related Strength Parameters and Conduction Velocity"

One of the most common changes exhibited by older adults is an age-related decline in muscle size (sarcopenia) and muscle strength (dynapenia) which is dependent on the integrity of the peripheral nerves. As evidenced, peripheral nerve function declines as early as 50 in healthy adults[67]. Consequently, this deterioration may lead to subsequent declines in functional ability. In a study of hand grip strength, Metter et al.[41] found a significant association between conduction velocity of the median nerve and grip strength in older adults. However, studies of lower body strength did not yield similar results in slowed conduction velocity[60,71] . Results from the lower body studies did indicate changes in the amplitude of the compound muscle action potential (CMAP) rather than the latency of the impulse. Those findings provide a greater understanding of axonal damage and weaker strength occurring in the lower body with age. It should be addressed that the differences seen in the upper versus lower body studies could be due to the size of the nerve supplying the muscles examined. There is limited research investigating age-related strength parameters on conduction velocity in limb differences. Moreover, there is a minimal understanding of the short-term effects of these variables as multiple studies were longitudinal.

2.5. Effects of Training on Motor Nerve Conduction Velocity in Injured Nerves

2.5.1. Resistance Training: Diabetic Peripheral Neuropathy

Kluding et al., 2012[31]

In this study, Kluding et al. examined the effects of a 10-week aerobic and resistance training program on patients with diabetic peripheral neuropathy. Peroneal and tibial nerves were stimulated before and after the intervention. Each training session contained either an aerobic workout or a resistance program which included a progressive overload in either duration or repetitions throughout the study. Exercises were performed 3 days per week for the first 3 weeks, then increased to 4 days per week until the conclusion of the study. Findings showed that no significant increases in peroneal and tibial conduction velocity were found. It should be noted that a lack of a control group could have limited the findings of this study.

Stubbs Jr. et al., 2019[61]

Stubbs and colleagues investigated the impact of 12 weeks of structured physical activity on four experimental groups in individuals with chronic type 2 diabetes and length-dependent distal symmetric polyneuropathy (≥ 10 yrs). Groups consisted of aerobic training, isokinetic strength training, aerobic-isokinetic (combined), and non-exercise. Each of the training groups exercised 3 times per week. Electrical stimulation was applied and recorded from the tibial and peroneal nerves at baseline, after the intervention, and 12 weeks post-intervention. When analyzed together, no exercise group exhibited significant changes in motor nerve conduction velocity. Moreover, no significant differences were observed within groups for either the tibial or peroneal nerves.

Gholami et al., 2021[20]

Gholami et al. studied the effects of 12 weeks of resistance training on nerve conduction velocity in older patients (≥ 60 yrs) with diabetic distal symmetrical polyneuropathy. Circuit training was conducted 3 times per week at 50-60% 1RM. Peroneal motor conduction velocity was obtained at baseline and 48 hours after the last exercise session. Results showed that 12 weeks of resistance training increased peroneal motor nerve conduction velocity by 7% in the intervention group. Additionally, increases in sensory conduction velocity were found. It was noted that these adaptations are likely due to the morphological and functional adaptations to a training stimulus.

2.5.2. Resistance Training: Multiple Sclerosis

Eslami et al., 2019[16]

Eslami et al. examined the effects of resistance training on nerve conduction speed in patients with multiple sclerosis. Ten participants were asked to participate in resistance training three times per week at 55 to 65% of their 1RM. The training protocol consisted of low resistance exercises such as pressing the foot, opening the knee, bending the knee, and lifting the heel. Results found that resistance training increased conduction speed in multiple sclerosis patients. These findings indicate that functional improvements can occur in patients with neurodegenerative diseases with appropriate training protocols.

2.5.3. Exercise Training: Nerve Crush

van Meeteren et al., 1997[64]

This study investigated the effects of exercise training after sciatic nerve crush in rats. This study aimed to determine if training improved sensorimotor recovery and regeneration of nerves after injury. Twenty Wistar rats were randomly selected to participate for 24 days by

having to maximally extend on both hind paws to drink bottles of water that were placed at a difficult height (approximately 4 hrs per day). Using needle electrodes, rats were anesthetized and the tibial and sciatic nerves were stimulated. Motor and sensory nerve conduction velocity were only measured in the later stages of the study at 50, 75, 100, 125, and 150 days post-operation. Conduction velocity results were established by expressing values of the crushed paw as a percentage of the non-injured paw. Findings showed that by day 125 motor conduction velocity of the trained paw was near normal values when expressed as a percentage of the non-injured paw. This study highlights conditions in which exercise training induces nerve regeneration after injury.

2.5.4. Neural Mobilization: Carpal Tunnel and Stroke

Goyal et al., 2016[23]

Goyal and colleagues investigated the effects of neural mobilization (loading and unloading) of muscles on motor nerve conduction velocity in patients with carpal tunnel syndrome. Participants included thirty females between the ages of 35 and 65 who had unilateral carpal tunnel syndrome. Patients were placed into two groups (Group A: therapeutic ultrasound, or Group B: neural mobilization). The procedure for Group B consisted of loading the median nerve (elbow extension) and unloading (cervical ipsilateral lateral flexion). This was done two times per week for three weeks. Stimulation was conducted on the median nerve at the carpal tunnel with recording electrodes placed on the abductor pollicis brevis. Results showed that after three weeks of neural mobilization (Group B) significant differences in conduction velocity were found. Findings from this study support the therapeutic effect neural mobilization may have on patients with neuropathic issues.

<u>Kang et al., 2018</u>[30]

In this study, Kang et al. explored changes in peripheral nerve conduction velocity in stroke patients using dynamic neural mobilization. Inclusion for the study consisted of stroke with a diagnosis of hemiplegia with an onset of fewer than six months, no limitation in passive range of motion on the paretic arm, and no paresthesia on the affected area. Participants were placed into one of two groups (Group I: neural mobilization or Group II: arm dynamic neural mobilization). Training for Group I consisted of having their arm extended for 20 seconds with no dynamic movement occurring. In training Group II, a therapist dynamically mobilized the nerve once every 2 seconds for 20 seconds with the use of a metronome in different maneuvers for each nerve. Each training session consisted of three sets of ten per session and was performed four times per week for four weeks. Stimulation of the radial, median and ulnar nerves was conducted pre and post-experiment. Recording electrodes were placed on the brachioradialis, abductor pollicis brevis, and abductor digiti minimi, respectively. It was reported that the conduction velocity of the radial, median and ulnar nerves was significantly different between groups at all segments, except the ulnar nerve when stimulated above the elbow. The authors concluded dynamic neural mobilization had a greater impact on increasing peripheral nerve function in stroke patients.

2.5.5. Summary of "Effects of Training on Motor Nerve Conduction Velocity in Injured Nerves"

Damage to the peripheral nerves frequently results in deficits to the motor and sensory response mechanism. This is due in part to a partial or total loss of motor neurons and may result in muscle weakness, delayed reflex time, or coordination issues. However, this damage is in not complete as it is generally accepted that nerve plasticity occurs in previously injured nerves

through the regeneration of damaged axons (MU remodeling). To counteract declines in nerve conduction velocity, several interventions have utilized various training modalities to offset the motor issues associated with peripheral nerve dysfunction.

Resistance training interventions frequently target diabetic peripheral neuropathy due to its high prevalence. However, there are no clear assumptions on resistance training's ability to address motor deficits in those individuals. Kluding et al.[31] and Stubbs Jr. et al.[61] reported no significant increases in conduction velocity speed after several weeks of aerobic and resistance training. Whereas, Gholami et al.[20] found a 7% increase in conduction velocity after 12 weeks of training in older adults. Similar to Gholami et al.[20], Eslami et al.[16] found increases in conduction speed when training at 55 to 65% 1 rep maximum in patients with multiple sclerosis. It's plausible to speculate that due to Kluding et al.'s [28] lack of a control group and the intensity of the training sessions the study designs may have overlooked possible adaptations that could occur.

Promising results have been observed in the manual loading and unloading (e.g. neural mobilization) of the upper body in studies of stroke and carpal tunnel syndrome patients[23,30]. These findings provide support for the therapeutic effect that neural mobilization has in the restoration of function in previously injured nerves. Moreover, van Metteren et al.[64] reported a regeneration in function and subsequent conduction velocity in rats after sciatic nerve crush. Findings showed normal conduction velocity values within 125 post-operation after rats completed 24 days of leg extension. Training has demonstrated the ability to alter conduction velocity in several studies, although it may be dependent upon the severity of one's condition and the intensity of the training. Consideration of the type of training should support the overall goals (i.e. increased function, or regeneration of nerves) of the patient.

2.6. Effects of Resistance Training on Motor Nerve Conduction Velocity in Non-Injured Motor Nerves

Sale et al., 1982[54]

Sale and colleagues examined neuromuscular adaptations following strength training and immobilization. Investigating the thenar muscles, one group participated in 18 weeks of training and 5 weeks of immobilization (Group A), while a second group underwent 5 weeks of immobilization and 18 weeks of training (Group B). Strength training consisted of sets of thumb abduction and isometric training three times per week. For the immobilization, the thumb, wrist, and elbow joints were immobilized using a fiberglass cast. Conduction velocity of the median nerve was conducted using supramaximal stimuli at the wrist and elbow. These measures were obtained within 2 hours of the end of immobilization and within 48 hours of the conclusion of training. With groups combined, immobilization and strength training did not affect motor nerve conduction velocity. However, Group B had a small but significant difference in conduction velocity from post immobilization to post-training. The authors concluded this difference may be due to method error.

Sale et al., 1983[55]

In a second study by Sale et al, the authors investigated neuromuscular function in a small population of bodybuilders and weightlifters (e.g. weight trainers). Median motor conduction velocity was measured from the thenar muscles of the weight trainers and a control group. Findings indicated that those who were weight trained had an 8% greater conduction velocity than those who did not. This result may be due in response to the functional overload weight trainers place on their nerves which may lead to increases in nerve diameter and myelin thickness.

Sleivert and colleagues examined the influence of a strength-sprint training sequence on multi-joint power output in untrained males. As a secondary measure, tibial nerve conduction velocity was investigated throughout the study. Thirty-two men participated in either a sprint-sprint, multi-joint, or single-joint strength-sprint group. Each group was tested before training, after 8 weeks of training, and after an additional 6 weeks of sprint training. Three trials were taken with the closest two values being averaged to determine the conduction velocity of the tibial nerve. Results showed that conduction velocity significantly increased from pre-values in all training groups after 14 weeks of training. Additionally, there was a significant difference in the conduction velocity of the multi-joint training group from pre-testing to 8 weeks of training.

Padkao and Prasertsri, 2019[46]

This study looked at the effects of high-intensity interval training and upper and lower limb resistance training in university athletes over 8 weeks. Nerve conduction velocity (both motor and sensory nerves) were evaluated as a secondary measure. The median and peroneal nerves of the dominant limbs were simulated at a maximal intensity at three segment points. There were no differences before and after training in motor nerve conduction velocity of the median nerve in both groups. The author's concluded that these findings may be explained by a hypertrophic muscle effect leading to compression of the nerve. However, the high-intensity training group showed a significant decrease in conduction velocity in the peroneal nerve pre- to post-intervention. This result was surprising and unexpected, although it could be due in part to an increased level of body fat which has been said to contribute to the slowing of nerve conduction velocity in studies of obese adults.

2.6.1. Summary of "Effects of Resistance Training on Motor Nerve Conduction Velocity in Non-Injured Motor Nerves"

There has been marginal interest in the effects of strength training on the conduction speed of young individuals with no prior evidence of nerve injury. Sale et al. [55] found that bodybuilders and weightlifters possessed an 8% faster conduction velocity than those of controls. Moreover, Sleivert et al.[57] observed significantly faster conduction velocities in the lower limb of those who completed 14 weeks of either sprint training, multi-joint training, or strength-sprint training. Though no differences were found in a study of university athletes after 8 weeks of high-intensity and upper and lower body training[46]. The evidence seems to encourage the idea of faster conduction velocity measures after training with speculation that increased overload may induce nerve diameter, however, Padkao and Prasertsri[46] counter that the hypertrophic muscle effect may lead to compression of the nerve.

