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## Assessment of Intrinsic Hand Neuromuscular Physiology

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*The University of Western Ontario*

Graduate Program in Health and Rehabilitation Sciences

A thesis submitted in partial fulfillment of the requirements for the degree in Doctor of  
Philosophy

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Supervisor

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## **Abstract**

Alterations to the peripheral nervous system and neuromuscular physiology may impact hand function in a typical or clinical population, such as individuals with ulnar neuropathy. The mechanisms that influence these positive and negative changes are still not well understood. The three studies within my thesis aim to validate the reliability of decomposition-based quantitative electromyography (DQEMG) measurements and explore the changes in intrinsic hand neuromuscular physiology in a typical aging population and individuals recovering from a surgical intervention for severe ulnar neuropathy.

The purpose of the first study was to determine the test-retest reliability of near-fibre (NF) jiggle, a measure of motor unit stability. I found that NF jiggle had good measurement reliability with low error, especially when contrasted with traditional jiggle. The context of this reliability was specific to the intrinsic hand muscles: first dorsal interosseus (FDI), abductor digiti minimi (ADM), and fourth dorsal interosseus (4DI).

The purpose of the second study was to compare the intrinsic hand neuromuscular physiology of a typical aging population using multivariate analyses. I determined that with aging, there are decreases in motor unit number estimations (MUNE) and motor unit stability (NF jiggle) with increases to motor unit potential (MUP) area in the intrinsic hand muscles. Using a multivariate approach allowed for age-related differences and the relationship between the variables to be further elucidated.

The purpose of the third study was to describe the responses, functional outcome, and motor unit physiology of three participants following an ulnar nerve transfer surgery to treat severe ulnar neuropathy and the rehabilitation that followed. I determined that functional outcomes were associated with improvements to neuromuscular physiology and may be influenced by rehabilitation adherence. Also, factors such as comorbidities, psychosocial barriers and delay in treatment may affect functional outcomes and rehabilitation adherence.

Overall, the progression of quantitative EMG measurements and exploring mechanisms of neuromuscular changes in aging and clinical populations provide foundational knowledge that may impact rehabilitation and treatment approaches. I hope that my thesis may provide new avenues of assessment, treatment, and prognosis for persons with pathologies that influence hand function and neuromuscular physiology.

**Keywords:** Intrinsic hand muscles; Electromyography; Reliability; Motor Unit; Motor Nervous System

## **Summary for Lay Audience**

Our hands are critical for achieving daily tasks like grabbing a cup of coffee or dressing ourselves. Changes to the muscles of the hand and nerves that connect to them, such as with aging or with diseases like compression of the nerve, may affect the ability of the hand to perform tasks. How these changes happen are not always well understood. The goal of the studies within my thesis are to check the stability of a measurement technique, known as electromyography (EMG), which is used to explore muscle and nerve physiology. Further, I used EMG to explore changes in the hand muscles and nerves in a healthy aging population and individuals recovering from a nerve surgery. This surgery is specifically used to treat cases of elbow nerve compression which has led to a decreased ability for the individuals to use their hand muscles.

The first study of my thesis checked the reliability of an EMG measurement in individual's hand muscles. When we tested and retested the same EMG measurement in the hand muscles, it showed good consistency. The purpose of my second study was to compare the hand muscles and nerves of young, middle, and older aged healthy individuals. When we compared older individuals to younger ones, we found that there are less nerve connections to the muscles and the consistency of this signal transmission from the nerves to the muscles decreases in quality with age. Finally, the third study of my thesis looked at three specific patients that received a new nerve surgery procedure to treat severe nerve compression at the elbow. My study looked at the recovery process of these three patients and used EMG to explore muscle and nerves of the hand. The success of their recovery not only related to the muscles and nerves of the hands but also to when the patient received the nerve surgery, other diseases they may have had, their mental health and social situations. Overall, I hope that the studies in my thesis, which measure the hand muscle and nerves. will contribute to new ways of treating people who have difficulties with their hand muscles.

## **Co-authorship Statement**

This thesis contains material from one published manuscript (Chapters 2) and two manuscripts awaiting reviews/revisions (Chapters 3 and 4). On all manuscripts, Philemon Tsang was the first author and Dr. Joy MacDermid, Dr. Thomas Miller, and Dr. Douglas Ross were coauthors. Dr. Christopher Doherty was a coauthor on Chapter 2 and 4. Dr. Timothy Doherty was a coauthor on Chapter 2 and 3. Juliana Larocerie-Salgado was a coauthor on Chapter 4 of the thesis. Michelle Eventov was a coauthor on Chapter 2. Philemon Tsang was the primary contributor to the data presented in this thesis with regards to collection, analysis, and interpretation.

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I would also like to thank my committee members for their help in this dissertation process. Dr. Thomas Miller and the EMG technicians (Jodi Beswick, Angela Scott, and Samuel Rioux), thank you for graciously accommodating my data collection within your facility. Dr. Timothy Doherty, thank you for your expertise regarding DQEMG. Your input and feedback have been invaluable as they have strengthened the quality of these research projects. Dr. Christopher Doherty and Dr. Douglas Ross, thank you for the access to the patient population for my investigations and your feedback as well. I would also like to thank my fellow coauthors Juliana Larocerie-Salgado and Michelle Eventov. Your contributions to the data acquisition and feedback for the manuscript have helped greatly.

Over the past few years, many individuals who are friends or strangers have generously volunteered their time to participate in my studies. These individuals kindly participated without any expectation of a tangible reward. Many participants volunteered knowing my data collection would involve some degree of discomfort. I am thankful for these participants; this thesis would not be possible without their generosity and kind spirit.

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thank my Lord Jesus Christ. Through Him all things were made; without Him nothing was made that has been made (John 1:3). Ultimately, this research work points to the majesty and glory of God's creation and Kingdom.



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## **List of Abbreviations**

AIN – anterior interosseous nerve  
ADL – activities of daily living  
ADM – abductor digiti minimi  
ALS – amyotrophic lateral sclerosis  
CAD – consecutive amplitude difference  
CIDP – chronic inflammatory demyelinating polyneuropathy  
CMAP – compound muscle action potential  
CNS – central nervous system  
CVA – cerebral vascular accident  
DASH – disability of arm, shoulder, and hand  
DE-STA – decomposition enhanced spiked triggered averaging  
DFA – discriminant function analysis  
DQEMG – decomposition-based quantitative electromyography  
EMG – electromyography  
ETE – end-to-end  
ETS – end-to-side  
FDI – first dorsal interosseus  
ICC – intra-class correlation coefficient  
IDI – inter-discharge interval  
QuickDASH – quick disability of arm, shoulder, and hand  
LOA – limits of agreement  
MA – middle-aged adult  
MANOVA – multivariate analysis of variance  
MDC – minimal detectable change  
MRC – medical research council  
MU – motor unit

MUNE – motor unit number estimation  
MUP – motor unit potential  
MVC – maximal voluntary contraction  
NF – near- fibre  
NMES – neuromuscular electrical stimulation  
OA – older adult  
PCA – posterior cerebral artery  
PD – Parkinson’s disease  
PPS – pulses per second  
PRUNE – patient rated ulnar nerve evaluation  
ROM – range of motion  
SD – standard deviation  
SEM – standard error of measurement  
SETS – supercharged end-to-side  
SMUP – surface motor unit potential  
TA – tibialis anterior  
TMS – transcranial magnetic stimulation  
UNE – ulnar nerve entrapment at the elbow  
UWO – University of Western Ontario  
YA – younger adult  
4DI – fourth dorsal interosseus

# Chapter 1- General Introduction

## 1. Human neuromuscular system and the motor unit

Any simple human action, whether it is throwing a ball or holding a cup of coffee requires the control of our musculoskeletal system. These actions require the interaction of the nervous system with the musculoskeletal system. Connecting the human central nervous system with muscles is the neuromuscular system, where the most fundamental unit for motor control is the motor unit. The motor neuron, its axon, and the muscle fibres that it innervates comprise the motor unit, which has been referred to as the final common pathway for motor control (Sherrington 1925).

Motor units have a large degree of variance in size and properties. The number of muscle fibers a motor unit innervates is known as the innervation number and can vary depending on the function and type of muscle (Feinstein et al. 1955). Likewise, the number of motor units in each muscle vary depending on the role of the muscle. It is generally proposed that motor neurons with a lower innervation number produce finer control and higher innervation numbers lead to greater resultant force production. It should be noted that even within a muscle, motor units do not have all the same innervation numbers with the first dorsal interosseous (FDI) muscle being one example (Kandel, E.; Schwartz, J.; Jessel 1991).

During voluntary contractions, motor units are typically recruited from the smallest to largest, a concept known as Henneman's size principle (Henneman 1957). This results in the initial recruitment of smaller and weaker muscle fibres progressing to larger, stronger, and faster fibres that are less fatigue resistant (Henneman and Olson 1965). Overall, the amount of force produced by a muscle is dependent on the number of motor units recruited and the rate that these motor units are discharged, also known as rate coding (Kandel, E.; Schwartz, J.; Jessel 1991). The control and modulation of these two mechanisms determine muscle forces and motor control.

## **2. Surface and Intramuscular Electromyography (EMG)**

Oftentimes, during muscle contractions several motor units are activated, which when summated, produce signals that can be detected by electromyography (EMG). Signals that are larger can be detected using surface electrodes placed over the skin of the muscle being recorded. The timing and amplitude of the signal recorded reflects the activation of the muscle fibres and motoneurons (Kandel, E.; Schwartz, J.; Jessel 1991). By stimulating along the motor pathway to activate some or all the muscle fibres, a recording via surface electrodes known as the compound muscle action potentials (CMAP) may be acquired. The synchronous activation of the muscle fibres provides an assessment of the motor pathway below the site of stimulation, the neuromuscular junction, and the muscle fibres activated (Daube and Rubin 2009a). To characterize the integrity of the motor units in more detail, intramuscular or needle EMG may be applied (Daube and Rubin 2009a). A voluntary muscle contraction with the detection of intramuscular EMG allows for motor unit potential (MUP) measurement and evaluate possible changes within the muscle.

## **3. Decomposition-based Quantitative Electromyography (DQEMG) and Motor Unit Number Estimation (MUNE)**

MUP acquisition is critical in the physiological assessment of motor units and pathologies. Although MUPs are frequently examined qualitatively, qualitative analysis can be prone to error and subjective interpretation (Pino et al. 2008). Quantitative analysis of motor units allows for baseline values and the ability to characterize pathological conditions further. Advancements to algorithms and technology have allowed for EMG signals to be acquired during muscular contractions and decomposed into trains of MUPs, a principle known as decomposition enhanced spiked triggered averaging (DE-STA) (Doherty and Stashuk 2003; Boe et al. 2004, 2005). Decomposition-based quantitative EMG (DQEMG) utilizes the principles of DE-STA and objectively acquires MUPs trains, providing clinically relevant insight regarding the MUP characteristics (Doherty and Stashuk 2003). Advantages to DQEMG include the increased speed and efficiency that MUPS are acquired. The temporal classification of



the MUP trains act as a trigger for extracting corresponding trains of MUPs from the surface EMG also known as surface MUPs (SMUP) (Boe et al. 2004).

Determining the number of motor units within a muscle is of great significance to neuromuscular physiology. Motor unit number estimation (MUNE) is a numeric estimation of the number of innervated axons within a muscle. MUNE is typically calculated based on the maximal CMAP divided by the average SMUP (McComas et al. 1971). Various approaches to MUNE have been developed such as the incremental method (McComas et al. 1971), multiple point stimulation (Doherty and Brown 1993), spike triggered averaging (Brown et al. 1988) and DE-STA (Boe et al. 2004). Using DQEMG and DE-STA to calculate MUNE allows for greater efficiency and for higher levels voluntary contraction, allowing for a sampling of a wider range of motor units.