Sale and colleagues[54] investigated the outcomes of immobilization and strength training on nerve conduction velocity during 18 weeks of training and 5 weeks of immobilization. Overall, they found no differences in conduction velocity. This study would be most similar to an investigation of nerve conduction velocity in non-trained older individuals, though it does not resemble the totality of our proposed study. Limb immobilization induces muscle atrophy and joint stiffness along with several other morphological and physiological factors. Additionally, this study investigated these outcomes in younger adults. To fully elucidate potential mechanisms for the trainability of the peripheral nerves an investigation of non-trained older and younger adults must be completed.

CHAPTER III

METHODS

3.1. Participants

The goal for this study was to recruit forty young (18-50 yr old) and forty older (60+ yr old) adults. Approval was secured by the Oklahoma State University Institutional review board for human participant research. All subjects were apparently healthy and reported having no neuromuscular disease or neurological disorders. Further, all subjects reported either having no upper body resistance training within the past six months or limited training ($\leq$ 2 x per week). All participants completed an informed consent and health history questionnaire before beginning the study. Additionally, participants disclosed current medication usage. To our knowledge, none of the prescribed medications listed by participants were known to influence the results of this study.

3.2. Research Design

This study consisted of three groups including a young training group (YT), young control group (YC), and older training group (OT). Due to recruitment issues, an older control (OC) group was not utilized for this analysis. Testing sessions were performed before (PRE) and (POST) four weeks of the study. Participants were asked to maintain normal daily activities throughout the study. On the first visit, participants completed an informed consent form and other required paperwork. Upon competition of the

documents, manual dexterity tests were performed on both limbs (i.e., Minnesota Manual

Dexterity Task). Next, ultrasound (US) of the flexor digitorum superficialis muscle

(FDS) and median nerve were conducted on both limbs to assess muscle size and nerve

size, respectively. Following this, motor nerve assessments were completed on both limbs

to quantify maximal m-wave (M-wave) and conduction velocity (NCV) of the median

nerves. To assess strength, maximal voluntary contractions (MVC's) were performed

bilaterally using an isometric hand dynamometer. Each of these tests were completed

PRE and POST 4-weeks of the protocol.

3.3 Instrumentation and Procedures

3.3.1. Manual Dexterity Tests

3.3.1.1. Placing Test

For the placing test, subjects were asked to place disks as quickly as possible into

an empty board starting from the top right while following a downward column format.

Disks were placed above the empty board in front of subjects in the same orientation as

the holes. Instructions were given to each subject to execute the test as quickly and

accurately as possible. Accurate placement ensured that each disk must be fully inserted

into the hole on the board. This test was conducted on both the right and left arms with

practice trials given prior to the testing. The time to complete the placing test was

recorded in seconds.

3.3.1.2. Turning Test

For the turning test, the disks were inserted into the board and placed within 1 in from the edge of the table closest to the subject. Subjects were asked to pick up the disk from the upper right-hand corner of the board with their left hand and turn it over while passing it to the right hand and returning it to the original hole. This action was repeated across the board in a row format until the completion of the task. As with the placing test, the time to complete was recorded in seconds. Prior to testing, practice trials with instruction were given.

3.3.2. Ultrasonography

Bilateral ultrasound (US) images of the flexor digitorum superficialis (FDS) muscle and the median nerve were obtained using a diagnostic imaging device (LOGIQs8; GE Healthcare Korea Ltd, Seongnam, South Korea) with a linear array probe (model ML6-15-D, 4-15 MHz, 50-mm field view). The FDS muscle was verified by externally resisting the fourth metacarpal and   palpating the forearm region. Participants were instructed to place their arms in a supine position on a standard table. To allow for blood flow redistribution, participants rested quietly for 5 minutes prior to imaging.

Panoramic US images of the left and right FDS muscle and median nerves were taken. The probe was placed perpendicular to the skin and moved from medial to lateral position across the muscle consistently. Water-soluble transmission gel was applied to the skin to enhance acoustic coupling for each image. One investigator (J.E.S.) performed three panoramic US scans on each arm. US Images were then used to quantify muscle

size (mCSA) and nerve size (nCSA). US analysis was performed using Image-J software (National Institutes of Health, USA, Version 1.50i). mCSA of the FDS muscle was measured in each image by defining a region of interest using the polygon function with inclusion of as much muscle as possible. nCSA was measured by identifying the hyperechoic honeycombed shape of the nerve bundle and defining its region of interest using the polygon function.

3.3.3. Motor Nerve Function Assessments

Motor nerve conduction velocity (NCV) was collected using the incremental method. This quantifies NCV by obtaining the supramaximal compound muscle action potential (CMAP) at different segments along the median nerve and dividing by the distance between segments. The formula is presented below:

Figure 1. Formula for calculating nerve conduction velocity

Using a transcutaneous electrical stimulator cart (Cadwell Sierra Summit, Cadwell

Industries, Inc., Kennewick, WA, USA), motor nerve function assessments were conducted

on the left and right median nerve. Disposable recording electrodes (20×27mm, Cadwell

Industries Inc., Kennewick, WA, USA) were placed on the belly of the FDS muscle as

verified by ultrasonography. The reference and the ground electrodes were placed on the

tendon (flexor carpi radialis tendon) and the back of the hand (metacarpals), respectively.

Prior to electrode placement, the skin over the specified sites were shaved, abraded, and

cleaned with alcohol to ensure optimal signal quality.

Maximal m-wave was obtained at the axilla region and below the elbow of each arm.

For assessment of the optimal stimulation site of the axilla region, the arm was palpated by

having the participant flex their bicep. The optimal stimulation site for the elbow was located

at the antecubital fossa near the biceps tendon. In a cathode-anode arrangement, a single

stimulus (single square wave impulse) was applied in step-wise increments starting at 5mA.

Each stimulus thereafter was increased by 5mA until no increases in maximal M-wave

amplitude was detected via visual inspection.

Following the assessment of maximal m-wave, motor nerve conduction velocity

measures (NCV) were obtained. A temperature probe was secured to the participant's wrist

to ensure consistent temperature (approx. 30°C) throughout testing (Med-Linket Ltd,

Shenzhen, Guangdong, China). A single supramaximal (e.g. 120% of maximal m-wave)

stimulation was applied to each proximal and distal site (axilla and below the elbow) on both

arms. The latency (m/s) of each stimulation was stored and recorded for later use in the

determination of NCV. Additionally, the distance (mm) from the proximal stimulation site to

the distal stimulation site was verified using a tape measure. NCV was derived by the

software included in the stimulation cart using the equation provided above.
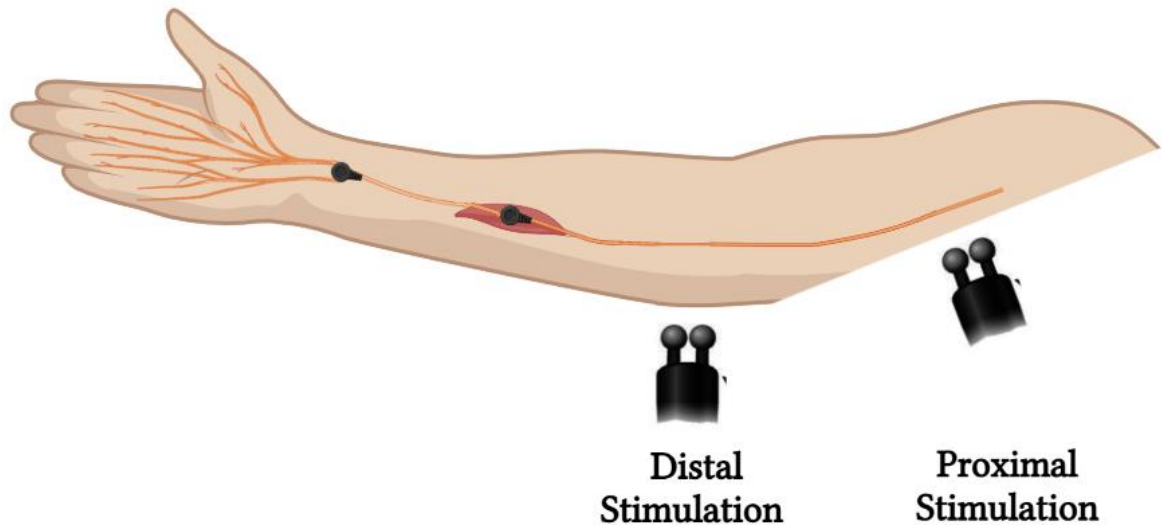
Figure 2. Stimulation sites for assessment of median nerve conduction velocity.

3.3.4. Hand Grip Strength Testing

Subjects were asked to hold a hand dynamometer by their side and perform two

maximal hand grip contractions per arm (Jamar, Sammons Preston Inc., Bolingbrook, IL,

USA). Prior to the contractions, subjects performed 2-3 warm-up contractions at about half

of their maximal effort. Upon directions, participants were asked to take a deep breath in and

raise the hand dynamometer to a 90° angle and contract maximally while exhaling each

breath. Each contraction lasted 4-5 seconds with strong verbal encouragement given by the

research team, and one minute of rest given between each trial. The highest value (kg) was

considered the participant's maximal hand grip strength.

3.3.5. Resistance Training Protocol

Subjects in the training groups performed bilateral resistance training of the forearm flexors 3 times per week for 4 weeks using a specialized hand-grip kit provided to them (NONJISPT, Shenzhen, Guangdong, China). Each kit contained an adjustable hand gripper, stress ball, grip ring, grip master, and finger stretcher resistance band. Additional grip rings (10-50 lbs; Refluxe, Shenzhen, Guangdong, China) and finger stretcher resistance bands (8-21 lbs; Portholic, Shenzhen, Guangdong, China) were used to induce a progressive overload in resistance for 4 weeks. Subjects were provided with pictures and instructions for each exercise upon completion of the initial testing (PRE) session. They were asked to perform 12 training sessions (approximately 30-45 mins) over the 4 weeks according to their schedule. Each participant was asked to keep a training log to assist with accountability. The PI also conducted weekly check-ins (via phone call or text) with each subject to ensure compliance to the protocol and answer any potential questions. Subjects were excluded from the study if they noted three or missed training sessions. Upon completion of the training, subjects revisited the lab for a (POST) testing session and all previous measures were assessed. training sessions. Upon completion of the training, subjects revisited the lab for a (POST) testing session and all previous measures were assessed.

3.3.6. Statistical Analyses

Initially, a four-way mixed factorial ANOVA model (age [young vs old] × group [training vs. control] × time [pre vs. post] × limb [left vs. right]) was conducted to determine changes in NCV. Because of the absence of an OC group in this data set, this model could not be used to further investigate interactions. Upon evidence of no limb interactions, two sets of a series of smaller three-way ANOVA models were performed. Three-way mixed factorial ANOVA model's (age [young vs old] × time [pre vs. post] × limb [left vs. right]) were performed to determine across the training groups for NCV, nerve CSA, muscle CSA, MVC strength, and the placing test for manual dexterity. A second series of three-way mixed factorial ANOVA model's (group [young training vs young control] × time [pre vs post] × limb [left vs. right]) were analyzed to detect differences between the young groups for NCV, nerve CSA, muscle CSA, MVC strength and the placing test for manual dexterity. If warranted, dependent paired samples t-test were performed. One-way ANOVAs were utilized to compare between subject's effects for the YT, YC and OT groups for each variable. When these findings were significant, Bonferroni post-hoc tests were run. For the turning test for manual dexterity, two separate 2-way mixed factorial ANOVA's were conducted (age [young vs old] x time [pre vs. post]) and (group [young training vs young control] x time [pre vs. post]). Additionally, correlation tests were run to determine if any associations occurred between NCV, nerve CSA, and MVC strength for all of the groups.

CHAPTER IV

RESULTS

4.1. Descriptives

Thirty-four apparently healthy adults participated in this study (see table

2). Thirteen young adults and seven older adults participated in four weeks of hand grip

resistance training, while fourteen young adults served as controls. As expected, there

were significant differences in age between groups ($p \leq 0.001$). There were no

differences in height and weight between any of the groups (Table 1).