#### **4. Motor Unit Potential Features and Jiggle**

Motor unit stability may be assessed through MUP shape variability. The term jiggle was originally described by Stålberg and Sonoo (1994) to characterize motor unit shape variability (Stålberg and Sonoo 1994). Likewise, jitter was a term used to describe the variation in the time interval between the firing of adjacent muscle fibres from the same motor unit (Stålberg and Sonoo 1994; Zalewska and Hausmanowa-Petrusewicz 2018). In the presence of increased neuromuscular transmission disturbance, impulse blocking may occur, which is caused by the loss of some action potentials believed to be due to impaired motor endplate transmission. Various factors such as background activity, needle movement, and physical noise may also influence MUP shape variability (Daube and Rubin 2009a; Rodríguez et al. 2011). Increases in MUP jiggle has been observed in patients with amyotrophic lateral sclerosis (ALS) (Stålberg and Sonoo 1994) and myasthenia gravis (Benatar et al. 2006).

In order to capture MUPs that are closer to the needle recording area, high-pass filtering may be used to generate near-fibre (NF) MUPs (Boe et al. 2004). Like jiggle, NF jiggle was developed to further investigate the integrity of neuromuscular transmission. DQEMG has been used to assess changes in NF jiggle in several clinical populations. Increased NF jiggle has been previously observed in individuals with diabetic neuropathy

(Allen et al. 2015) and chronic inflammatory demyelinating polyneuropathy (CIDP) (Gilmore et al. 2017a).

Motor unit properties may be characterized by multiple MUPs and their appearances, including features like amplitude, duration, and area. Histological features like the innervation ratio and fibre density (number of muscle fibers in a cross-sectional area) can also affect the characteristics of the MUPs (Daube and Rubin 2009a). MUP amplitude is usually measured from the negative to the positive peak of the main spike (peak-to-peak amplitude). Similarly, MUP duration is defined as the time window of initial deflection from baseline to the time when the shape has returned to baseline. MUP amplitude and duration collectively reflect the MUP area of the motor unit. Some pathological conditions have been associated with increases in MUP duration and area such as diabetic neuropathy (Allen et al. 2015).

## **5. Reliability of DQEMG**

The validity and reliability of DQEMG measurements have been explored in various contexts. Specifically, DQEMG's calculation of MUNE has demonstrated high reliability for the test-retest and intra-rater reliability (Boe et al. 2006; Ives and Doherty 2012; Piasecki et al. 2018). Measurement of the maximal CMAP has been previously reported to have moderate and high levels of reliability for the biceps brachii and upper trapezius, respectively (Ives 2012). Similarly, SMUP reliability was high for both the biceps brachii and trapezius (Ives and Doherty 2012). The reliability of DQEMG applied to larger lower extremity muscles demonstrated high levels of reliability when estimating the motor unit numbers (Piasecki et al. 2018).

Previous investigations have also reported DQEMG's reliability for needle MUP parameters such as amplitude, area, and duration. The biceps brachii and FDI muscles' MUP duration and area demonstrated moderate levels of inter-rater and intra-rater reliability (Boe et al. 2010; Ives and Doherty 2012). NF jiggle, a measure of motor unit stability, demonstrated good levels of inter-rater reliability in the tibialis anterior muscle (Allen et al. 2015).

## **6. The Aging Hand**

### **6.1 Age-related decreases in upper extremity control**

With aging there are several changes that may be observed in upper extremity motor control and hand function. For example, older adults demonstrate altered prehension strategies (Shiffman 1992). When examined with functional capacity evaluations, older adults demonstrated diminished finger and hand coordination on tasks such as the Purdue Pegboard Test and the Complete Minnesota Dexterity Test (Soer et al. 2012). Likewise, there is a decline in independent finger movement and force production in a healthy aging population in contrast to younger adults (VanBeek et al. 2019).

Aside from motor control, strength declines with aging in the upper extremity have been explored in multiple contexts. Finger capacity in movements such as pinch, palmar, and key pinch strength may decline as early as 45 years of age (Mathiowetz et al. 1985). Aside from hand muscles, aging is associated with decreases in strength at the shoulder which has been observed in multiple tasks (Vidt et al. 2012). In contrast, no age-related strength decreases were seen at the elbow joint (Plow et al. 2014). Some suggested mechanisms contributing to age-related strength decreases include lower muscle volume, diminished maximal isometric joint moment-generating capacity, and altered sensorimotor cortical excitability (Vidt et al. 2012; Plow et al. 2014).

### **6.2 Age-related changes to sensorimotor physiology and sarcopenia**

Age-related changes in hand function and motor control may stem from various changes in the central nervous system. Using transcranial magnetic stimulation (TMS), previous reports have identified decreases in motor cortical excitability and sensorimotor integration (Bhandari et al. 2016). Similarly, neuroimaging studies using diffuse tensor imaging demonstrate changes in cortical white matter, specifically within the interhemispheric pathways (Salat et al. 2005) and corticospinal tract (Lebel et al. 2012). In healthy aging, there are changes to muscle spindle responses, resulting in alterations to spinal motor circuitry which have been observed via Hoffman reflexes (H-reflexes) (Geertsens et al. 2017; Lavender et al. 2019).

Various changes in muscle physiology have been observed in a typical aging populations. The phenomenon sarcopenia has been defined as the loss of muscle mass and strength as a result of aging (Doherty 2003; Power et al. 2013). Inactivity, increased muscle fat, insulin resistance, and nutrition contribute to the genesis of sarcopenia (Rosenberg 2011). However, the full mechanisms and etiology of sarcopenia are still not well understood. As sarcopenia onsets, decreases in the number of muscle fibres and reduced size of the remaining fibres have been previously observed in the lower extremity (Lexell et al. 1988; Hunter et al. 2016).

Several changes at the level of the motor unit can be observed in sarcopenia. First, at the level of the neuromuscular junction, several alterations have been observed in animal aging models. Examples of morphological changes include increased presynaptic branching and dispersion of postsynaptic endplate regions (Hepple and Rice 2016). At the metabolic and cellular level, mitochondrial impairments may also lead to neuromuscular junction instability (Hepple and Rice 2016; Rygiel et al. 2016). In humans, neuromuscular instability and changes have been observed in lower extremity muscles via EMG through the measurements NF jiggle and jitter (Hourigan et al. 2015; Gilmore et al. 2017b). In addition to impairments at the neuromuscular level, cellular death of motor neurons is a widely accepted mechanism and precursor to several of the deficits observed in sarcopenia (McNeil et al. 2005). One protective mechanism that has been established is the subsequent collateral reinnervation of orphaned muscle fibres following motor neuron death (Gordon et al. 2004). This increase in axonal sprouting temporarily maintains muscular function, but may still ultimately result in neuromuscular deficits such as impaired motor unit stability (i.e. increased jiggle) or increased metabolic demands and oxidative stress on the surviving motor neurons (Gordon et al. 2004; Hourigan et al. 2015; Gilmore et al. 2017b).

## **7. Ulnar Neuropathy and Nerve Transfers**

### **7.1 Ulnar Neuropathy Pathophysiology**

Ulnar neuropathy at the elbow is the second most prevalent compressive neuropathy with an annual incidence rate of 21 in 100 000 (Mondelli et al. 2005). Typical clinical

signs and symptoms of ulnar neuropathy include presentations of clawing, significant weakness, and eventually atrophy at the hands (Palmer and Hughes 2010). Sensory complaints from patients are initially intermittent paresthesia and motor symptom complaints of achiness (Mackinnon 2002). As the natural course of the pathology advances, symptoms may progress to constant numbness and weakness/atrophy, for sensory and motor symptoms, respectively. Electroneurography and EMG are commonly utilized to confirm the underlying neural pathology. Risk factors for ulnar neuropathy may include forceful work (Svendsen et al. 2012), obesity, and smoking (Frost et al. 2013).

There are three proposed causes for ulnar neuropathy including external compression, a tight humeroulnar arcade, elbow flexion leading to nerve traction or a combination of these factors (Stewart 2006; Omejec and Podnar 2016). Sites of entrapment or compression are typically the medial intermuscular septum, the retroepicondylar groove and under the humeroulnar aponeurotic arcade (also known as the cubital tunnel) (Caputo and Watson 2000). There are increases in connective tissue when a nerve crosses a joint, possibly as a response to repetitive loading (Armstrong et al. 1984; Rempel and Diao 2004). Animal models of repetitive loading have revealed a significant decrease in motor nerve conduction (Rempel et al. 2001; Rempel and Diao 2004)

Several mechanisms of pathogenesis, pathohistology and pathophysiology of compressive neuropathies have been previously examined. During the acute and initial phases of nerve compression, there is an increase in vascular permeability due to a breakdown of the blood nerve barrier (Mackinnon 2002). There is eventual edema formation within the nerve which continually builds up in the endoneurial space as there is no lymphatic drainage to decrease fluid accumulation (Lundborg 1983; Rempel 2004). Increase of compression duration or pressure leads to greater edema formation in a dose-response relationship (Rempel 2004; Mackinnon 2002). Eventually, macrophage recruitment occurs resulting in fibrosis and demyelination. As the pathology persists, there is eventual nerve degeneration (Rempel 2004).

## 7.2 Surgical Interventions for Ulnar Neuropathy

Several surgical interventions may be performed to treat ulnar nerve entrapments to resolve the pressure at the site of compression. Cubital Tunnel Release can be performed via open surgery or endoscopically with similar results reported (Aldekhayel et al. 2016). However, performing the release endoscopically may allow for the surgical intervention to be less invasive and permit for faster rates of recovery (Cobb 2010). There are several clinical scenarios that are contraindications to the surgical technique such as space occupying lesions, long-standing elbow contractures, and other conditions requiring the nerve to be repositioned (Cobb 2010). When decompression is unsuccessful, other surgical approaches may be utilized like anterior transpositions, where the ulnar nerve is relocated to an anterior submuscular or subcutaneous site to prevent recurrent compression or subluxation (Caputo and Watson 2000). One critique and disadvantage to anterior transposition is that it may devascularise the nerve (Ogata et al. 1985; Geutjens et al. 1996). Finally, in cases where proximal nerve injuries or neuropathies have poor functional recovery, nerve transfers have been recommended as a means of intervening (Tung and Mackinnon 2010; Kale et al. 2011). A previously recommended approach to transfers is end-to-end (ETE), where the donor nerve is coapted to the end of the recipient nerve (Tung and Mackinnon 2010; Kale et al. 2011). It should be noted that these surgical approaches can and have been used in combination, depending on the patient's clinical context (Jarvie et al. 2018). Overall, the prognosis and recovery following some of these surgical interventions are sometimes less than optimal for functional outcomes (Lan et al. 2019).

One relatively novel nerve transfer approach has been utilized by transferring one end of the anterior interosseous nerve (AIN) as a donor nerve to the side of the ulnar nerve. Past reports have named the procedure as the supercharged end-to-side (SETS) AIN to ulnar nerve technique (Barbour et al. 2012). Typically, the surgical process involves an initial release of the Guyon canal. The motor fascicles of the ulnar nerve are then identified via electrical stimulation. The AIN is then harvested and coapted to the motor fascicles of the ulnar nerve from the side (Barbour et al. 2012). Theoretically, the AIN “supercharges” the motor aspects of the ulnar nerve, allowing for reinnervation of the

hand musculature (Kale et al. 2011). Initial animal models have demonstrated increased nerve regeneration, muscle mass, and improved quality of nerve regeneration (Farber et al. 2013a). Further, the SETS AIN to ulnar nerve has shown promising clinical improvements such as increased pinch strength, improved grip strength, and increased ability to abduct the affected hand (Kale et al. 2011; Barbour et al. 2012; Baltzer et al. 2016; Jarvie et al. 2018). One recent systematic review further emphasized the effectiveness of restoring intrinsic function following the SETS AIN to ulnar nerve surgery (Dunn et al. 2019). However, to optimize surgical approaches for success, guidelines and indications for the SETS AIN to ulnar nerve were also recently developed (Power et al. 2020).

### **7.3 Rehabilitation for Ulnar Neuropathy and Nerve Transfer**

In some scenarios, ulnar neuropathy can be treated with conservative management alone. Prior to surgery, options for treatments may include splints, neural mobility exercises, or patient education. Splints are commonly applied at the elbow nocturnally to prevent excessive flexion at night, which is known to increase cubital tunnel pressure (Coppieters et al. 2004; Svernlöv et al. 2009). Goals of neural mobilization include reducing intraneural and extraneural edema, increasing blood circulation and improving neural tissue mobility (Coppieters et al. 2004). Patient education includes avoiding factors that would provoke symptoms (Robertson and Saratsiotis 2005). One clinical trial compared the effectiveness of splints, neural mobilization and education alone and found comparable outcomes with all three interventions (Svernlöv et al. 2009). Additional strategies may also involve the use of cortisone injections. However, when comparing placebo to cortisone injections, there was no superiority found with cortisone injections for ulnar neuropathy management (vanVeen et al. 2015).

Following nerve transfers, rehabilitation protocols are necessary to maximize functional outcomes of patients. Having specific stages and structured protocols to guide therapist and patient goals and expectations following nerve transfer surgery may optimize outcomes. One specific concept that has been emphasized is the idea of donor activation, where the patient focuses on the previous function of the donor nerve in order

to activate and strengthen the new recipient muscle (Kahn and Moore 2016). A recent review, known as The Birmingham Protocol, has proposed specific stages of rehabilitation to optimize functional recovery following nerve transfers (Hill et al. 2019). The protocol is divided into six stages (pre-operative, protection, prevention, power, plasticity, and purpose) that are relatively easy to understand and encourages patient participation. Similarly, a recent structured rehabilitation protocol was developed by Sturma et al (2019). The protocol is subdivided into four components (patient education, enhancing cortical representation of the denervated body part, motor activation using donor side approach, and re-learning the original movement pattern) (Sturma et al. 2019). To date, there have been no investigations to observe the measurement and efficacy of these protocols and stages. Further, with nerve transfer and rehabilitation, aside from motor outcomes like the medical research council (MRC) muscle scale (James 2007), there are no formally agreed upon outcome measurements from these protocols (Hill et al. 2019; Sturma et al. 2019). Generic patient reported outcome measures include the Disability of Arm, Shoulder and Hand or Patient Experience Measure score (Macey et al. 1995; Hudak et al. 1996; Hill et al. 2019). One specific outcome measure that has been validated for ulnar neuropathy surgery is the Patient Rated Ulnar Nerve Evaluation (PRUNE) (MacDermid and Grewal 2013).

## **8. Goal of Thesis**

The purpose of my thesis was to contribute to the knowledge of intrinsic hand neuromuscular physiology and its possible clinical applications. I did this by investigating persons with ulnar neuropathy, examining typical age-related changes to motor unit physiology, and exploring the outcomes following a nerve transfer intervention. Motor unit physiology was measured utilizing decomposition-based quantitative EMG (DQEMG). Near-fiber (NF) jiggle, a relatively novel and specific DQEMG measure of motor unit stability was explored across the various investigations. The initial study within the thesis explored the test-retest reliability of NF jiggle in the intrinsic hand muscles. The second manuscript utilized DQEMG to describe age-related changes in intrinsic hand neuromuscular physiology in typical adults in various age groups. Finally, utilizing a repeated case study design, I explored the clinical trajectory



and hand motor unit physiology of individuals who had severe ulnar neuropathy and received the SETS AIN to ulnar nerve procedure and the subsequent hand rehabilitation.

## 9. References

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## Chapter 2- Test-retest reliability of near-fibre jiggle in the ulnar intrinsic hand muscles

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### Introduction

Measurement of motor unit potentials (MUP) via quantitative electromyography is an objective and *in vivo* method of studying alpha motor neuron health and muscle innervation (Stålberg 1966). The stability of neuromuscular transmission may be assessed through MUP shape variability from a single motor unit (MU). Stålberg and Sonoo (1994) had originally described motor unit shape variability, describing the terms jitter, impulse blocking, and jiggle (Stålberg and Sonoo 1994). In a recent investigation, jitter was described as the variation in the time interval between the firing of adjacent muscle fibres from the same motor unit (Zalewska and Hausmanowa-Petrusewicz 2018). In severe cases of neuromuscular transmission disturbance, there may be loss of some action potentials believed to be due to impaired motor endplate transmission, known as impulse blocking. Finally, jiggle refers to the MUPs' shape variability across multiple discharges within a single motor unit. Collectively, jitter, impulse blocking of the single fibre action potentials are believed to contribute to jiggle (Stålberg and Sonoo 1994). However, other technical factors like background activity, needle movement, and physical noise may also contribute to EMG jiggle (Daube and Rubin 2009b; Rodríguez et al. 2011).

Decomposition-based quantitative EMG (DQEMG) concurrently uses needle and surface electromyography to measure motor unit physiology, offering clinically relevant data. DQEMG has been used as an approach and technique to capture near fibre (NF) jiggle and jitter. Similar to jiggle as originally described, NF jiggle was developed to further investigate the integrity of neuromuscular transmission (Allen et al. 2015). NF

MUP is generated by high-pass filtering the MUP template waveform and is therefore primarily composed of fibres that are close to the recording area of the needle (Boe et al. 2004). MU stability is believed to be inversely related to increases in NF jiggle and jitter (Stålberg et al. 1996).

Changes in NF jiggle have been previously observed in several clinical populations. Increased NF jiggle has been previously observed within the lower extremity muscles in individuals with amyotrophic lateral sclerosis (ALS) (Campos et al. 2000), diabetic neuropathy (Allen et al. 2015), chronic inflammatory demyelinating polyneuropathy (CIDP) (Gilmore et al. 2017a), and older adults (Hourigan et al. 2015; Gilmore et al. 2017b). Likewise, increases in MUP jiggle have been observed in facial muscles of patients with myasthenia gravis (Benatar et al. 2006) and ALS (Stålberg and Sonoo 1994). However, to date, there have been no investigations that have explored the test-retest reliability of NF jiggle measurements, specifically, within the intrinsic hand muscles. Measurements of reliability are critical for the usage of a measurement tool, particularly if this tool will be used for clinical assessments. The purpose of the present study was to investigate the reliability of NF jiggle in the ulnar nerve innervated intrinsic hand muscles.

## **Methods**

### **Participants**

Twenty healthy adults (Mean age =  $23.2 \pm 1.9$ ; 8 females) volunteered to participate in the study. All subjects gave informed consent in accordance with University of Western Ontario's ethics review board (Reference: 2016-107863-2120).

### **Data Acquisition**

Measurements of DQEMG NF jiggle were made with a standard single-strand 25 mm disposable stainless-steel concentric needle (Model N53153; Teca Corp., Hawthorne, NY) with an inner tungsten core. The concentric needle was connected to a single wire lead. Needle EMG signals were acquired using a standard clinical EMG system Cadwell



and Sierra Summit and bandpass filtered at 10 Hz to 10 kHz with a sampling rate of 48 kHz.

Participants were comfortably positioned with their arm supported during data acquisition. Participants were instructed to immobilize and maintain the other digits in a relaxed position. This allowed for resistance during voluntary contractions and minimized movement artifacts. The concentric needle (the needle has a stainless-steel cannula to increase the comfort of insertion) was inserted into the largest portion of the muscle belly of the muscles being examined (~10 mm in depth). Participants were asked to contract the muscle being examined to produce a mild to moderate intensity voluntary isometric contraction. Following each contraction, subjective feedback was provided by the researcher to the participant to reach a contraction intensity to approximately 40-60 pulses per second (pps). Participants were initially asked to minimally contract the muscle isometrically and the needle position was adjusted until it minimized the rise time of the first few motor units. Rise time was evaluated subjectively through auditory and visual feedback as the Sierra system did not provide an objective measure of rise time. Once the needle was in a satisfactory and stable position, the contraction was sustained for ~30 seconds where MUPs from several MU were detected. Participants were coached to maintain the contraction at the same mild-moderate intensity throughout the 30 seconds through auditory feedback and verbal cueing from the investigator. Approximately four to six contractions were collected to acquire 20 or more MUP trains for each muscle. The needle position was adjusted between contractions to minimize the chances of sampling the same motor units. To obtain NF MUPs, we used a high-pass filter using a second ordered low-pass differentiator. The second order filter equation is:  $x_t = y_{t+2} - y_{t+1} - y_t + y_{t-1}$ . The  $y_t$  is the sampled raw signal and  $x_t$  is the sampled filtered signal. The formula and methods for the filters have been reported elsewhere (McGill et al. 1985; Stashuk 1999b; Allen et al. 2015). Figure 1 provides an example of MUP shimmer plots before and after filtering. NF jiggle was obtained from the first dorsal interosseous (FDI), the abductor digiti minimi (ADM), and the fourth dorsal interosseous (4DI) muscles. Calculations of NF jiggle were quantified with the consecutive amplitude difference (CAD) statistic previously described by Stålberg and Sonoo (Stålberg and Sonoo 1994; Stashuk 1999b). The consecutive amplitude difference is calculated using an

absolute value of the amplitude integrated for time and normalized to the MUP area with a median correction utilized. However, this statistic was applied to NF MUPs rather than the original MUPs.

One of the authors (P.T.) collected and reviewed the MUP trains. For the retest portion of the study, the data collection was repeated on the same day. The same concentric needle was used for the retest portion but performed after a brief 15-minute break. Data analysis was only performed following both the test and retest portions. Data review was not performed with the author blinded.

### **Data Analysis**

EMG data was then inspected and analyzed following the sessions. Approximately 20 to 30 MUP trains were acquired for each participants' hand muscles (FDI, ADM and 4DI) during the test and retest session. In order to ensure that there was a consistent MU firing pattern represented, visual checks were made for each MUP train. Also, the inter-discharge-interval (IDI) histogram was inspected to confirm that the distribution was Gaussian in nature and with a coefficient of variation <0.3. MUP trains were required to have >50 detected potentials. Any MUP trains that did not meet the inclusion criteria stated were not included further in the analysis. NF MUP parameters include NF count, NF jiggle, NF jitter, NF dispersion and maximum NF interval. However, for the purpose of this investigation, NF jiggle will be the focus. NF jiggle is a statistical measurement used to represent the shape variability of the MUPs produced by a single MU. Analysis of shape variability requires that the MUPs be representative of a single MU. The investigator viewed raster plots of the NF MUPs of each MUP train analyzed and excluded contaminated NF MUPs.

### **Statistical Analyses**

Mean values of jiggle and standard deviations of jiggle are represented on Table 2. Relative test-retest reliability was calculated using the intraclass correlation coefficient (ICC) (Shrout and Fleiss 1979). Further, standard error of measurement (SEM) was calculated using the following formula  $SD_{pooled} \times \sqrt{1 - ICC}$  (Harvill 1991). SEM is an

indication of the expected measurement error in a single individual's score using the same metric of jiggle. Minimal detectable change (MDC) was calculated at the 90% level, which is appropriate for assessing change in clinical practice. For the rater to be 90% confident that true change occurred, a threshold value of jiggle was calculated using the formula  $MDC_{90} = SEM \times \sqrt{2} \times 1.65$  (Leslie G. Portney 2009).