Table 1. Descriptive Statistics

Group	Young Training	Young Control	Older Training	
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**p-value**
Age (yrs)	23.15 ± 7.5	20.29 ± 1.2	65.67 ± 4.9	**≤ 0.001***
Height (cm^2)	172.13 ± 10.3	168.00 ± 7.4	170.54 ± 6.3	= 0.453
Weight (kg)	80.18 ± 18.2	70.64 ± 18.96	74.59 ± 13.1	= 0.481

* = Significant relationship at the 0.05 level.

Table 2. Demographic Data

	Young Training	Young Control	Older Training
Sex (male/female)	Female*: n = 8*	Female: *n = 14*	Female: *n = 4*
	Male: *n = 5*	Male: *n = 0*	Male: *n =3*
Handedness (left/right)	Left: *n = 2*	Left: *n = 0*	Left: *n = 1*
	Right: *n = 11*	Right: *n = 14*	Right: *n = 6*
Total	*n = 13*	*n = 14*	*n = 7*

4.2. Nerve Conduction Velocity

4.2.1. Young Training vs. Older Training Groups

For NCV, findings showed no significant limb $\times$ time $\times$ age interaction ($p = 0.966$) for the training groups. There was also no significant time $\times$ age interaction ($p = 0.433$) interaction (see Figure 3). Additionally, no significant limb $\times$ age ($p = 0.433$) and limb $\times$ time ($p = 0.966$) interactions were reported. A significant main effect for time ($p \leq 0.001$, partial $\eta^2 = 7.77$) was found indicating that NCV was different pre to post.

4.2.2. Young Training vs. Young Control Groups

Due to missing data for the YC group only ten participants were included in this data set. A violation of equal variances for the pre-right NCV and post-right NCV resulted in running a separate one-way ANOVA to determine if assumptions were met (pre-right NCV: ($F_{(1,24)} = 0.252$, $p = 0.620$), post-right NCV($F_{(1,22)} = 3.190$, $p = 0.088$).The subsequent repeated measures ANOVA revealed no significant limb $\times$ time $\times$ group interaction ($p = 0.903$). However, there was a time $\times$ group interaction ($p = 0.001$) for the YT vs. YC groups (see Figure3). T-tests revealed that the NCV for the YT group were statistically different pre to post ($t(12) = -5.903$, $p \leq 0.001$). As expected, NCV for the YC group was not statistically

significant after four-weeks ($t(9) = -0.070$, $p = 0.946$). No significant limb $\times$ group ($p = 0.826$) and limb $\times$ time ($p = 0.761$) interactions were identified. A significant main effect for time ($p = 0.001$, partial $\eta^2 = 4.28$) was discovered.

4.2.3. Young Training vs. Young Control vs. Older Training Groups

No significant differences in NCV were found between groups at baseline for either the left or right limb (left: ($F_{(2,27)} = 0.920$, $p = 0.411$; right ($F_{(2,27)} = 1.761$, $p = 0.191$). Similarly, there were also no significant differences in NCV between groups post study (left:($F_{(2,27)} = 1.499$, $p = 0.241$; right ($F_{(2,27)} = 1.491$, $p = 0.243$). right)($F_{(2,27)} = 1.491$, $p = 0.243$).

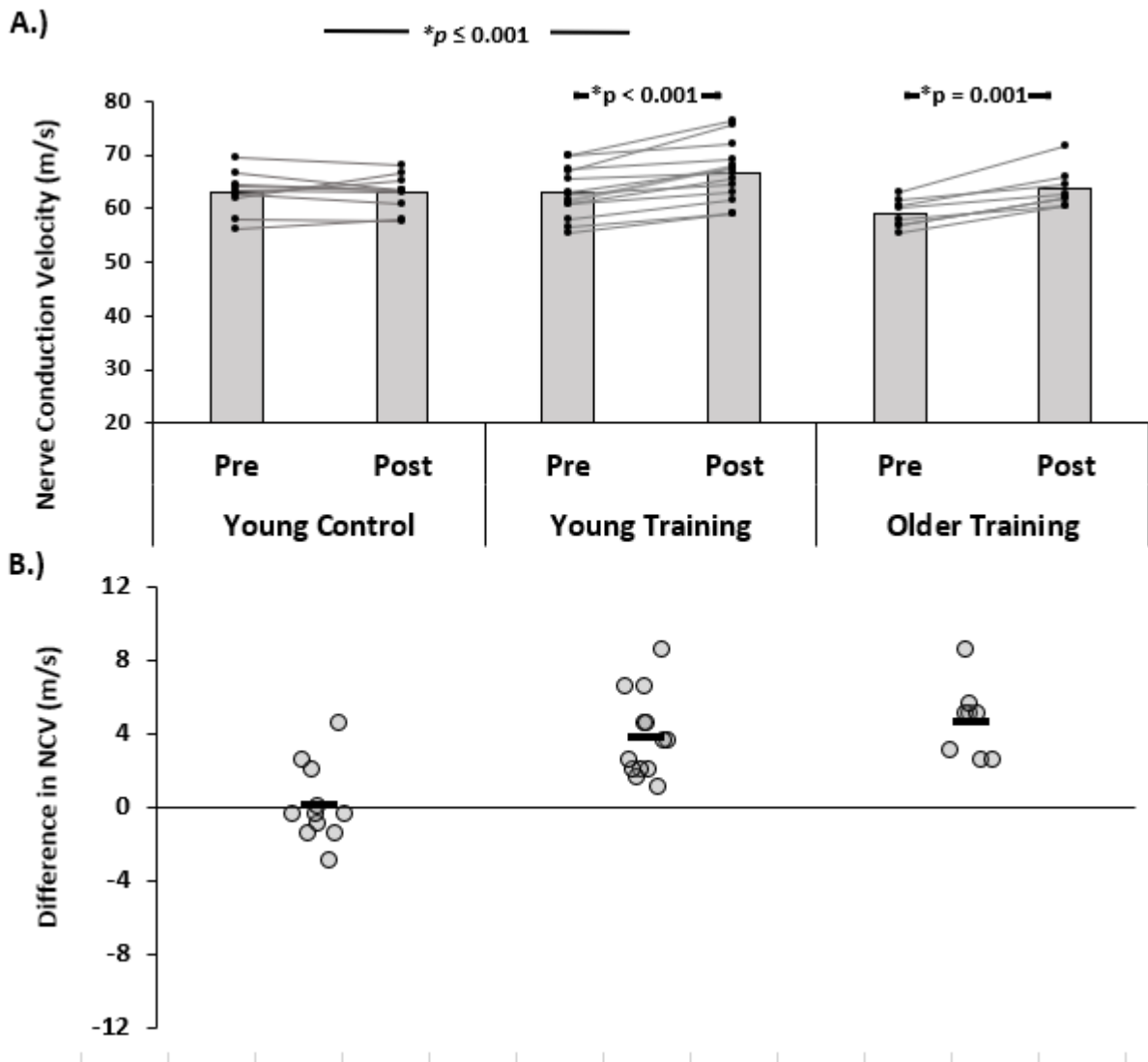**Figure 3.** A.) Nerve conduction velocity for all groups (averaged between limbs) at PRE and POST four weeks. B.) Change scores in Nerve Conduction Velocity. ⎯ = Significant group × time interaction: ⊢⎯⊣ = Significant main effect for time: * = Significant differences at the 0.05 level.

4.3. Ultrasound Measurements

4.3.1. FDS muscle CSA

4.3.1.1. Young Training vs. Older Training Groups

No limb $\times$ time $\times$ age interaction ($p = 0.820$) was identified. However, a time $\times$ age interaction ($p = 0.036$) was reported (see Figure 4). Follow-up t-test showed that FDS muscle CSA changed pre to post in for the YT *(t(12)* = -4.915, $p \leq 0.001$). There was no statistically significant change for time in the OT group: (t(6) = -1.322, $p = 0.234$) No significant limb $\times$ age ($p = 0.982$) and limb $\times$ time ($p = 0.314$) interactions were noted. A main effect for time ($p = 0.001$, partial $\eta^2 = 4.72$) found.

4.3.1.2. Young Training vs. Young Control Groups

Due to a violation of equal variances for the post-left FDS muscle CSA a separate one-way ANOVA was conducted to determine if assumptions were met ($F_{(1,25)}$ = 1.613, $p = 0.216$). The following repeated measures ANOVA revealed no limb $\times$ time $\times$ group interaction ($p = 0.509$). However, a statistically significant ($p \leq 0.001$) time $\times$ group interaction was identified (see Figure 4). As previously mentioned, the FDS muscle was statistically different in size pre to post in the YT group (*t(12)* = -4.915, $p \leq 0.001$). Interestingly, significant differences were also observed in the YC group (t(13) = 2.593, $p = 0.022$). No significant limb $\times$ group ($p = 0.767$) and limb $\times$ time ($p = 0.761$) interactions were noted.   A significant main effect for time *(p = 0.002*, partial $\eta^2 = 3.13$) and limb (*p = 0.017*, partial $\eta^2 = 2.08$) was found indicating change in FDS muscle CSA.

4.3.1.3. Young Training vs. Young Control vs. Older Training Groups

No significant differences were reported between groups at baseline for either the left or right limb FDS muscle CSA (left: ($F_{(2,31)}$ = 0.758, $p = 0.477$; right ($F_{(2,31)}$ = 0.484, $p = 0.621$). There were also no significant differences in FDS muscle CSA between groups post study (left: ($F_{(2,31)}$ = 1.272, $p = 0.295$; right ($F_{(2,31)}$ = 0.969, $p = 0.391$).
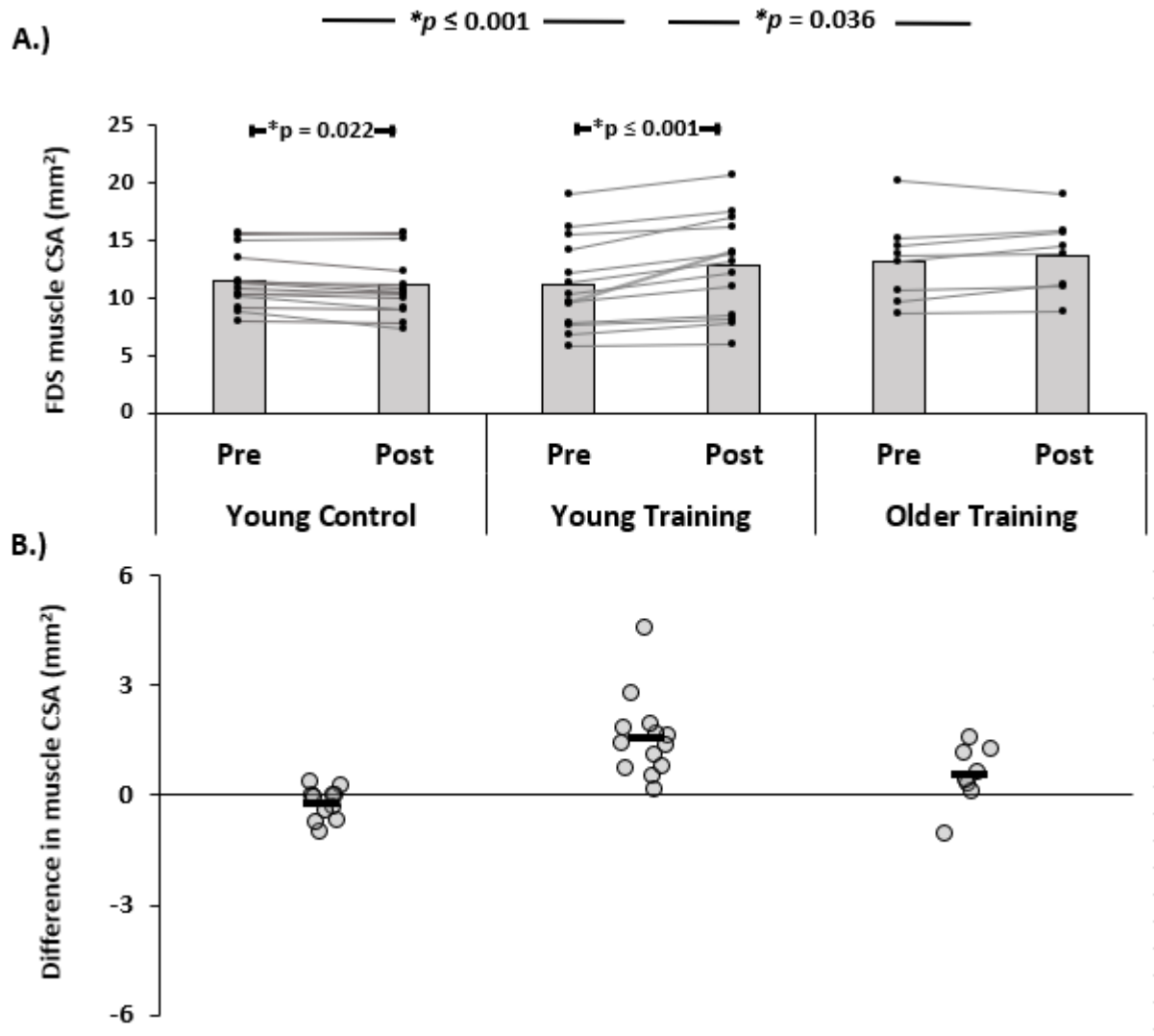
Figure 4. A.) FDS muscle CSA for all groups (averaged between limbs) at PRE and POST four weeks. B.) Change scores in FDS muscle CSA. — = Significant group × time interaction/age × interaction: * = Significant differences at the 0.05 level.