The Bland-Altman technique was used to determine the distribution of differences between the test and retest scores for NF jiggle. As per Bland and Altman, the differences between test and retest NF jiggle scores were plotted against the mean of their scores (Martin Bland and Altman 1986). Limits of agreement (LOA) were placed at  $\pm 1.96$  standard deviations (SD) around the mean difference, which was also indicated by a line. A patterned relationship between the score differences with the means would indicate a systematic bias. This was done through visual inspection of the plot, but also through the use of a linear regression model. Similarly, the plot allows for a visual inspection of the LOAs, where a narrower range would suggest better agreement between the two measures.

## Results

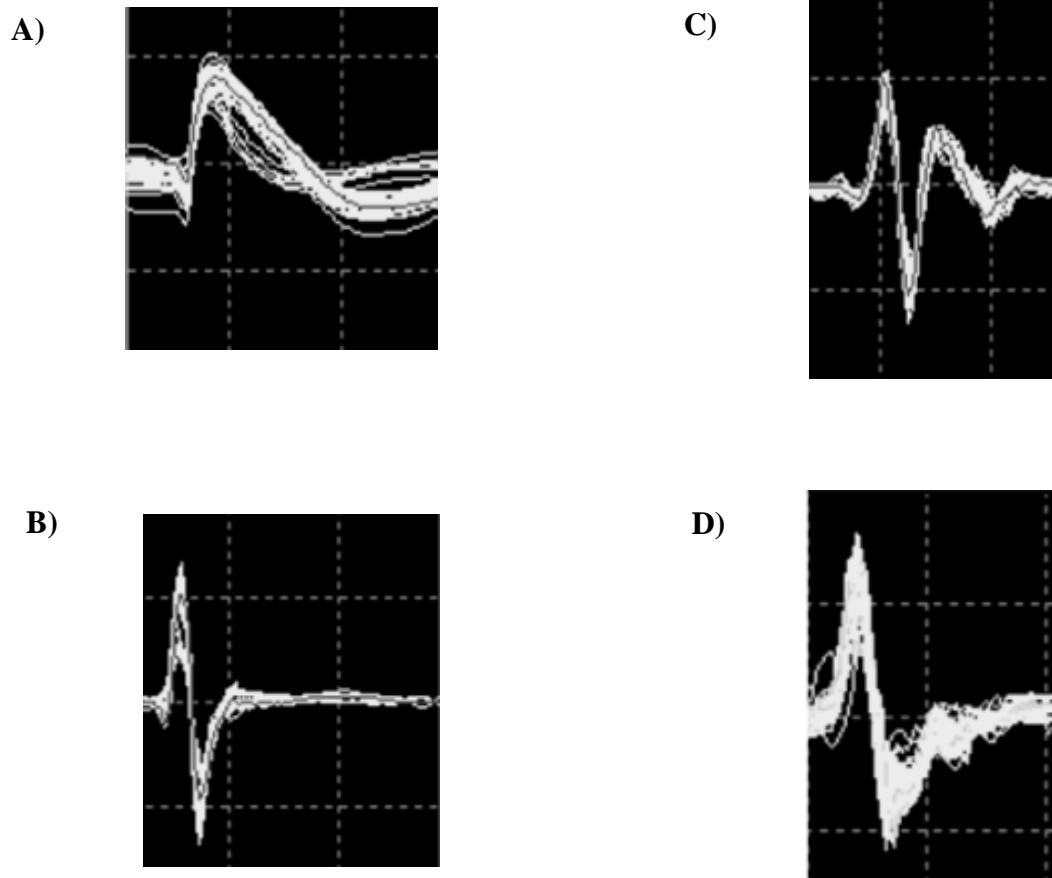
All twenty healthy adults successfully completed the study (Mean age =  $23.2 \pm 1.9$ ; 8 females) (See Table 1 for demographics).

The mean value of NF Jiggle values for the FDI, ADM, and 4DI were 32.5%, 32.4%, and 34%, respectively (Table 2). The mean value of Traditional Jiggle values for the FDI, ADM and 4DI were 59.5%, 55.1%, and 57.4%, respectively (Table 2).

Figure 2 represents the Bland-Altman plot for the FDI, ADM and 4DI muscles. Upon visual inspection of the scatterplot for the FDI and 4DI, the points indicate no observable systematic bias due to the relative even distribution. In contrast, the ADM scatterplot shows small increases in the mean difference range as the mean scores increase. This suggests a small systematic bias between the NF jiggle test and retest measurements. The mean differences for the FDI, ADM and 4DI muscles were -0.82%, 0.56%, and 0.47%, respectively. The limits of agreement (LOA) for the test and retest

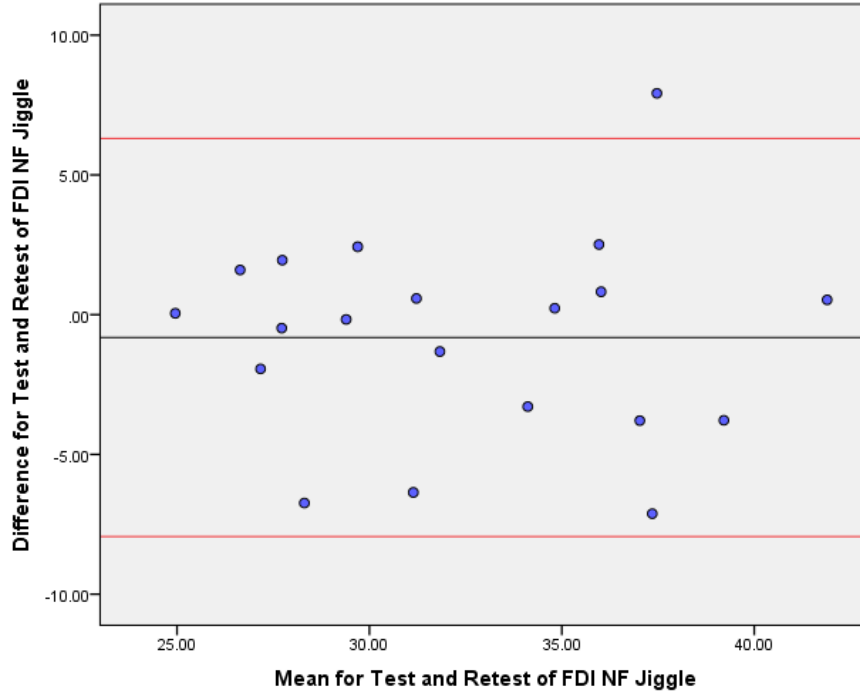
measurements were defined as 2 standard deviations (of the score differences) away from the mean difference. The LOA for the FDI, ADM and 4DI were -7.9% to 6.3% (range of 14.2%), -7.5% to 8.6% (range of 16.1%) and -9.2 to 10.1% (range of 19.3%), respectively. The ranges for the LOA suggest that there are greater score differences in the test and retest scores for 4DI NF jiggle in comparison to the other two muscles. However, the small asymmetry to the upper and lower limits for all three plots suggests minimal bias between the test and retest session in the FDI, ADM and 4DI. The linear regression models for the test and retest scores of all 3 hand muscles (FDI, ADM, and 4DI) indicated that NF jiggle averages were not a significant predictor of NF jiggle differences. Collectively, the low mean difference scores, the LOA and the regression model suggest a small amount of bias between the test and retest scores of NF jiggle in all 3 hand muscles.

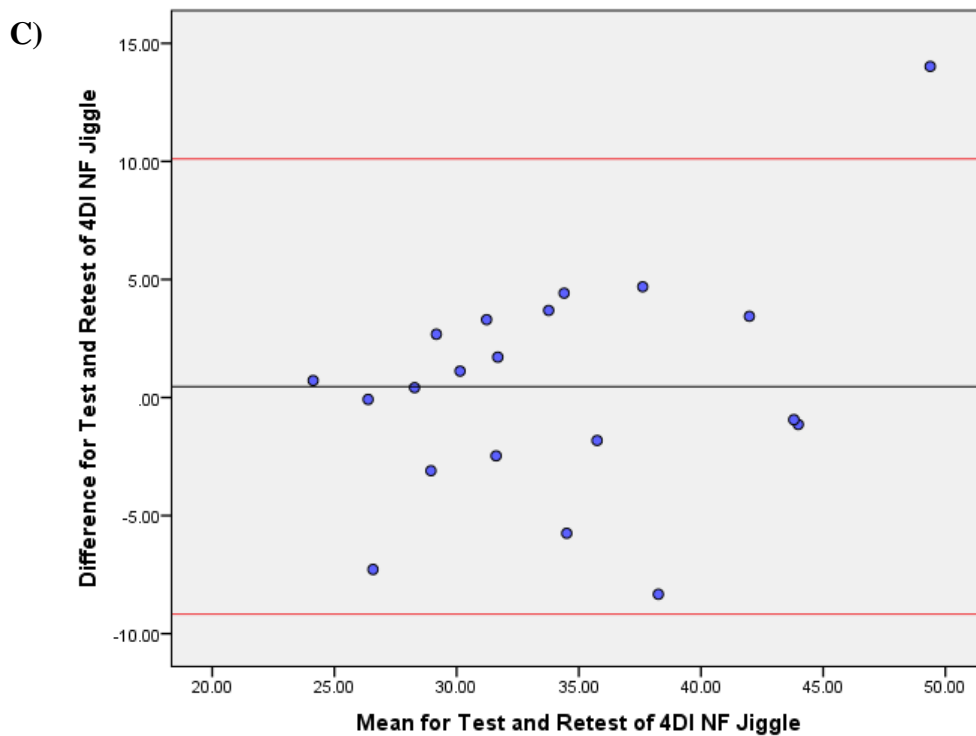
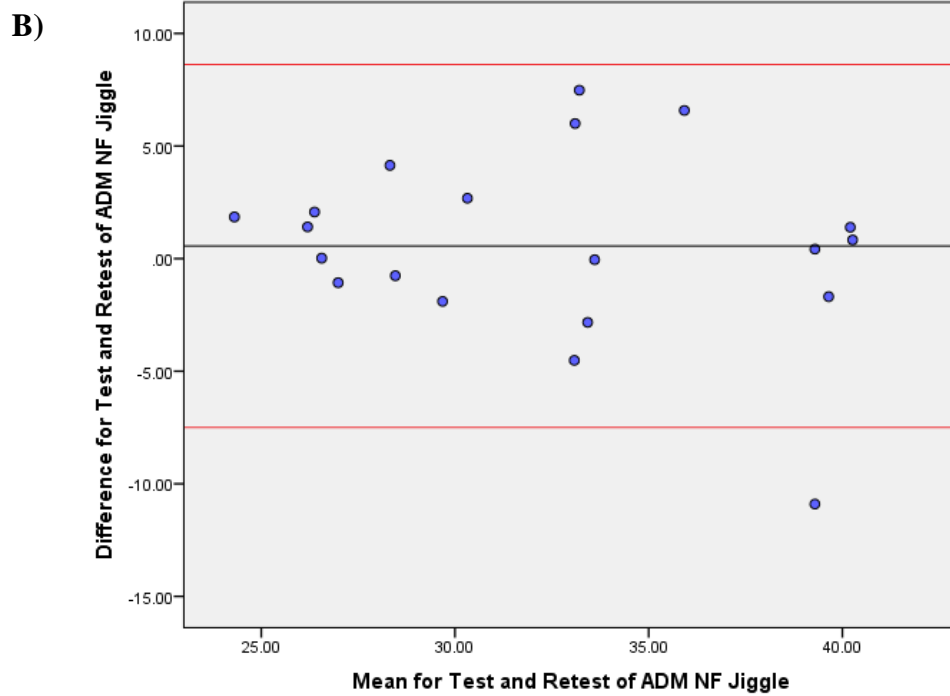
Table 3 presents the ICC, SEM and MDC values for all 3 hand muscles' NF Jiggle. Test-retest reliability was good in all three muscles' NF Jiggle (FDI, ADM and 4DI) with ICCs of 0.86, 0.85, and 0.87, respectively. The SEM and MDC were slightly smaller for the FDI and ADM muscles in comparison to the 4DI. Table 4 presents the ICC values for Traditional Jiggle of all 3 hand muscles. Test-retest reliability was moderate in the FDI (0.59) and 4DI muscle (0.55), the ADM muscle (0.79) demonstrated good reliability.



**Figure 1.** Examples of MUP shimmer plots from the FDI muscle of one participant **A)** MUP shimmer plot (before high pass filter) **B)** NF MUP shimmer plot (after high pass filter) **C)** NF MUP shimmer plot from test session (NF jiggle = 30.7%) **D)** NF MUP shimmer plot from re-test session (NF jiggle = 47.4%)

A)





**Figure 2.** Bland-Altman analysis comparing the test and retest session of NF jiggle **A)** first dorsal interosseous (FDI) muscle **B)** abductor digiti minimi muscle (ADM) **C)** fourth dorsal interosseous muscle (4DI)

**Table 1.** Study Demographics

<b>Demographics (n = 20)</b>	
Age	23.2 ( $\pm$ 1.9) <sup>a</sup> years
Men	12 (60%)
Women	8 (40%)
Right Hand Dominant	18 (90%)

<sup>a</sup> Standard Deviation

**Table 2.** Descriptive statistics for Near-fiber (NF) Jiggle and Traditional Jiggle

<b>Muscles</b>	<b>NF Jiggle (%)</b>			<b>Traditional Jiggle (%)</b>		
	<b><i>FDI</i></b> <sup>a</sup>	<b><i>ADM</i></b> <sup>b</sup>	<b><i>4DI</i></b> <sup>c</sup>	<b><i>FDI</i></b> <sup>a</sup>	<b><i>ADM</i></b> <sup>b</sup>	<b><i>4DI</i></b> <sup>c</sup>
<b>Mean</b>	32.5	32.4	34	59.4	55.1	57.4
<b>Standard Deviation</b>	5.1	5.6	7.1	30.1	25.6	25.7

<sup>a</sup> First Dorsal Interosseous (FDI)

<sup>b</sup> Abductor Digiti Minimi (ADM)

<sup>c</sup> Fourth Dorsal Interosseous (4DI)



**Table 3.** Intraclass Correlation Coefficient (ICC), Standard Error of Measurement (SEM) and Minimal Detectable Change (MDC) for near-fiber jiggle of the intrinsic hand muscles

	<b>FDI<sup>a</sup></b>	<b>ADM<sup>b</sup></b>	<b>4DI<sup>c</sup></b>
<i>Intraclass Correlation Coefficient (ICC)</i>	0.86	0.85	0.87
<i>Standard Error of Measurement (SEM)</i>	1.9	2.1	2.5
<i>Minimal Detectable Change (MDC)</i>	4.4	5.0	7.1

<sup>a</sup> *First Dorsal Interosseous (FDI)*

<sup>b</sup> *Abductor Digiti Minimi (ADM)*

<sup>c</sup> *Fourth Dorsal Interosseous (4DI)*

**Table 4.** Intraclass Correlation Coefficient (ICC) for traditional jiggle of the hand muscles

	<i><b>FDI</b></i> <sup>a</sup>	<i><b>ADM</b></i> <sup>b</sup>	<i><b>4DI</b></i> <sup>c</sup>
<i>Intraclass Correlation Coefficient (ICC)</i>	0.59	0.79	0.55

<sup>a</sup> *First Dorsal Interosseous (FDI)*

<sup>b</sup> *Abductor Digiti Minimi (ADM)*

<sup>c</sup> *Fourth Dorsal Interosseous (4DI)*

## Discussion

This study has demonstrated that the physiological measurement of NF jiggle, a quantitative electromyography measurement of motor unit shape variability, can be reliably obtained using DQEMG in the ulnar innervated intrinsic hand muscles FDI, ADM and 4DI. In contrast to traditional jiggle, NF Jiggle for FDI, ADM and 4DI demonstrated good reliability through the ICC values. SEM and MDC90 values were determined based on the ICC values. Capturing the reliability of NF jiggle allows future clinicians and investigators to follow the natural history of diseases and the response to treatments of disorders. Collectively, these measurements may provide useful insight regarding where pathological changes may have occurred.

Reliability is affected by the overall consistency of the NF jiggle technique but is also context specific to the tested muscles and population. Different clinical populations may have different inherent levels of variability, both error variability and participant variability. When examining ICC calculations, higher participant variability increases the denominator of the ICC, which may enhance relative reliability. In contrast, SEM and mean error are not ratio-based, so represent absolute size of measurement error. Overall, our data is specific to the reliability of jiggle in the hand muscles, in a relatively young and healthy population. Under these circumstances, all three hand muscles demonstrated good reliability. Further, the Bland-Altman plots demonstrated reasonable agreement between the test and retest trials of NF jiggle in all three hand muscles. When compared to traditional jiggle, NF jiggle demonstrated greater reliability (higher ICCs) in all 3 hand muscles. NF MUPs are obtained by high pass filtering MUP templates and therefore are comprised of fiber contribution that are closer to the needle detection surface (Stashuk 1999b; Allen et al. 2015). Measuring MUP configurations in more detail from the subset of motor units closer to the needle detection surface, the NF MUP may provide more detailed information regarding neuromuscular transmission in contrast to traditional MUP measurements. Previous investigation of NF jiggle vs. traditional jiggle in healthy participants have shown lower values of jiggle in the NF measurements in contrast to traditional jiggle (Stashuk 1999b; Allen et al. 2015). Considering the differences between these two approaches of measuring motor unit stability, the overall statistic of NF jiggle

appears to be more reliable and consistent when it was measured in the hand muscles of healthy participants.

Previous investigations have explored the test-retest and intra-rater reliability of DQEMG, particularly for the measurement of MUNE (Boe et al. 2004, 2006; Ives and Doherty 2012; Piasecki et al. 2018). Likewise, other studies have reported DQEMG's reliability for needle MUP parameters such as amplitude, area, and duration (Calder et al. 2008; Boe et al. 2010; Ives and Doherty 2012; Piasecki et al. 2018). The reliability coefficients in the previous investigations ranged from 0.53 (MUP area intra-rater reliability) (Ives and Doherty 2012) to 0.99 (MUP amplitude intra-rater reliability) (Calder et al. 2008). Moderate levels of reliability have been observed in MUP parameters like duration and area (Boe et al. 2010; Ives and Doherty 2012). Conceptually, these parameters should influence MUP configuration and create fluctuations in NF jiggle (shape variability) (Daube and Rubin 2009b). However, by specifically evaluating reliability of NF jiggle in the context of the intrinsic hand muscles, the measurement demonstrates good test-retest reliability for all the muscles observed. The current study's reliability coefficients of NF jiggle were similar to a previous investigation by Allen et al. (2015) where the tibialis anterior (TA) muscle's NF jiggle inter-rater reliability was reported to be 0.81 (Allen et al. 2015). The present study's SEM of 1.9 (FDI), 2.1 (ADM), and 2.5 (4DI) indicates the amount of variation that might be expected on repeated testing. Similarly, the MDC90 values of 4.4 (FDI), 5.0 (ADM), and 7.1 (4DI) indicates that if there was a change greater than these reported values, the user can be 90% confident that a change has occurred. These numbers provide a quantitative indicator of how much variation might be due to measurement error. Understanding how much error or random variation occurs in the normal population is the important prerequisite to understanding when variability is abnormal.

Previous studies have investigated DQEMG NF jiggle in healthy younger and older adults' lower extremity muscles (i.e. TA muscle). These studies have reported NF jiggle values of 34.3% (Gilmore et al. 2017a) and 33.8% (Allen et al. 2015), in the TA muscle. The current investigation is the first to provide data on hand muscles, and it is noteworthy that the estimates are similar to the lower extremity. Whether this range of

values can be expected in all muscles will only become apparent as data on a larger pool of muscles is published. DQEMG has been previously used to investigate motor unit number estimation and other motor unit properties in the FDI muscle (Boe et al. 2006, 2010; Allen et al. 2015), although NF jiggle was not reported. Jiggle adds important information about neuromuscular transmission stability. Unstable MUPs are shown by the change in the characteristics of the MUPs including prolonged durations, low amplitude and polyphasic shape (Krarup et al. 2016). This is believed to be associated with influential factors such as damaged motor axons or unstable conduction along immature terminal fibers during remodeling (Stålberg et al. 1996; Krarup et al. 2016). These pathophysiological characteristics and increases in NF jiggle have been observed in age-related muscular changes (i.e. sarcopenia) (Hourigan et al. 2015; Gilmore et al. 2017b) and other neuromuscular pathologies such as diabetic neuropathy (Allen et al. 2015), myasthenia gravis (Benatar et al. 2006), ALS (Stålberg and Sonoo 1994), and CIDP (Gilmore et al. 2017a).

While this study provides preliminary positive results that support the use of NF jiggle to assess motor unit stability in the hand, limitations must be considered when interpreting our results. First, our sample cannot be considered a normative population since we sampled a relatively younger age group and had insufficient numbers to identify reliability across the age span. Changes in motor unit stability have been previously reported in an aging population (Hourigan et al. 2015; Gilmore et al. 2017b). Second, test-retest reliability was determined by one rater, using an intra-rater reliability approach. Considering that various neuromuscular conditions are treated from multiple centers and clinicians, it would be important for future investigations to measure the inter-rater reliability of the technique as it is applied.

## **Conclusions**

The results of this study demonstrate that NF jiggle produces highly reliable results in healthy participants' intrinsic hand muscles, both in terms of detecting group differences (relative reliability), and absolute reliability (small SEM and MDC). NF jiggle may be a potentially useful measurement for measuring changes in motor unit

stability for future investigations such as age-related changes in hand muscles and investigations of nerve injuries.

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# **Chapter 3- Assessment of age-related differences in decomposition-based quantitative EMG in the Intrinsic Hand Muscles: A Multivariate Approach**

## **Introduction**

Hand control is arguably one of the most critical components for accomplishing activities of daily living. However, with aging there are several changes and declines that may be observed in the upper extremity such as altered strategies in the prehension of an object (Shiffman 1992). Other deficits such as decreases in grip and pinch strength may also contribute to a decline in hand function within an aging population (Puh 2010). Likewise, there is a decline in independent finger movement and force production in a healthy aging population in contrast to younger adults (VanBeek et al. 2019). Changes in hand function and motor control may stem from various factors. Studies using transcranial magnetic stimulation have identified decreases in motor cortical excitability and sensorimotor integration. (Bhandari et al. 2016). Alterations to muscle properties and tissue compliance also occur during normal aging (Tuite et al. 2007). Motor neuron and neuromuscular junction changes may also contribute to the decline in hand function in the elderly (Brown 1972; Doherty and Brown 1993, 1997; Doherty and Stashuk 2003). Specifically, the phenomenon sarcopenia has been defined as the loss of muscle mass and strength as a result of aging (Doherty 2003; Power et al. 2013). The mechanisms and etiology of sarcopenia are still not fully understood. However, factors such as inactivity, increased muscle fat, insulin resistance, and nutrition contribute to the genesis of sarcopenia (Rosenberg 2011).