4.3.2. Nerve CSA

4.3.2.1. Young Training vs. Older Training Groups

All variables were not equally distributed therefore multiple one-way ANOVA's were used to determine if assumptions were met. There were no statistically significant differences in group means as determined by the one-way ANOVA's (pre-left nerve CSA ($F_{(1,18)} = 2.997$, $p = 0.101$), post-left ($F_{(1,18)} = 2.889$, $p = 0.106$), pre-right ($F_{(1,18)} = 3.805$, $p = 0.067$), and

post-right ($F_{(1,18)}$ = 3.771, p = 0.068). The subsequent repeated measures ANOVA showed no limb × time × age interaction (p = 0.791). Additionally, there was no time × age interaction (p = 0.508) (see Figure 5). No significant limb × age (p = 0.216) and limb × time (p = 0.791) interactions were noted. Findings showed a significant main effect for time ($p \leq 0.001$, partial η^2 = 8.36) indicating changes in nerve CSA pre to post.

4.3.2.2. Young Training vs. Young Control Groups

There was no significant limb × time × group interaction (p = 0.790). However, a significant time × group interaction ($p \leq 0.001$) was found (see Figure 5). Follow-up t-tests showed that nerve CSA for the YT group was statistically different pre to post training (t(12) = -9.519, $p \leq 0.001$). Not surprising, the YC group was not statistically significant pre to post (t(12) = -1.829, p = 0.090). Additionally, no significant limb × group (p = 0.235) and limb × time (p = 0.284) interactions were identified. A main effect for time ($p \leq 0.001$, partial η^2 = 6.44) and limb (p =0.049, partial η^2 = 1.46) was also noted.

4.3.2.3. Young Training vs. Young Control vs Older Training Groups

Significant differences were reported between groups at baseline for both left and right limb nerve CSA (left: ($F_{(2,31)}$ = 5.472, p = 0.09; right ($F_{(2,31)}$ = 3.390, p = 0.047). Similarly, there were also significant differences in nerve CSA between groups post intervention (left: ($F_{(2,31)}$ = 8.673, p = 0.01; right ($F_{(2,31)}$ = 4.638, p = 0.017). Bonferroni post-hoc tests showed that pre-left nCSA was significant different between the YC and OT groups (-1.79 (95% CI –3.16 to –4.19) p = 0.007). Additionally, the post-left nCSA was significant different between the YC and OT groups (-2.10 (95% CI –3.41 to –0.79) p = 0.001). Similar findings were reported for these groups for post-right nCSA (-2.28 (95% CI 0.38 to 4.19) p = 0.015)
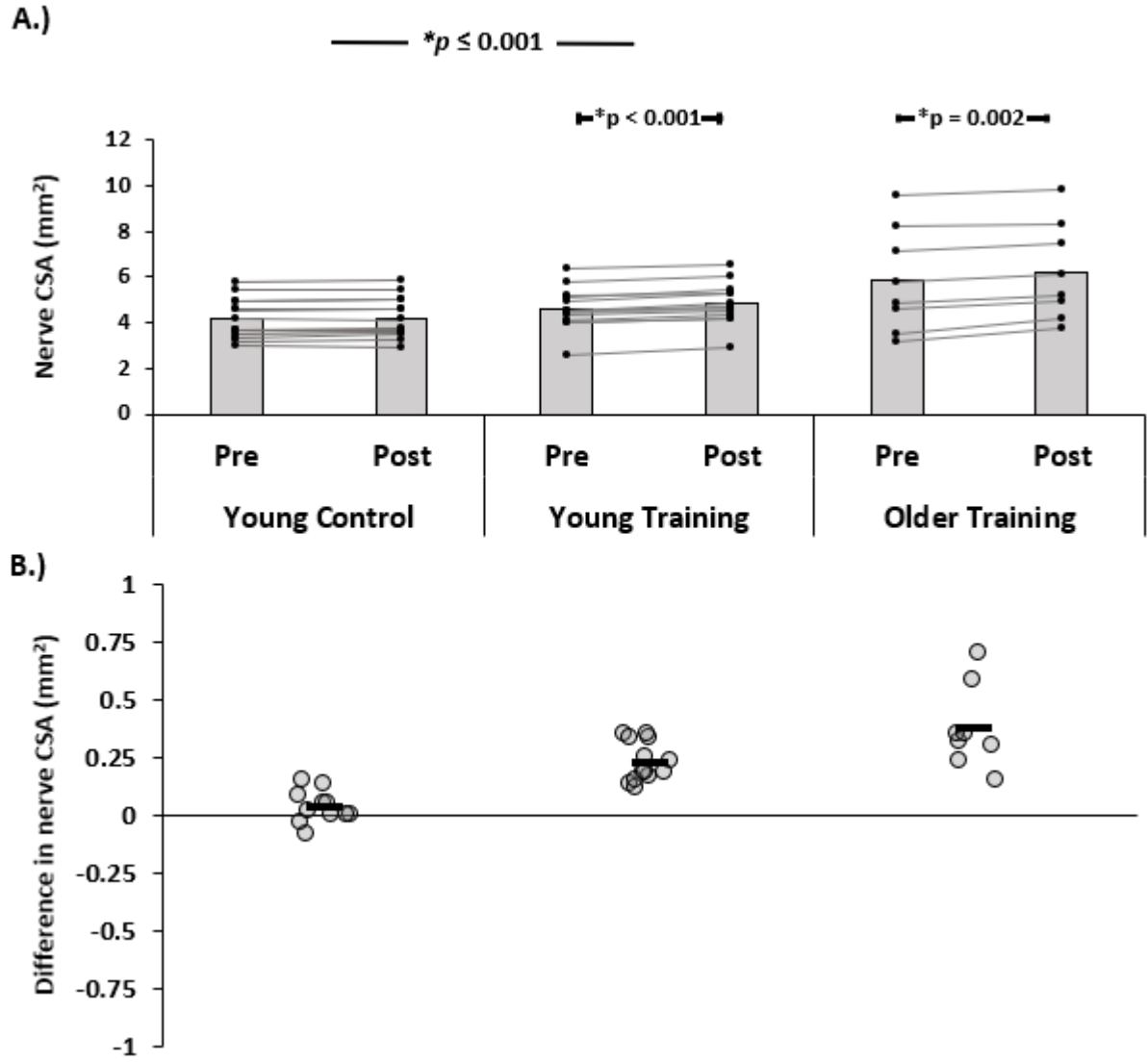
Figure 5. A.) Nerve CSA for all groups (averaged between limbs) at PRE and POST four weeks. B.) Change scores in Nerve CSA. — = Significant group × time interaction: ⊢⊣ = Significant main effect for time: * = Significant differences at the 0.05 level.

4.4. NCV and nerve CSA Correlations

4.4.1. All Groups

Because of inconsistent data for the YC group, only ten participants NCV measures were analyzed in this data set. Results showed a significant correlation between NCV and

nerve CSA for all groups ($r = .455$, $p = 0.011$). These findings indicate that there is a

moderate relationship between NCV and nerve CSA (see Figure 6).
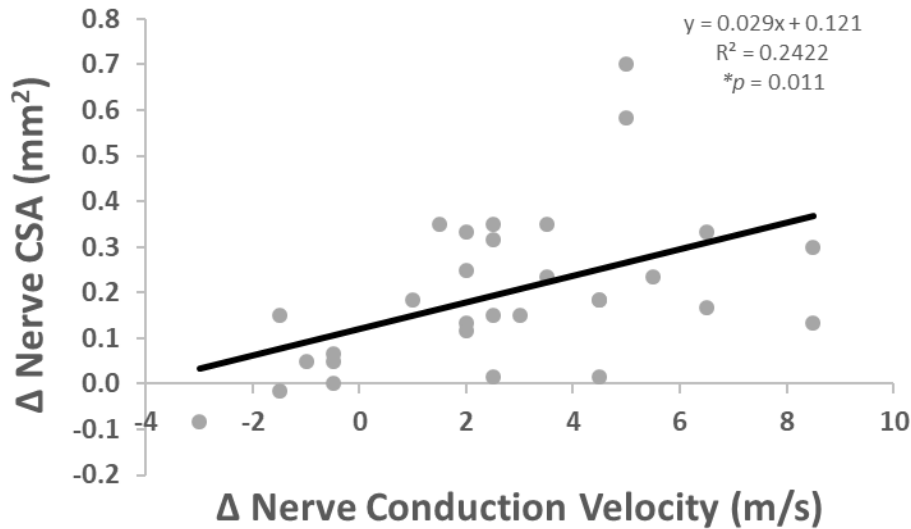

Figure 6. Moderate relationship between Nerve CSA and Nerve Conduction Velocity for all groups. ***** = Significant relationship at the 0.05 level.

4.5. Handgrip Strength MVC's

4.5.1. Young Training vs. Older Training Groups

For the MVC's, there was no significant limb × time × age interaction for either

training group ($p = 0.673$). A significant time × age interaction ($p = 0.040$) was identified

(see Figure 7). T-tests showed a significant difference in pre to post MVC for the YT group

($t(12) = -5.752$, $p \leq 0.001$). However, the OT group did not report any significant differences

between time ($t(6) = -0.813$, $p = 0.477$). No significant limb × age ($p = 0.361$) and limb ×

time ($p = 0.236$) interactions were noted. A significant main effect for time ($p = 0.001$, partial

$\eta^2 = 4.44$) was found identifying differences in strength pre to post. Also, a significant main

effect for limb ($p = 0.023$, partial $\eta^2 = 2.57$) was reported indicating differences in hand grip

strength between limbs.

4.5.2. Young Training vs. Young Control Groups

The left-post and right-pre MVC's were not equally distributed therefore multiple one-way ANOVA's was used to determine if assumptions were met. There were no statistically significant differences in group means as determined by the one-way ANOVA's for the right-pre ($F_{(1,25)}$ = 2.013, p = 0.168). However, a Welch's adjustment was needed for the left-post MVC ($F_{(1, 21.425)}$ = 4.631, p = 0.043). The resulting repeated measures found no limb × time × group interaction (p = 0.361). Not surprising, there was significant time × group interaction ($p \leq 0.001$) (see Figure 7). As previously mentioned, the YT group showed significant differences in MVC strength pre to post ($t(12)$ = -5.752, $p \leq 0.001$). Although, the YC group did not report any significant differences between time *($t(13)$ = 1.149, p =0.271)*. There was also no significant limb × group (p = 0.099) and limb × time (p = 0.968) interactions. A significant main effect for both time and limb were also reported (time: p = 0.022, partial η^2 = 1.92; limb: p = 0.016, partial η^2 = 2.12).