Past reports have used techniques such as magnetic resonance imaging (MRI) to explore muscle volume or muscle protein quantity (Sinclair et al. 2010). However, using quantitative electrophysiological techniques allows for motor unit physiology and quality to be systematically examined within an aging population (Power et al. 2014). One approach to investigating neuromuscular physiology in-vivo is using decomposition-based quantitative electromyography (DQEMG). DQEMG simultaneously uses needle and surface electromyography (EMG) to objectively measure motor unit physiology,

offering clinically relevant insight (Doherty and Stashuk 2003). The fidelity of neuromuscular transmission and degree of reinnervation can be measured by DQEMG through spike trigger averaging to perform motor unit estimations (MUNE) and examine the stability of the functioning motor units (MU). DQEMG increases the speed and efficiency of motor unit potential (MUP) sampling. Similarly, near fibre (NF) jiggle and jitter are measurements that have been developed to further investigate the integrity of neuromuscular transmission (Stashuk 1999b; Allen et al. 2015). Collectively, DQEMG may allow clinicians to understand the neuromuscular mechanisms underpinning declines in motor control and performance; thereby providing avenues for future rehabilitation and treatments in response to these changes.

Age-related changes in the motor unit properties of the ulnar nerve innervated intrinsic hand muscles have not been investigated using DQEMG. The purpose of the current investigation was to compare the motor unit physiology of typical younger adults (YA) (20 to 40-year-old), middle-aged adults (MA) (41-60-year-old) and older adults (OA) (>60 years old) using DQEMG to examine the ulnar intrinsic hand muscles. Further, our investigation used a multivariate approach to analyze the findings from the intramuscular and surface EMG.

## **Methods**

### **Participants**

In total, forty-two participants were recruited to participate in this study. Fourteen participants were between 20-40 years old (mean age =  $26.6 \pm 2.9$  years), thirteen participants were between 41-60 years old (mean age =  $50.5 \pm 6.3$  years), and fifteen were >60 years old (mean age =  $73.5 \pm 7.4$  years). Participants in the 20-40 years old range were recruited from the University of Western Ontario (UWO) community. Participants from the other two age groups were either recruited from the Canadian Center for Activity and Aging, a local exercise group associated with UWO or from St. Joseph's Hospital. Participants in the three groups were excluded if there was any evidence of neurological or neuromusculoskeletal disease that would affect the findings. Informed consent was obtained from all participants in accordance with the University of

Western Ontario Health Science Research Ethics Board, which approved of this study (File number: 107863).

### **Data Acquisition**

DQEMG and the Sierra EMG system software (Sierra Inc) were used to collect the EMG data. Self-adhesive Silver Mactrode electrodes (GE Medical Systems, Milwaukee, WI) were used to detect surface signals with bandpass setting of 5 Hz to 5000 Hz. Intramuscular EMG signals were detected using 25 mm x 30-gauge disposable concentric needle electrodes (TECA elite, CareFusion, Middleton, WI) with bandpass settings of 10Hz to 10KHz.

For EMG data collection, each participant's skin was cleansed with isopropyl alcohol before surface electrodes were placed. For the FDI and ADM, the active electrode was positioned over the motor point of the muscle, whereas the reference electrode was positioned over the 2<sup>nd</sup> and 5<sup>th</sup> metacarpal phalangeal joint line, respectively. For all EMG collections, the ground electrode was positioned over the ipsilateral ulnar styloid process. No surface EMG was recorded from 4DI. To stimulate the ulnar nerve at the wrist (~7 cm proximal to the active electrode), a handheld bipolar stimulator was used to elicit a maximum CMAP. The stimulus intensity was gradually increased by the investigator in small increments until CMAP negative peak amplitude no longer increased.

A concentric needle was inserted into the muscle belly of the FDI, ADM and 4DI. For FDI and ADM, the needle electrode was always positioned a minimum of 2 mm away from the active surface electrode. Participants were asked to perform a mild to moderate isometric finger abduction contraction, while an optimal needle position was determined using the minimal rise times of the MUPs generated. Once an optimal position was obtained, participants were asked to maintain a mild to moderate contraction, which was evaluated by EMG intensity via pulses per second (pps). EMG intensity of approximately 70 pps corresponds with ~23% of MVC (Allen et al. 2015). Each contraction was held for ~30 seconds. During each contraction, participants received verbal feedback from the investigator to maintain the desired contraction

intensity. Subsequent contractions were performed until a minimum of 20 suitable MUP trains were collected. Contractions were separated by approximately ~30 second breaks or longer if needed by the participant. To capture motor units from various parts of the muscle, the needle was repositioned slightly between contractions.

### **Data Analysis**

The algorithms used in DQEMG have been described previously (Doherty and Stashuk 2003). The acceptability of MUP trains and decomposed EMG signals were reviewed offline. A minimum of 51 MUPs with a consistent and physiological MU firing rate were required for MUP trains to be accepted. MUP train's firing rates were considered physiological and consistent if the inter-discharge interval (IDI) histogram had a Gaussian-shaped main peak and a coefficient of variation of the IDI of less than 0.3 (Stashuk 1999a). MUP trains that had shapes indicating that it was a cannula-recorded potential were excluded, but the surface MUP (SMUP) template was still accepted. MUP raster plots were examined visually to determine whether they originated from the same MU. A MUNE for FDI and ADM were calculated by dividing the maximum CMAP mean negative peak amplitude by the SMUP negative peak amplitude mean.

Near fibre (NF) MUP is calculated by high pass filtering a MUP template waveform. Therefore, it is primarily composed of fiber contributions that are close to the recording area of the needle (Stashuk 1999b; Allen et al. 2015). NF MUP parameters include NF count (density) and NF Jiggle in this investigation. Jiggle is a statistic that calculates the variability in the overall MUP shape from 1 MUP discharge to the next within a single motor unit. NF jiggle demonstrates adequate reliability, specifically within the intrinsic hand muscles as shown in our previous study (Tsang et al. 2019). Higher NF jiggle values indicate decreased motor unit stability.

All statistics were analyzed using SPSS version 23.0 (IBM- SPSS, Chicago, Illinois). Normality was performed by visual inspection of histogram plots of the dependent variables. Box's Test was used to examine the equality of covariances. For all three intrinsic hand muscles (FDI, ADM and 4DI), a multivariate analysis of variance (MANOVA) was performed for the intramuscular EMG dependent variables (MUP Area,

MUP Duration, NF Count, and NF Jiggle) and surface EMG dependent variables (SMUP negative peak amplitude and MUNE). If statistical significance was observed with the MANOVA, a discriminate function analysis (DFA) was performed as a subsequent post hoc analysis. Effect sizes of the MANOVAs and DFAs were examined using partial eta squared ( $\eta_p^2$ ) and  $R^2$ , respectively. Similarly, magnitude of difference was calculated using Cohen's  $d$ . An  $\alpha \leq 0.05$  was considered statistically significant for all tests. Bonferroni correction was applied to the statistical significance levels to account for multiple MANOVAs ( $\alpha \leq 0.025$ ).

## **Results**

Forty-two adults successfully completed the study (See Table 1 for demographics). Group means and standard deviations for all intramuscular EMG and surface EMG are presented in Table 2A and 2B, respectively.

Two MANOVAs were performed with the independent variable AGE (YA vs. MA vs. OA). One MANOVA was performed for the intramuscular EMG variables (NF jiggle, MUP Area, MUP duration, NF Count) for all 3 intrinsic hand muscles (FDI, ADM and 4DI) for a total of 12 dependent variables to create a canonical construct we named as *intrinsic hand muscle intramuscular EMG*. A second MANOVA was performed for the surface EMG variables (SMUP amplitude and MUNE) for two intrinsic hand muscles (FDI and ADM) for a total of 4 dependent variables to create a canonical construct named as *intrinsic hand muscle surface EMG*. Follow-up DFA were performed for each of the MANOVAs, which creates a model that predicts group membership based on the predictor variables.

### **Intramuscular EMG Variables**

Using Pillai's Trace, there was a significant effect of AGE on the canonical variable *intrinsic hand muscle intramuscular EMG*,  $V = 0.88$ ,  $F(24, 58) = 1.91$ ,  $p < 0.025$ . Separate univariate ANOVAs indicated a significant effect of AGE on 4DI NF Jiggle,  $F(2, 39) = 3.72$ ,  $p < 0.05$ ; FDI Area,  $F(2, 39) = 4.66$ ,  $p < 0.05$ ; ADM Area,  $F(2, 39) = 3.30$ ,  $p < 0.05$ ; and 4DI NF Count,  $F(2, 39) = 4.06$ ,  $p < 0.05$ . The rest of the other

dependent variables' univariate ANOVAs were not statistically significant. The MANOVA's eta-squared indicated that the independent variable of AGE explained 44% ( $\eta_p^2 = 0.44$ ) of the variance in the canonical construct: *intrinsic hand muscle intramuscular EMG*, which would be considered a large effect size (Cohen 2013).

The MANOVA was followed up with a DFA, which produced two discriminant functions. The first discriminant function explained 58.7% of the variance of the discriminant model,  $R^2 = 0.49$  whereas the second discriminant function explained 41.3% of the variance of the discriminant model,  $R^2 = 0.40$ . Both functions had a large effect size in the prediction of group membership of AGE (Cohen 2013). Collectively, these two discriminant functions were significantly able to predict group membership of the AGE groups based on intramuscular EMG variables,  $\Lambda = 0.31$ ,  $\chi^2(24) = 39.3$ ,  $p < 0.05$ . The correlations between the outcomes and the functions revealed that there was a strong relation for the following variables: NF Jiggle (FDI, ADM and 4DI) and Area (FDI, ADM and 4DI) and FDI Duration contributed the most to the first function (see Table 3 for variables and the loading on the functions). 4DI NF count, 4DI duration and ADM duration contributed the most to the second function (See Table 3). The discriminant function plot (Figure 1A) revealed that the first function discriminated the young age group from the middle age and older age group, and the second function differentiated the middle age group from the other two groups.

When using Cohen's  $d$  to examine the magnitude of difference of the intramuscular EMG variables between the YA and OA, there was a large effect size for: FDI NF Jiggle, 4DI NF Jiggle, FDI MUP Area, and ADM MUP Area. A medium effect size was observed for variables: ADM NF Jiggle, FDI MUP Duration, and 4DI MUP Area. Mean differences and effect sizes between the YA and OA group for the intramuscular EMG variables are presented in Table 4.