4.5.3. Young Training vs. Young Control vs. Older Training Groups

No significant differences were reported between groups at baseline for either the left or right MVC strength (left: ($F_{(2,31)}$ = 0.748, p = 0.482; right ($F_{(2,31)}$ = 1.529, p = 0.233). There were also no significant differences in MVC strength between groups post study (left: ($F_{(2,31)}$ = 3.014, p = 0.064; right ($F_{(2,31)}$ = 3.056, p = 0.061).
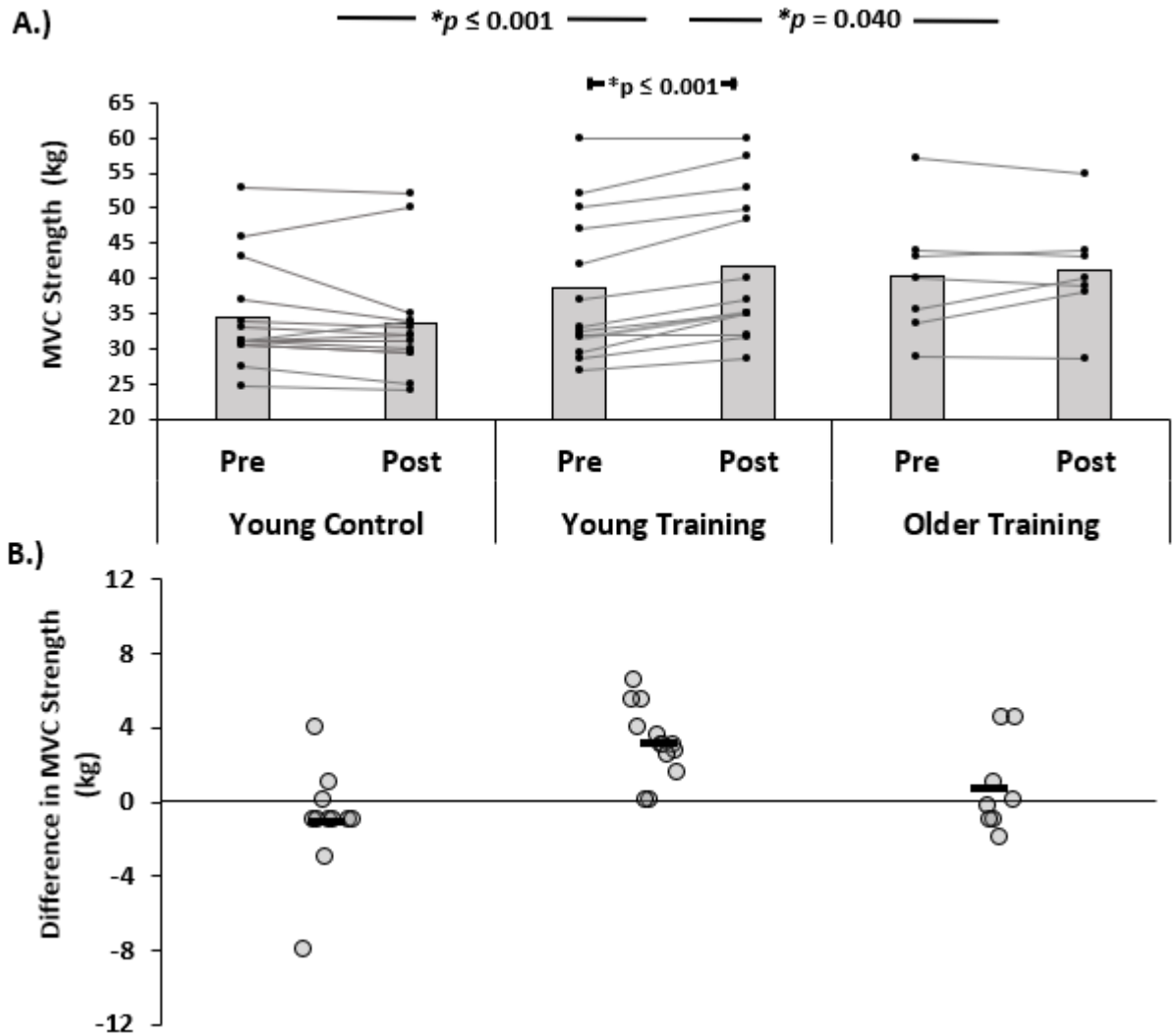
Figure 7. A.) Handgrip strength (MVC's) for all groups (averaged between limbs) at PRE and POST four weeks. B.) Change scores in MVC Strength. — = Significant group × time interaction/age × interaction: ⊢—⊣ = Significant main effect for time: * = Significant differences at the 0.05 level.

4.6. NCV and MVC Correlations

4.6.1. All groups

Due to missing data in the YC group for NCV, only ten participants from that group were analyzed in this data set. Results indicated a significant correlation between NCV and

MVC strength for all groups ($r = .597$, $p \le 0.001$). These findings suggest a strong positive

relationship exists between NCV and MVC strength (see Figure 8).
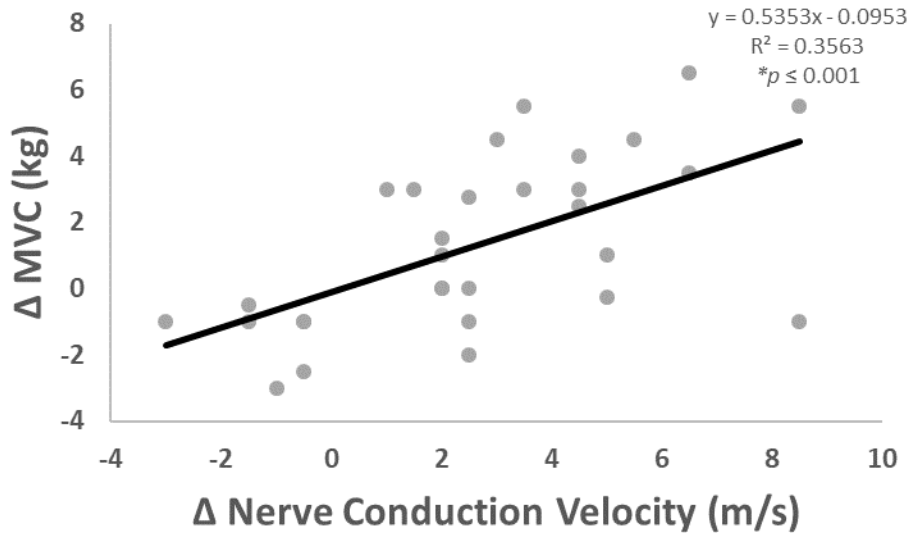
Figure 8. Moderate relationship between Nerve CSA and Nerve Conduction Velocity for all
groups. ***** = Significant relationship at the 0.01 level.

4.7. MVC and Nerve CSA Correlations

4.7.1. All groups

Due to missing data in the YC group for NCV, only eleven participants from that

group were analyzed in this data set. Results found no significant correlation between MVC

strength and nerve CSA for all groups ($r = .116$, $p = 0.534$). These findings suggest a weak

negative relationship exists between MVC strength and nerve CSA (see Figure 9).
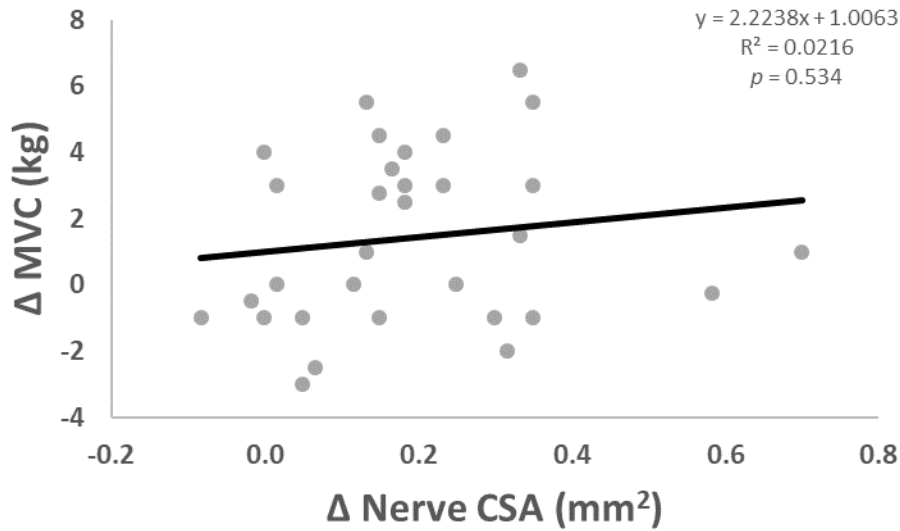
Figure 9. Weak negative relationship between MVC strength and Nerve CSA for all groups.

4.8. Manual Dexterity Tests

4.8.1. Placing Test

4.8.1.1. Young Training vs. Older Training Groups

For the placing test, there was no limb × time × age interaction ($p = 0.913$) for the training groups. Additionally, there was no time × age interaction ($p = 0.626$). No significant limb × age ($p = 0.289$) and limb × time ($p = 0.506$) interactions were noted. A significant main effect for time ($p = 0.021$, partial $\eta^2 = 2.63$) was found revealing that time for the placing test was significantly different before and after four weeks of training. Further, a significant main effect for limb ($p = 0.012$, partial $\eta^2 = 3.04$) identified highlighting interlimb differences in placing speed (see Figure 10).

4.8.1.2. Young Training vs. Young Control

Results showed no significant limb × time × group interaction ($p = 0.589$) for the placing test in the young groups. Moreover, no time × group interaction ($p = 0.582$) was reported. No significant limb × group ($p = 0.078$) and limb × time ($p = 0.240$) interactions

63

were noted. A significant main effect for time ($p = 0.029$, partial $\eta^2 = 1.78$) was found showing that placing speed was significantly different before and after four weeks. Additionally, a significant main effect for limb ($p \leq 0.001$, partial $\eta^2 = 4.75$) observed (see Figure 10).