### **Surface EMG**

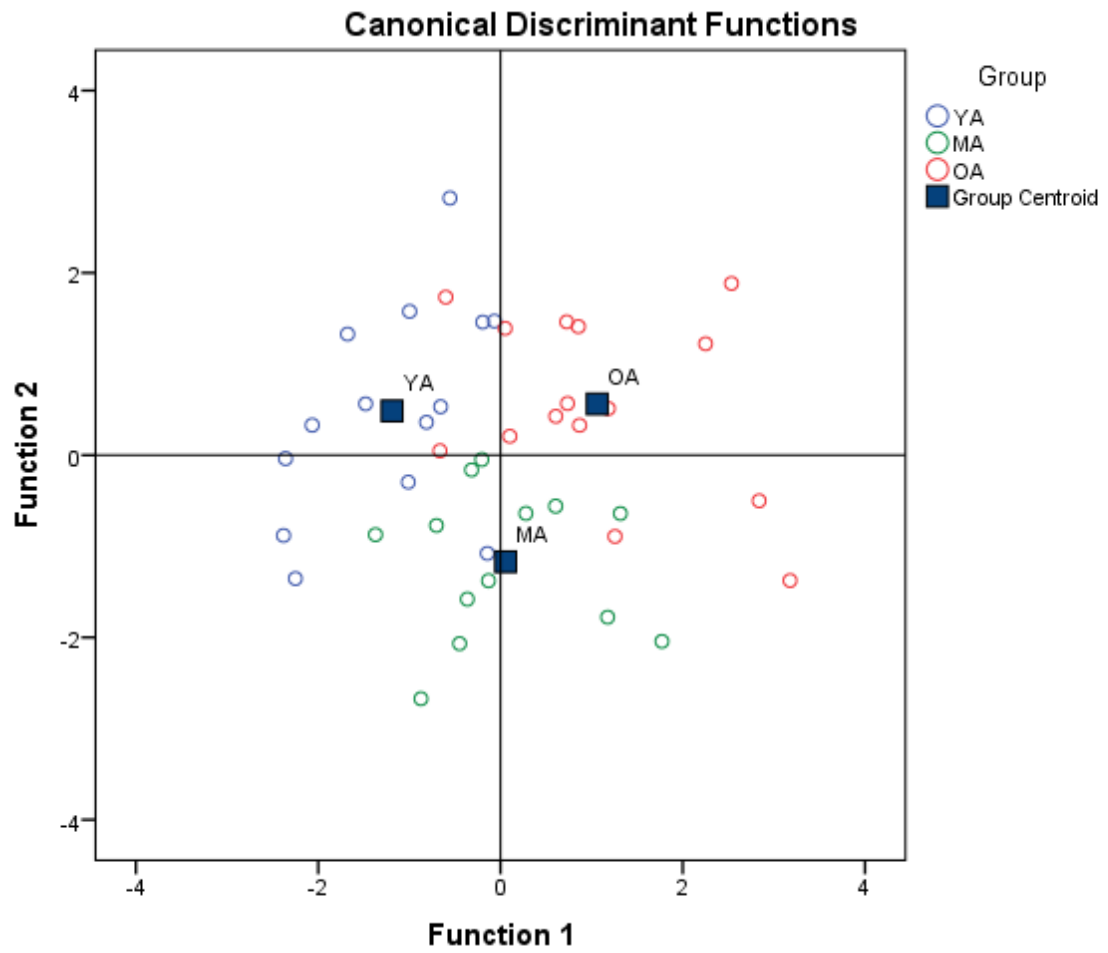
Using Pillai's Trace, there was a significant effect of AGE on the canonical variable *intrinsic hand muscle surface EMG*,  $V = 0.541$ ,  $F(8, 72) = 3.33$ ,  $p < 0.025$ . Separate univariate ANOVAs indicated a significant effect of AGE on ADM MUNE,

$F(2, 38) = 7.13, p < 0.05$ ; FDI MUNE,  $F(2, 38) = 5.11, p < 0.05$ ; and FDI SMUP,  $F(2, 38) = 6.19, p < 0.05$ . ADM SMUP was not statistically significant in the univariate analysis. Overall, the surface EMG's MANOVA eta-square indicated that the independent variable of AGE explained 27% ( $\eta_p^2 = 0.27$ ) of the variance within the canonical variable, *intrinsic hand muscle surface EMG*, which would be considered a large effect size (Cohen 2013).

The MANOVA was followed up with DFA, which produced two discriminant functions. The first discriminant function explained 90% of the variance of the discriminant model,  $R^2 = 0.46$ , whereas the second discriminant function explained 10% of the variance of the discriminant model,  $R^2 = 0.08$ . The first discriminant function had a large effect size and the second discriminant function had a small effect size in the prediction of group membership of AGE (Cohen 2013). Collectively, these two discriminant functions significantly differentiated the AGE groups,  $\Lambda = 0.50, \chi^2(8) = 25.5, p < 0.05$ . The correlations between the outcomes and the functions reveal that there was a strong relationship for the following variables: ADM MUNE, FDI MUNE and FDI SMUP seemed to contribute most to the first function (See Table 5). Likewise, ADM SMUP seemed to contribute the most to the second function (See Table 5). The discriminant function plot (Figure 1B) showed that the first function discriminated the old age group from the young age and middle age group, and the second function differentiated the middle age group from the other two groups.

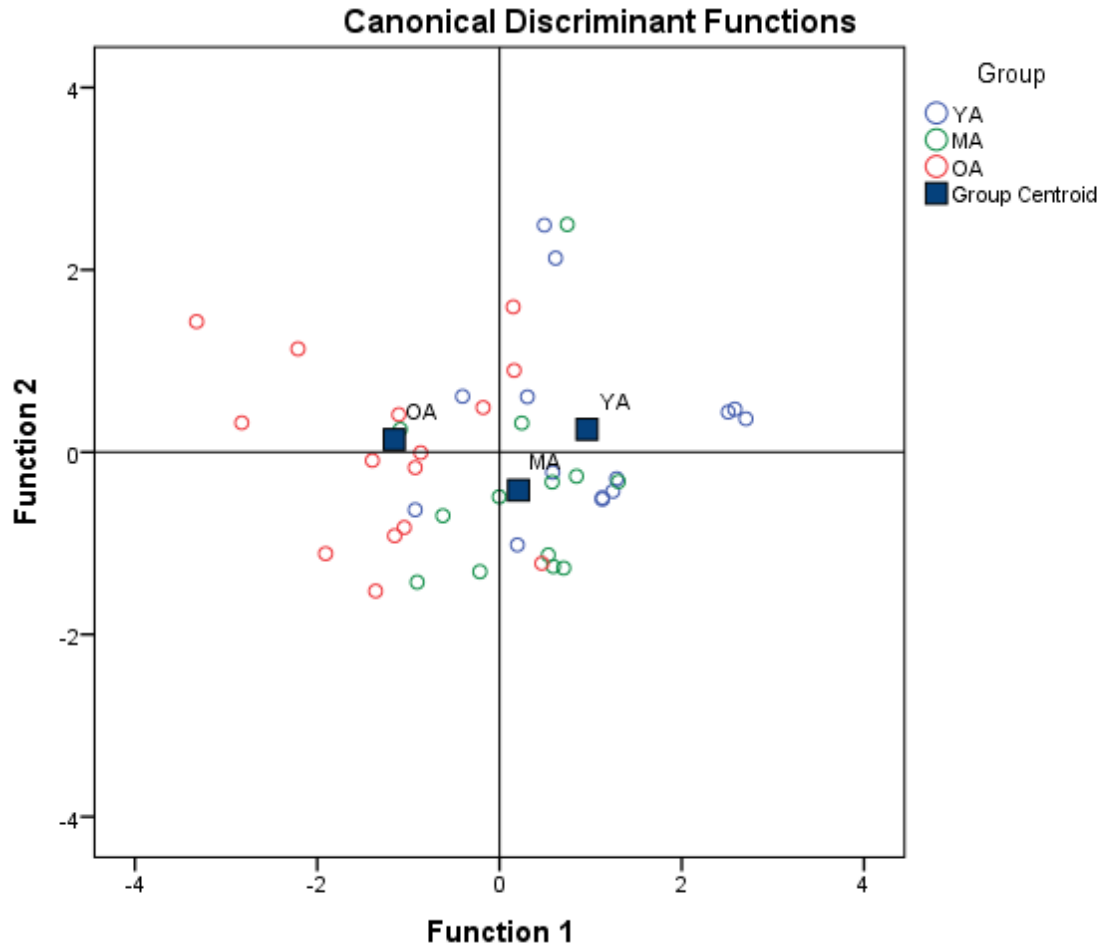
Using Cohen's *d* to explore the magnitude of difference of the surface EMG variables between the YA and OA groups, there were large effect sizes for: ADM MUNE, FDI MUNE, and FDI SMUP. A medium effect size was observed for the variable ADM SMUP. Mean differences and effect sizes between the YA and OA group are presented in Table 6.

A)





B)



**Figure 3.** Discriminant function plots for the EMG canonical variates: Group means of the canonical variates or centroids (square) were plotted for the three age groups (YA vs. MA vs. OA). Each data point (circular) corresponds to individuals in a group. The x-axis represents Function 1 of the discriminant model. The y-axis represents Function 2 of the discriminant model. Reference lines are situated at the 0 position of each function. Overlaps are considered to be similarities of groups, but distinct areas are considered group differences.

A) Intramuscular EMG discriminant function plot. Although some overlaps are observed for some individuals' variates, the overall group variate mean, represented by the centroids, demonstrate distinct areas as seen by the separation from the reference lines.

B) Surface EMG discriminant function plot. In contrast to the intramuscular EMG discriminant function plot, there are more overlaps for the individuals' variates. This may be related to the smaller effect size of the discriminant functions for the surface EMG's DFA (smaller  $R^2$  values (seen in the Results section)). However, there are still distinct areas for the overall group variate means represented by the group centroids which are separated by the reference lines.

**Table 5. Study Demographics**

<b>Subject demographics and characteristics (N = 42)</b>			
	<b>YA (n = 14)</b>	<b>MA (n = 13)</b>	<b>OA (n = 15)</b>
<i>Men/Women (number)</i>	9/5	7/6	7/8
<i>Handedness- Right/Left (number)</i>	13/1	11/2	13/2
<i>Age (years)</i>	26.6 ± 2.9	50.5 ± 6.3	73.5 ± 7.4

**Table 6.** Descriptive statistics for A) Intramuscular EMG Data and B) Surface EMG Data

A)

<b>Intramuscular EMG Descriptive Statistics (Means with Standard Deviations)</b>									
<i>Muscle</i>	<b>FDI</b>			<b>ADM</b>			<b>4DI</b>		
<i>Group</i>	<b>YA</b>	<b>MA</b>	<b>OA</b>	<b>YA</b>	<b>MA</b>	<b>OA</b>	<b>YA</b>	<b>MA</b>	<b>OA</b>
<i>NF Jiggle (%)</i>	34.6 ± 7.5	39.6 ± 10.1	43.5 ± 13.5	33 ± 7.4	35.2 ± 5.8	38.9 ± 7.7	34.8 ± 7.5	44.5 ± 9.1	44.5 ± 14.4
<i>MUP Amplitude (µV)</i>	489.5 ± 175.2	580.1 ± 200.4	664.9 ± 266.9	551.1 ± 200.5	571 ± 238.6	693.9 ± 213.6	554.7 ± 232.3	562.5 ± 207.9	668.0 ± 188.5
<i>MUP Duration (ms)</i>	6.8 ± 1.1	7.5 ± 1.2	7.8 ± 2.1	8.1 ± 2.1	7.3 ± 1.3	8.2 ± 1.1	6.7 ± 1.8	6.4 ± 0.9	7.7 ± 1.8
<i>MUP Area (µVms)</i>	585.8 ± 183.5	772.2 ± 206.3	974.0 ± 509.2	756.3 ± 286.8	754.2 ± 324.1	992.7 ± 250.7	730.9 ± 377.1	731.8 ± 270.3	982.7 ± 465.6
<i>NF Count</i>	2.4 ± 0.7	2.5 ± 0.7	2.4 ± 0.3	2.6 ± 0.5	2.3 ± 0.4	2.4 ± 0.5	2.2 ± 0.4	2.6 ± 0.5	2.2 ± 0.5

B)