4.8.1.3. Young Training vs. Young Control vs. Older Training Groups

Significant differences were reported between groups at baseline for both left and right placing test speed (left: ($F_{(2,31)} = 9.593$, $p = 0.001$; right ($F_{(2,31)} = 14.741$, $p \leq 0.001$). Similarly, there were also significant differences in placing test speed between groups post study (left: ($F_{(2,31)} = 11.857$, $p \leq 0.001$; right ($F_{(2,31)} = 10.623$, $p \leq 0.001$). Bonferroni post-hoc tests showed that pre-left placing speed was significantly different at baseline between the YT and OT groups (-13.6 (95% CI –21.9 to –5.4) $p = 0.001$). Moreover, pre-left placing speed was significant different between the OT and YC groups at baseline (11.9 (95% CI 3.79 to 20.0) $p = 0.002$). For the pre-right placing speed there were significant differences between the YT and OT groups pre-study (-10.4 (95% CI –16.4 to –4.5) $p \leq 0.001$). Significant differences were also observed between the OT and YC groups (12.2 (95% CI 6.3 to 18.1) pre-study. There were significant post study differences reported between the YT and OT groups for post-left placing speed (-12.6 (95% CI –19.3 to -5.8) $p \leq 0.001$). For the OT and YC groups, significant differences were observed in the post-left placing test (10.6 (95% CI 3.9 to 17.3) $p = 0.001$). The YT and OT groups showed significant differences in post-right placing speed (-9.6 (95% CI –15.7 to –3.6) $p = 0.001$). Finally, the OT and YC groups were found to have significantly different post-right placing speed (10.2 (95% CI 4.2 to 16.1) $p \leq 0.001$).
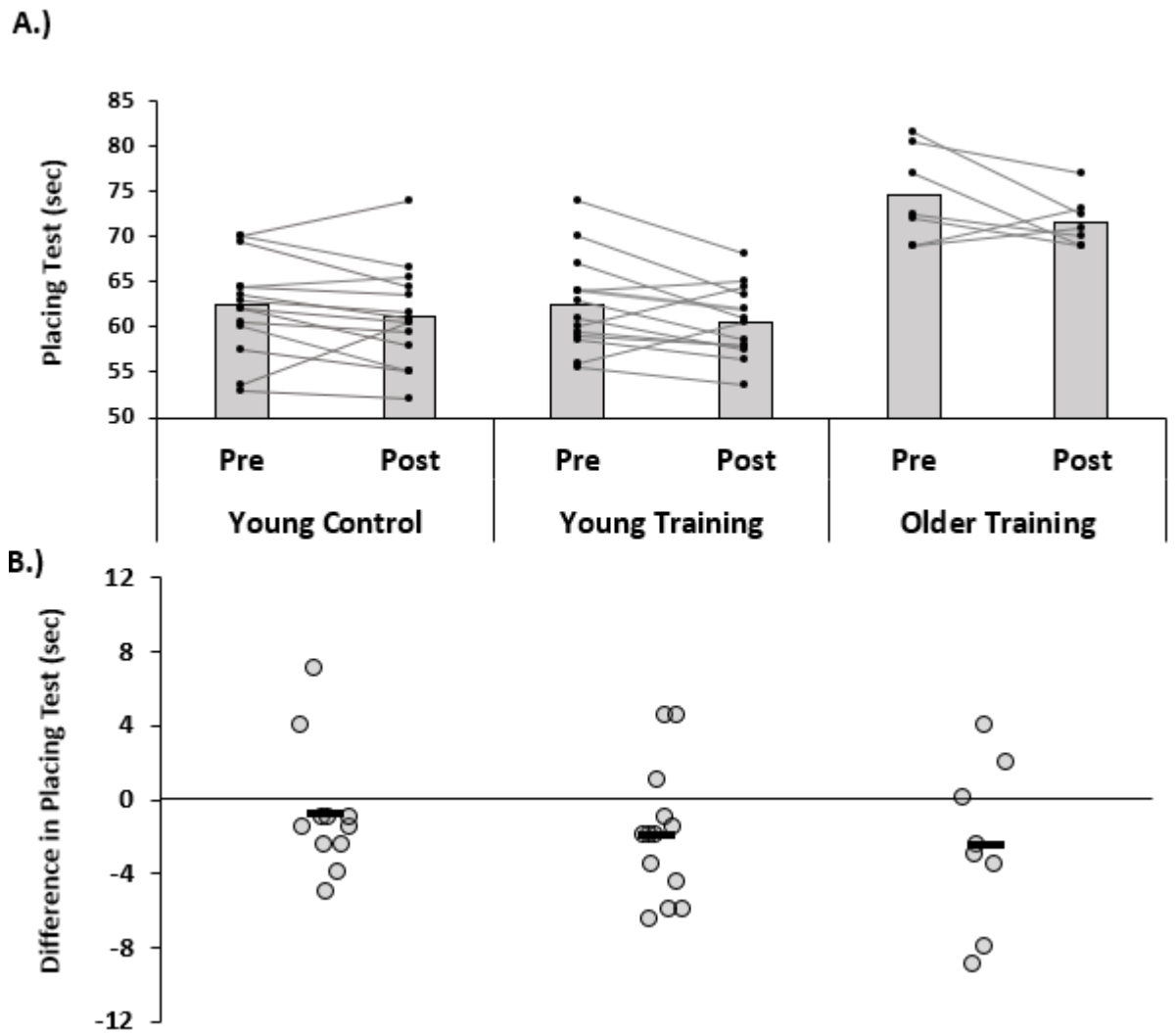
Figure 10. A.) Placing test for all groups (averaged between limbs) at PRE and POST four weeks. B.) Change scores in Placing Test speed. No significant group × time interaction/age × interaction: No significant within group differences in placing speed.

4.8.2. Turning Test

4.8.2.1. Young Training vs. Older Training Groups

For the turning test, no time × age interaction ($p = 0.616$) was identified. As

expected, there was a significant main effect for time ($p = 0.016$, partial $\eta^2 = 2.84$) revealing

differences in turning speed pre and post four weeks (see Figure 11).

4.8.2.2. Young Training vs. Young Control Groups

There was no time × group interaction ($p = 0.903$) for the turning test. Like the training groups, there was a significant main effect for time ($p = 0.033$, partial $\eta^2 = 1.70$) (see Figure 11).

4.8.2.3. Young Training vs. Young Control vs. Older Training Groups

Significant differences in pre-turning test speed were found between all groups at baseline ($F_{(2,31)} = 12.0$, $p \leq 0.001$). Moreover, significant differences were noted between all groups for post-turning test speed ($F_{(2,31)} = 9.0$, $p = 0.001$). Bonferroni post-hoc tests showed that the YT and OT groups significantly differed in pre-turning speed (-13.6 (95% CI –21.7 to –5.5) $p = 0.001$). Findings showed that the OT and YC groups also had different pre-turning speeds (14.7 (95% CI 6.7 to 22.8) $p \leq 0.001$). For the post-turning test, the YT and OT groups showed significant differences in speed –14.6 (95% CI –23.7 to –5.5) $p = 0.001$). Further, the OT and YC group were found to have significant differences post study 12.5 (95% CI 3.6 to 21.5) $p = 0.004$).
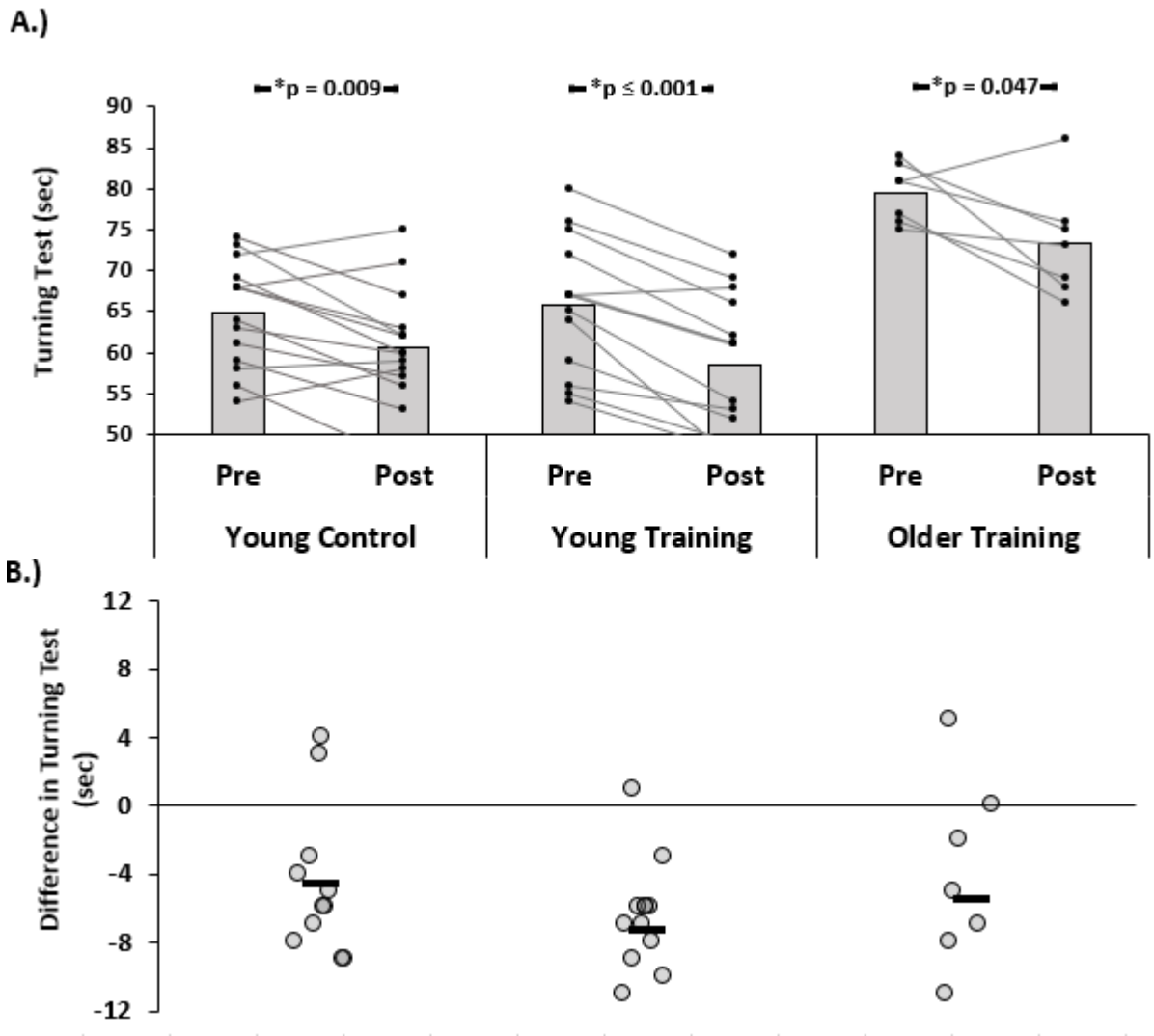
Figure 11. A.) Turning test for all groups at PRE and POST four weeks. B). Change scores in Turning Test speed. ⊢⊣ = Significant main effect for time: * = Significant differences at the 0.05 level.

CHAPTER V

DISCUSSION

The study aimed to examine the trainability of peripheral nerve function as it relates to age. A secondary emphasis of this study was to determine if a relationship between nerve conduction velocity and nerve CSA exists. This experiment applied unique approaches to answer questions regarding the adaptability of the PNS. As a result, our study identified increases in median nerve speed after training in both young and older adults. Moreover, this study also quantified changes in nerve morphology in both training groups. The findings from this investigation may provide helpful information to clinicians and physical therapists regarding the influence of resistance training on the function and plasticity of the nerves.

Declining PNS function often leads to neuromuscular dysfunction. It has been reported that ,age-related slowing of healthy motor nerves occurs in both humans and rodents[44,68,69]. Further, previous research identifies a linear relationship between a slowing in nerve speed and age ($\geq$ 60 yrs.) in those who are free of neuromuscular disease[67]. Therefore, we aspired to identify if a training program would elicit alterations in nerve speed in untrained adults. As such, identifying interventions to improve nerve function may be useful in avoiding age-related adverse outcomes. Additionally, of the few studies investigating training effects on nerve function, only one has examined

untrained young males[57]. Our exploration targeted not only untrained young adults, but older adults as well.

5.1. Adaptations to the Peripheral Nervous System

The effects of resistance training on nerve speed have been demonstrated in previous studies, although mainly in chronically trained athletes. Like those investigations [54,55], our study showed that nerve speed changed similarly over time in both training groups. Moreover, compared with the YT group, the YC group did not exhibit significant changes in NCV. While previous studies [20,23,57], demonstrated changes in NCV due to long-term training programs (12-14 weeks), this study took a short-term approach to determine nerve speed Although our study was shorter in duration, our positive findings may be due to the rapid movement speed and range of motion that participants were asked to complete the exercises. Moreover, because of the limited research regarding training and NCV, this study intended to assess easily quantifiable and superficial nerves to target the muscles responsible for hand grip. The findings of these data may have implications for our aging populations concerning increasing functional mobility.

5.2. Morphological Adaptations to Training

In addition to our results on nerve speed, this study aimed to assess the relationship between nerve plasticity and age. Utilizing ultrasonography, we determined a change in axonal nerve size for both our YT and OT groups. These findings conflict with a previous study on nerve size in trained adults [42]. Previously it was speculated that increased overload might lead to nerve compression; however, that study only determined NCV, not nerve diameter[46]. Our study identified a moderate correlation between NCV and nerve CSA when

looking at all groups leading one to surmise that there may be physiological and morphological associations of the nerve. While it is still being determined why this was the case in this study, further research should consider additional methods (i.e., a larger cohort, older control group, or technician oversight) to further validate these results. Changes in muscle size were found in the YT group after four weeks of training; however, those changes were not present in the OT group. Not surprisingly, the YC demonstrated declines in muscle size after four weeks. It is reasonable to suggest that the absence of muscle hypertrophy in the OT group may be due to the duration of (e.g., four-weeks) the training. It has been noted that muscle hypertrophy in older adults can be observable within nine weeks of training[38]. Therefore, the time course of our investigation may have inhibited our ability to identify significant changes in FDS muscle size. Moreover, our understanding of the level of MU remodeling occurring within the muscle fibers was not investigated. It is possible that the OT group had substantial losses in fast-twitch type II fibers which may have attenuated their ability to increase muscle size.

Changes in muscle size were found in the YT group after four weeks of training; however, those changes were not present in the OT group. Not surprisingly, the YC demonstrated declines in muscle size after four weeks. It is reasonable to suggest that the absence of muscle hypertrophy in the OT group may be due to the duration of (e.g., four-weeks) the training. It has been noted that muscle hypertrophy in older adults can be observable within nine weeks of training [38]. Therefore, the time course of our investigation may have inhibited our ability to identify significant changes in FDS muscle size. Moreover, our understanding of the level of MU remodeling occurring within the muscle fibers was not

investigated. It is possible that the OT group had substantial losses in fast-twitch type II fibers which may have attenuated their ability to increase muscle size.

5.3. Associated Changes in Strength

Loss of muscle mass is commonly associated with declines in muscular strength. Our study identified changes in hand grip strength in our YT group, although not in our OT and YC groups. It is well-established that neural adaptations may begin between four and six weeks after the onset of a new stimulus [11]. Therefore, one likely scenario for the outcome of our present study is that our OT group needed a longer duration to attain such changes. Moreover, there were no significant correlations found between MVC strength and NCV. Our findings contradict a previous study in which correlations were found between hand grip strength and NCV [41]. However, others have found no such associations in lower body strength parameters [60,71].

5.4. Alterations in Manual Dexterity

Manual dexterity was determined using two different testing measures. For the placing test, all groups (YT, OT, and YC) were significantly faster before and after four weeks. Additionally, there was a difference in limb placing speed in all groups, highlighting interlimb differences in manual dexterity. All groups were significantly faster pre to post intervention for the turning test. While the outcomes of these measures may be due, in fact, to the training, the YC group was also significantly faster. One should consider the possibility of a learning effect with these types of tests in future assessments.

5.5 Limitations

There are some conceivable limitations to this study design. The primary factor was our sample size ($n = 34$). Additionally, there was not a matched control for the OT group. It was previously noted in a study investigating long-term resistance training on NCV that a lack of a control group might contribute to limited findings [31]. Additional data collection is being planned to increase the sample of this cohort. As previously mentioned, a learning effect may have been present in the manual dexterity tests. In retrospect, this variable could have benefited from familiarization in order to reduce the impact of a learning effect. With assessment of nerve CSA, we should be careful not to insinuate that the changes observed equate to bigger neurons. Our findings coupled with the increases in NCV suggest that hypertrophy is occurring at the axonal level. Another factor that should be considered is the level to which our participants were "untrained." While inclusion criteria allowed participants to exercise (≤ 2 x per week), this may have contributed to some of our moderate findings. Several older adults reported being active, which may have influenced the minimal changes observed. Additionally, it is possible that this intervention contained a compliance factor. While participants were asked to track their workouts, one can never entirely ensure participant compliance with the training program.

5.6. Future Research and Recommendations

A proposed follow-up to this project would be an examination of the impact of training on lower body nerve function. Lower body mobility is said to deteriorate more rapidly than the upper body, which has significant implications on fall risk in older adults. The slowing of nerves may result in slower movement speed, thus altering an individual's

response time. It is important to identify potential interventions that may support prevention of these consequences of aging. Moreover, an investigation on the deeper nerves as well as a more extended duration protocol may provide better answers to our findings. In addition, a proper analysis of the entire motor pathway (cortical to spinal to peripheral) should be considered to isolate the specificity of adaptations.

5.7. Conclusions

These findings support our hypothesis that hand grip training would increase NCV in both young and older adults. Moreover, our study showed successful nerve plasticity in older adults. These data suggest that resistance training may be a reliable method to counteract NCV deficits in the short term. This study also identified changes in nerve size that were not previously shown. The results of this study could aid clinicians and physical therapists in exercise prescription in individuals needing to improve nerve speed and motor function. The significance of this study has the potential to improve the quality of life and generate greater independence for our older populations.

REFERENCES

1. Awang, M. S., Abdullah, J. M., Abdullah, M. R., Tharakan, J., Prasad, A., Husin, Z. A., Hussin, A. M., Tahir, A., & Razak, S. A. (2006). Nerve conduction study among healthy Malays. The influence of age, height and body mass index on median, ulnar, common peroneal and sural nerves. *The Malaysian journal of medical sciences: MJMS*, *13*(2), 19.

2. Bean, J., Kiely, D. K., Herman, S., Leveille, S. G., Mizer, K., Frontera, W. R., & Fielding, R. A. (2002). The relationship between leg power and physical performance in mobility-limited older people. *Journal of the American Geriatrics Society*, *50*(3), 461-467.

3. Bouche P, C. F., Saint-Jean O, Leger JM, Queslati S, Guez D, Moulonguet A, Brault Y, Aquino JP, and Simunek P. . (1993). Clinical and electrophysiological study of the peripheral nervous system in the elderly. *240*, 263-268.

4. Buschbacher, R. M. (1998). Body mass index effect on common nerve conduction study measurements. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *21*(11), 1398-1404.

5. Campbell Jr, W. W., Ward, L. C., & Swift, T. R. (1981). Nerve conduction velocity varies inversely with height. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *4*(6), 520-523.

6. Campbell, M., McComas, A., & Petito, F. (1973). Physiological changes in ageing muscles. *Journal of Neurology, Neurosurgery & Psychiatry*, *36*(2), 174-182.

7. Carmeli E, P. H., and Coleman R. . (2003). The Aging Hand. *Journal of Gerontology*, *58A*.

8. Choy, N. L., Brauer, S., & Nitz, J. (2003). Changes in postural stability in women aged 20 to 80 years. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *58*(6), M525-M530.

9. Clark, B. C., Clark, L. A., & Law, T. D. (2016). Resistance exercise to prevent and manage sarcopenia and dynapenia. *Annual Review of Gerontology and Geriatrics*, *36*(1), 205-228.

10. De Jesus, P., Hausmanowa-Petrusewicz, I., & Barchi, R. L. (1973). The effect of cold on nerve conduction of human slow and fast nerve fibers. *Neurology*, *23*(11), 1182-1189.

11. Defreitas, J. M., Beck, T. W., Stock, M. S., Dillon, M. A., & Kasishke, P. R. (2011). An examination of the time course of training-induced skeletal muscle hypertrophy. *European Journal of Applied Physiology*, *111*(11), 2785-2790.

12. Deschenes, M. R. (2011). Motor unit and neuromuscular junction remodeling with aging. *Current aging science*, *4*(3), 209-220.

13. Doherty, T. J., & Brown, W. F. (1997). Age-related changes in the twitch contractile properties of human thenar motor units. *Journal of Applied Physiology*, *82*(1), 93-101.

14. Dorfman, L. J., & Bosley, T. M. (1979). Age-related changes in peripheral and central nerve conduction in man. *Neurology*, *29*(1), 38-38.

15. Elam, R. P. (1987). Body fat and its relationship to tibial nerve conduction velocity in a specific population. *Journal of Orthopaedic & Sports Physical Therapy*, *8*(10), 495-497.

16. Eslami, R., Tartibian, B., & Najarpour, M. (2019). Effect of six weeks resistance training on nerve conduction velocity, strength, balance and walking speed in Multiple Sclerosis patients. *Journal of Gorgan University of Medical Sciences*, *21*(3), 63-68.

17. Fragala, M. S., Cadore, E. L., Dorgo, S., Izquierdo, M., Kraemer, W. J., Peterson, M. D., & Ryan, E. D. (2019). Resistance training for older adults: position statement from the national strength and conditioning association. *The Journal of Strength & Conditioning Research*, *33*(8).

18. Gakhar, M., Verma, S., & Lehri, A. (2014). A comparison of nerve conduction properties in male and female of 20 to 30 years of age group. *Journal of Exercise Science and Physiotherapy*, *10*(1), 16-20.

19. Geerlings, A. C., & Mechelse, K. (1985). Temperature and nerve conduction velocity, some practical problems. *Electromyography and clinical neurophysiology*, *25*(4), 253-259.

20. Gholami, F., Khaki, R., Mirzaei, B., & Howatson, G. (2021). Resistance training improves nerve conduction and arterial stiffness in older adults with diabetic distal symmetrical polyneuropathy: A randomized controlled trial. *Experimental Gerontology*, *153*, 111481.

21. Gilmore, K. J., Kirk, E. A., Doherty, T. J., & Rice, C. L. (2018). Effect of very old age on anconeus motor unit loss and compensatory remodelling. *Muscle & Nerve*, *57*(4), 659-663.

22. Gordon, T., Hegedus, J., & Tam, S. L. (2004). Adaptive and maladaptive motor axonal sprouting in aging and motoneuron disease. *Neurological research*, *26*(2), 174-185.

23. Goyal, M., Mehta, S. K., Rana, N., Singal, R., Mittal, A., Goyal, K., Sharma, S., Chatterjee, S., & Sharma, M. (2016). Motor nerve conduction velocity and function in carpal tunnel syndrome following neural mobilization: A randomized clinical trial. *Int J Health Allied Sci*, *5*(2), 104-110.

24. Haff, G. G., & Triplett, N. T. (2015). *Essentials of strength training and conditioning 4th edition*. Human kinetics.

25. Halar, E., DeLisa, J., & Soine, T. (1983). Nerve conduction studies in upper extremities: skin temperature corrections. *Archives of physical medicine and rehabilitation*, *64*(9), 412-416.

26. Halar, E. M., DeLisa, J. A., & Brozovich, F. (1980). Nerve conduction velocity. Relationship of skin, subcutaneous and intramuscular temperatures. *Archives of physical medicine and rehabilitation*, *61*(5), 199-203.

27. Hennessey, W. J., Falco, F. J., Goldberg, G., & Braddom, R. L. (1994). Gender and arm length: influence on nerve conduction parameters in the upper limb. *Archives of physical medicine and rehabilitation*, *75*(3), 265-269.

28. Henrikson, J. (1956). Conduction velocity of motor nerves in normal subjects and patients with neuromuscular disorders. *Minnesota University, Master's Thesis*.

29. Izquierdo, M., Aguado, X., Gonzalez, R., Lopez, J., & Häkkinen, K. (1999). Maximal and explosive force production capacity and balance performance in men of different ages. *European journal of applied physiology and occupational physiology*, *79*(3), 260-267.

30. Kang, J. I., Moon, Y. J., Jeong, D. K., Choi, H., Park, J. S., & Choi, H. H. (2018). Muscle activity in relation to the changes in peripheral nerve conduction velocity in stroke patients: Focus on the dynamic neural mobilization technique. *Journal of International Academy of Physical Therapy Research*, *9*(2), 1447-1454.

31. Kluding, P. M., Pasnoor, M., Singh, R., Jernigan, S., Farmer, K., Rucker, J., Sharma, N. K., & Wright, D. E. (2012). The effect of exercise on neuropathic symptoms, nerve function, and cutaneous innervation in people with diabetic peripheral neuropathy. *Journal of Diabetes and its Complications*, *26*(5), 424-429.

32. Kumar, A., & Prasad, A. (1970). Nerve conduction velocity in median nerve and tibial nerve of healthy adult population with respect to gender. *National Journal of Physiology, Pharmacy and Pharmacology*, *6*(5), 368-368.

33. Kung, T. A., Cederna, P. S., van der Meulen, J. H., Urbanchek, M. G., Kuzon Jr, W. M., & Faulkner, J. A. (2014). Motor unit changes seen with skeletal muscle sarcopenia in oldest old rats. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *69*(6), 657-665.

34. LaFratta, C. W., & Smith, O. H. (1964). A study of the relationship of motor nerve conduction velocity in the adult to age, sex, and handedness. *Archives of physical medicine and rehabilitation*, *45*, 407-412.

35. Landau, M. E., Barner, K. C., & Campbell, W. W. (2005). Effect of body mass index on ulnar nerve conduction velocity, ulnar neuropathy at the elbow, and carpal tunnel syndrome. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *32*(3), 360-363.

36. Lauretani, F., Bandinelli, S., Bartali, B., Di Iorio, A., Giacomini, V., Corsi, A. M., Guralnik, J. M., & Ferrucci, L. (2006). Axonal degeneration affects muscle density in older men and women. *Neurobiology of aging*, *27*(8), 1145-1154.

37. Lexell, J. (1997). Evidence of Nervous System Degeneration with Advancing Age. *The Journal of Nutrition*, *127*.

38. Lixandrão, M. E., Damas, F., Chacon-Mikahil, M. P. T., Cavaglieri, C. R., Ugrinowitsch, C., Bottaro, M., Vechin, F. C., Conceição, M. S., Berton, R., & Libardi, C. A. (2016). Time Course of Resistance Training–Induced Muscle Hypertrophy in the Elderly. *The Journal of Strength & Conditioning Research*, *30*(1), 159-163.

39. Mayer, R. F. (1951). Nerve conduction studies in man. . *Neurology* (13), 1021-1030.

40. McNeil, C. J., Doherty, T. J., Stashuk, D. W., & Rice, C. L. (2005). Motor unit number estimates in the tibialis anterior muscle of young, old, and very old men. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *31*(4), 461-467.

41. Metter EJ, C. R., Metter B, Pacheco T, and Tobin J. (1998). The Relationship of Peripheral Motor Nerve Conduciton Velocity to Age-Associated Loss of Grip Strength *Aging Clinical and Experimental Research*, *10*, 471-478.

42. Molin CJ, W. J., and Runga AR. . (2017). High-resistance strength training does not affect nerve cross-sectional area- an ultrasound study. *Clin Neurophysiol Pract*, *2*, 163-169.

43. Moses, B., Nelson, R., Nelson Jr, A., & Cheifetz, P. (2007). The relationship between skin temperature and neuronal characteristics in the median, ulnar and radial nerves of non-impaired individuals. *Electromyography and clinical neurophysiology*, *47*(7-8), 351-360.

44. Norris AH, S. N., and Wagman IH. (1953). Age Changes in the Maximum Conduction Velocity of Motor Fibers of Human Ulnar Nerves. *Journal of Applied Physiology*, *5*, 589-593.

45. Oh, S. J., Kim, H. S., & Ahmad, B. K. (1985). The near-nerve sensory nerve conduction in tarsal tunnel syndrome. *Journal of Neurology, Neurosurgery & Psychiatry*, *48*(10), 999-1003.

46. Padkao T, a. P. P. (2019). Effectiveness of an upper and lower limb resistance training program on body composition, nerve conduction velocity, adn cardiac autonomic nervous system activity in university athletes. *J Exerc Physiol Online*(22).

47. Palve, S. S., & Palve, S. B. (2018). Impact of aging on nerve conduction velocities and late responses in healthy individuals. *Journal of neurosciences in rural practice*, *9*(01), 112-116.

48. Piasecki, M., Ireland, A., Piasecki, J., Stashuk, D. W., Swiecicka, A., Rutter, M., Jones, D., & McPhee, J. (2018). Failure to expand the motor unit size to compensate for declining motor unit numbers distinguishes sarcopenic from non-sarcopenic older men. *The Journal of physiology*, *596*(9), 1627-1637.

49. Rami, S. H. (2012). Effect of body mass index on parameters of nerve conduction study in Indian population. *Indian J Physiol Pharmacol*, *56*(1), 88-93.

50. Richards, J., Gechey A, Alexander J, Macedo L, May K.A., and Lindley SB. . (2021). The effect of local cooling at the elbow on nerve conduction velocity and motor unit behavior. An exploration of a novel neurological assessment. . *Sensors* (21), 6703.

51. Rivner, M. H., Swift, T. R., Crout, B. O., & Rhodes, K. P. (1990). Toward more rational nerve conduction interpreations: The effect of height. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *13*(3), 232-239.

52. Rivner, M. H., Swift, T. R., & Malik, K. (2001). Influence of age and height on nerve conduction. *Muscle & Nerve*, *24*(9), 1134-1141.

53. Robinson, L., Rubner, D., Wahl, P., Fujimoto, W., & Stolov, W. (1993). Influences of height and gender on normal nerve conduction studies. *Archives of physical medicine and rehabilitation*, *74*(11), 1134-1138.

54. Sale, D., McComas, A., MacDougall, J., & Upton, A. (1982). Neuromuscular adaptation in human thenar muscles following strength training and immobilization. *Journal of Applied Physiology*, *53*(2), 419-424.

55. Sale, D., Upton, A., McComas, A., & MacDougall, J. (1983). Neuromuscular function in weight-trainers. *Experimental Neurology*, *82*(3), 521-531.

56. Simmons, Z., Nicholson, T., Wilde, C., & Manders, E. K. (1997). Variation of calculated ulnar motor conduction velocity across the elbow with body mass index. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *20*(12), 1607-1608.

57. Sleivert GG, B. R., and Wenger HA. (1995). The influence of a strength-sprint training sequence on multi-joint power output. *Medicine and Science in Sports and Exercise*(27), 1655-1665.

58. Soudmand, R., Ward, L. C., & Swift, T. R. (1982). Effect of height on nerve conduction velocity. *Neurology*, *32*(4), 407-407.

59. Stetson DS, A. J., Silverstein BA, and Wolfe RA. . (1992). Effects of age, sex, and anthropometric factors on nerve conduction measures. *Muscle & Nerve*, *15*, 1095-1104.

60. Strotmeyer, E. S., De Rekeneire, N., Schwartz, A. V., Resnick, H. E., Goodpaster, B. H., Faulkner, K. A., Shorr, R. I., Vinik, A. I., Harris, T. B., & Newman, A. B. (2009). Sensory and motor peripheral nerve function and lower-extremity quadriceps strength: the health, aging and body composition study. *Journal of the American Geriatrics Society*, *57*(11), 2004-2010.

61. Stubbs Jr, E. B., Fisher, M. A., Miller, C. M., Jelinek, C., Butler, J., McBurney, C., & Collins, E. G. (2019). Randomized controlled trial of physical exercise in diabetic veterans with length-dependent distal symmetric polyneuropathy. *Frontiers in neuroscience*, *13*, 51.

62. Thakur, D., Jha, S., Pandey, N., Jha, C., Bajaj, B., & Paudel, B. (2011). Influence of height on the nerve conduction study parameters of the peripheral nerves. *J Clin Diagn Res*, *5*(2), 260-263.

63. Tomlinson, B., & Irving, D. (1977). The numbers of limb motor neurons in the human lumbosacral cord throughout life. *Journal of the neurological sciences*, *34*(2), 213-219.

64. van Meeteren, N. L., Brakkee, J. H., Hamers, F. P., Helders, P. J., & Gispen, W. H. (1997). Exercise training improves functional recovery and motor nerve conduction velocity after sciatic nerve crush lesion in the rat. *Archives of physical medicine and rehabilitation*, *78*(1), 70-77.

65. Verdú, E., Ceballos, D., Vilches, J. J., & Navarro, X. (2000). Influence of aging on peripheral nerve function and regeneration. *Journal of the Peripheral Nervous System*, *5*(4), 191-208.

66. VH, A. N., Govindan, R., Zubaida, P., & Jose, J. (1970). Normative data of upper limb motor nerve conduction in Northern Kerala population and effect of height on motor nerve conduction velocity. *National Journal of Physiology, Pharmacy and Pharmacology*, *6*(4), 340-340.

67. Wagman, I., & Lesse, H. (1952). Maximum conduction velocities of motor fibers of ulnar nerve in human subjects of various ages and sizes. *Journal of neurophysiology*, *15*, 235-244.

68. Walsh, M. E., Sloane, L. B., Fischer, K. E., Austad, S. N., Richardson, A., & Van Remmen, H. (2015). Use of nerve conduction velocity to assess peripheral nerve health in aging mice. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *70*(11), 1312-1319.

69. Wang, F. C., de Pasqua, V., & Delwaide, P. J. (1999). Age-related changes in fastest and slowest conducting axons of thenar motor units. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *22*(8), 1022-1029.

70. Ward, R. E., Boudreau, R. M., Caserotti, P., Harris, T. B., Zivkovic, S., Goodpaster, B. H., Satterfield, S., Kritchevsky, S., Schwartz, A. V., & Vinik, A. I. (2015). Sensory and motor peripheral nerve function and longitudinal changes in quadriceps strength. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *70*(4), 464-470.

71. Ward, R. E., Caserotti, P., Faulkner, K., Boudreau, R. M., Zivkovic, S., Lee, C., Goodpaster, B. H., Cawthon, P. M., Newman, A. B., & Cauley, J. A. (2014). Peripheral

nerve function and lower extremity muscle power in older men. *Archives of physical medicine and rehabilitation*, *95*(4), 726-733.

72. Yarasheski, K. (2002). Managing sarcopenia with progressive resistance exercise training. *Journal of nutrition health and aging 6*(5), 349-356.

APPENDICIES

Appendix A – IRB Approval Letter

Oklahoma State University Institutional Review Board

Date:	07/29/2022
Application Number:	IRB-22-270
Proposal Title:	Quantifying the trainability of peripheral nerve function in young and older adults.
Principal Investigator:	JoJo Shields
Co-Investigator(s):	
Faculty Adviser:	Jason Defreitas
Project Coordinator:	
Research Assistant(s):	Claire Smith, Shawn Reese
Processed as:	Expedited
Expedited Category:	

Status Recommended by Reviewer(s): Approved
Approval Date: 07/28/2022

The IRB application referenced above has been approved. It is the judgment of the reviewers that the rights and welfare of individuals who may be asked to participate in this study will be respected, and that the research will be conducted in a manner consistent with the IRB requirements as outlined in section 45 CFR 46.

This study meets criteria in the Revised Common Rule, as well as, one or more of the circumstances for which <u>continuing review is not required.</u> As Principal Investigator of this research, you will be required to submit a status report to the IRB triennially.

The final versions of any recruitment, consent, and assent documents bearing the IRB approval stamp are available for download from IRBManager. These are the versions that must be used during the study.

As Principal Investigator, it is your responsibility to do the following:
1. Conduct this study exactly as it has been approved. Any modifications to the research protocol must be approved by the IRB. Protocol modifications requiring approval may include changes to the title, PI, adviser, other research personnel, funding status or sponsor, subject population composition or size, recruitment, inclusion/exclusion criteria, research site, research procedures and consent/assent process or forms.
2. Submit a status report to the IRB when requested
3. Promptly report to the IRB any harm experienced by a participant that is both unanticipated and related per IRB policy.
4. Maintain accurate and complete study records for evaluation by the OSU IRB and, if applicable, inspection by regulatory agencies and/or the study sponsor.
5. Notify the IRB office when your research project is complete or when you are no longer affiliated with Oklahoma State University.

If you have questions about the IRB procedures or need any assistance from the Board, please contact the IRB Office at 405-744-3377 or irb@okstate.edu.

Sincerely,
Oklahoma State University IRB

VITA

JoCarol E. Shields

Candidate for the Degree of

Doctor of Philosophy

Dissertation: QUANTIFYING THE TRAINABILITY OF PERPIPHERAL NERVE
FUNCTION IN YOUNG AND OLDER ADULTS

Major Field: Health, Leisure, and Human Performance

Biographical:

Education:

Completed the requirements for the Doctor of Philosophy in Health, Leisure, &
Human Performance at Oklahoma State University, Stillwater, OK in May
2023.

Completed the requirements for the Master of Science in Exercise Science at
Texas Tech University, Lubbock, TX in 2013.

Completed the requirements for the Bachelor of Science in Movement Science
at Delaware State University, Dover, DE in 2010.

Experience:

Graduate teaching associate Aug '19 – Present
Department of Health and Human Performance
Oklahoma State University

Professional Memberships:

American College of Sports Medicine; 2013 – Present
National Strength and Conditioning Association; 2013 – Present