<b>Surface EMG Descriptive Statistics (Means with Standard Deviations)</b>						
<i>Muscle</i>	<b>FDI</b>			<b>ADM</b>		
<i>Group</i>	<b>YA</b>	<b>MA</b>	<b>OA</b>	<b>YA</b>	<b>MA</b>	<b>OA</b>
<i>SMUP Amplitude (µV)</i>	49.4 ± 22.7	56.4 ± 32.3	101.0 ± 60.6	69.2 ± 20.2	63.0 ± 21.6	77.7 ± 14.8
<i>Max CMAP Amplitude (mV)</i>	13.3 ± 2.5	13.6 ± 3.0	12.7 ± 2.9	11.2 ± 1.6	9.5 ± 1.2	8.9 ± 1.4
<i>MUNE (number)</i>	313.9 ± 126.1	287.2 ± 123	175.1 ± 115.4	173.3 ± 54.0	162.0 ± 42.9	116.9 ± 23.4

*Table 7. Correlation of Intramuscular EMG Variables to the Discriminant Functions*

<b>Intramuscular EMG Variables</b>	<b>Discriminant Function</b>	
	<b>1</b>	<b>2</b>
<i>FDI Area</i>	.50	.05
<i>4DI Jiggle</i>	.41	-.24
<i>FDI Jiggle</i>	.37	-.01
<i>ADM Jiggle</i>	.37	.09
<i>ADM Area</i>	.36	.27
<i>FDI Duration</i>	.31	-.08
<i>4DI Area</i>	.28	.21
<i>4DI Count</i>	.11	-.55
<i>4DI Duration</i>	.26	.34
<i>ADM Duration</i>	.02	.33
<i>FDI Count</i>	-.04	-.11
<i>ADM Count</i>	-.13	.19

**Table 8.** Intramuscular EMG Variables: Mean Differences between the YA and OA groups and Effect Size (Cohen's *d*)

<b>Intramuscular EMG Variable</b>	<b>Mean Difference<sup>a</sup> between YA and OA groups</b>	<b>Effect Size (Cohen's <i>d</i>)</b>
FDI NF Jiggle	-8.94	0.82**
ADM NF Jiggle	-5.88	0.78*
4DI NF Jiggle	-9.73	0.84**
FDI MUP Duration	-1.07	0.60*
ADM MUP Duration	-0.12	0.06
4DI MUP Duration	-0.96	0.56*
FDI MUP Area	-388.22	1.01**
ADM MUP Area	-238.54	0.88**
4DI MUP Area	-251.82	0.59*
FDI NF count	0.06	0
ADM NF Count	0.13	0.4
4DI NF Count	-0.09	0

(a) Mean Difference = YA Mean – OA Mean

(\*) Indicates a Medium Effect Size

(\*\*) Indicates a Large Effect Size

**Table 9.** Correlation of Surface EMG Variables to the Discriminant Functions

<b>Surface EMG Variables</b>	<b>Discriminant Function</b>	
	<b>1</b>	<b>2</b>
<i>ADM MUNE</i>	.66	-.34
<i>FDI SMUP</i>	-.60	.43
<i>FDI MUNE</i>	.56	-.30
<i>ADM SMUP</i>	-.29	.82

**Table 10.** Surface EMG Variables: Mean Differences between the YA and OA groups and Effect Size (Cohen's *d*)

Surface EMG Variable	Mean Difference between YA and OA groups <sup>a</sup>	Effect Size (Cohen's <i>d</i> )
FDI MUNE	138.8	1.2**
ADM MUNE	56.4	1.4**
FDI SMUP	-51.6	1.1**
ADM SMUP	-8.5	0.5*

(a) Mean Difference = YA Mean – OA Mean

(\*) Indicates a Medium Effect Size

(\*\*) Indicates a Large Effect Size

## Discussion

This study demonstrated changes in neuromuscular physiology in the intrinsic hand muscles within a typical aging population, particularly between young adults (20 to 40-years-old) and older adults (>60 years old). Specifically, we used a multivariate and discriminant analysis to examine the differences between the groups. Through the multivariate analyses (MANOVA), a large difference was identified between the groups for the canonical constructs *intrinsic hand muscle intramuscular EMG* and *intrinsic hand muscle surface EMG*. Discriminant analysis confirmed a large effect and ability for these canonical variates to predict group membership (YA vs. MA vs. OA). Between the OA and YA groups, intramuscular measurements like NF jiggle and MUP Area demonstrated medium to large group differences in all three intrinsic hand muscles. Likewise, the YA and OA demonstrated medium to large group differences for surface EMG variables SMUP amplitude and MUNE for the FDI and ADM muscles. Novel contributions from our investigation include examining age-related changes to motor unit physiology via DQEMG in the ulnar intrinsic hand muscles (i.e. ADM and 4DI). To our knowledge, there have been no previous reports examining the motor unit physiology of the ulnar intrinsic hand muscles collectively. Further, quantitative EMG variables have typically been examined using univariate models. Multivariate modelling of multiple EMG variables and muscles from the same peripheral nerve may provide unique insights regarding motor unit changes that occur due to alterations of the peripheral nerve. Utilizing a modelling approach like the present one may provide future avenues to further explore motor unit physiology within clinical populations such as persons with compressive neuropathies (i.e. cubital tunnel syndrome). Finally, there are few quantitative EMG reports of age-related changes to motor unit physiology within the age span of 40 to 60-year-old adults (MA adults). The current investigation provides some insight regarding neuromuscular changes that may occur within this age demographic.

There is strong rationale to analyze EMG data using a multivariate approach. First, by using a multivariate test, we minimize the chances of committing a Type I or experimental-wise error (Huberty and Morris 1989). DQEMG provides several salient variables regarding motor unit properties and neuromuscular physiology (Doherty and



Stashuk 2003). However, with increasing number of variables (i.e. our study examined 12 intramuscular variables) that are examined using univariate statistical tests, there becomes a greater risk of committing Type I error. Secondly, by using a multivariate approach we were able to further examine underlying interactions and factors that may have influenced the group differences. Relationships and interactions between intramuscular and surface EMG variables have been previously reported in other EMG studies (Rodríguez et al. 2011; Allen et al. 2015; Hourigan et al. 2015). Indeed, it is reasonable in the context of our investigation to consider all the intramuscular EMG and surface EMG collectively as canonical variables, which explore the motor unit properties of the ulnar-innervated intrinsic hand muscles. Our findings identify that there is large age-related multi-dimensional shift in motor unit physiology within the ulnar-innervated hand muscles. The extent and magnitude of this shift in motor unit physiology within the intrinsic hand muscles may not have been fully captured if our study had only performed univariate analyses. We also used discriminant analyses, a subsequent post-hoc procedure that has been recommended by previous reports (Warne 2014; Barton et al. 2016). The discriminant analysis for intramuscular EMG revealed that NF jiggle and MUP Area strongly contributed to the differentiating functions that discriminate the age groups. Likewise, the surface EMG discriminant analysis revealed ADM MUNE, FDI MUNE, and FDI SMUP most strongly contributed to the differentiating functions. Collectively, additional studies may prove these variables and models to be useful as prognostic biomarkers, such as identifying those who may be at risk of “aging” hand muscles.

In comparison to younger adults, older adults demonstrated large decreases in MUNE in the ADM (~33% less in the OA group) and FDI (~44% less in the OA group), respectively. It should be noted that the FDI MUNE values observed in our study are atypically high in contrast to previous reports (i.e. approximately 144 motor units) (Feinstein et al. 1955; Doherty and Stashuk 2003; Bromberg 2020). It is likely that the MUNE in our study were unusually high due to the low SMUP negative peak amplitude recorded in our DQEMG trials. Our study encouraged participants to produce a mild to moderate contraction, which may have led to low force production. Muscle contractions at lower percentage of MVC have been shown to produce smaller amplitude SMUPs and greater estimations of motor unit numbers (Boe et al. 2005). However, the percentage and

effect size in MUNE change between the groups is similar to previous reports of aging (Gawel and Kostera-Pruszczyk 2014; Gilmore et al. 2018) and pathological populations (Allen et al. 2015). These studies typically observed ~25-35% decreases in MUNE. With motor unit loss, there are progressive increases in the motor unit sizes, usually leading to increased surface MUP amplitudes (McNeil et al. 2005), similar to the greater SMUP amplitude observed in the OA group in this study. Motor unit loss may be attributed to an age-related pathological process known as sarcopenia (Narici et al. 2010). Declines in muscle performance such as decreased peak muscle power (McKinnon et al. 2015), lower maximal voluntary contraction strength (Gilmore et al. 2017b) and torque (Kirk et al. 2018) have been previously observed in an aging population alongside decreased MUNE. However, in some cases, muscular strength may be maintained until a very old age (>80 years old) through the process of collateral reinnervation to maintain muscle fibers (McNeil et al. 2005). Ultimately, sarcopenia-related loss of muscle mass and strength may contribute to the decline in functional motor control and independence in the elderly (Larsson et al. 2019).

Altered motor unit properties, specifically NF jiggle and MUP area, were observed in all three intrinsic hand muscles via intramuscular EMG. The older group in comparison to the younger group demonstrated a medium to large increase in NF jiggle in all three intrinsic hand muscles, suggesting an overall decrease in motor unit stability in the ulnar intrinsic hand muscles. Jiggle is inversely related to motor unit stability (Stålberg and Sonoo 1994). Age-related decreases in motor unit stability have been previously reported; most of these investigations were in the context of the lower extremity (Hourigan et al. 2015; Gilmore et al. 2017b). With aging and the loss of motor units, collateral reinnervation and an enlargement of the remaining motor units is a proposed compensatory mechanism to maintain muscle function (Power et al. 2013). In addition to decreased motor unit stability, we observed increases in MUP area with aging. Increased MUP area may also be attributed to collateral sprouting of new nerves and muscle fiber atrophy leading to decreased muscle fiber conduction velocity; resulting in longer MUP durations and larger MUP areas (Stålberg and Sonoo 1994). Similar to our investigation, MUP area increases has been previously reported to be positively correlated to decreases in motor unit stability (i.e. NF jiggle) (Hourigan et al. 2015). NF jiggle and MUP area

have also been previously associated with declines in muscle performance. Decreases in MVC strength, peak twitch tension (Gilmore et al. 2017b) and overall strength (Gilmore et al. 2017a) have been observed alongside decreases to motor unit stability.

There are some strengths and limitations to our current investigation that should be addressed. One limitation of our study is the discrepancy of MUNE in contrast to previous investigations of hand muscles (Feinstein et al. 1955; Doherty and Stashuk 2003; Bromberg 2020). For unknown reasons, the acquisition of SMUP negative peak amplitudes acquired on our DQEMG system were very small, leading to an abnormally high FDI MUNE for all our groups. Although the absolute MUNE is atypically high, the percent differences in motor unit between the age groups is similar to previous reports as mentioned above. Likewise, another limitation to our study is the lack of a subgroup for “very old” adult (>80 years old). This specific demographic demonstrates even greater magnified effects of motor unit loss and other neuromuscular changes (McNeil et al. 2005; Reid and Fielding 2012; Gilmore et al. 2018). One strength of our study is the sufficient power and equal sample size across the various age groups (young vs. middle vs old). Further, our study examines whether neuromuscular changes occur even earlier in life with middle-aged adults (41-60 years old). Exploring motor unit changes at earlier ages and demographics may allow for possible avenues to intervene prior to the onset of sarcopenia. Lastly, we were able to utilize a multivariate approach to examine differences in hand neuromuscular physiology.

In conclusion, it has been demonstrated that MUNE and intramuscular variables like NF jiggle and MUP area significantly differ in older adults when compared to younger adults. Age-related changes to upper extremity performance such as decreased upper extremity force production (Puh 2010), increased fatigability (Yoon et al. 2013) and decreased independent control of individual digits (VanBeek et al. 2019) have all been observed in healthy aging populations. Motor neuron and neuromuscular junction changes observed in the current study may contribute to the aging-related changes described. However, it is important to consider other factors that contribute to decreases in hand control and performance such as changes to the sensorimotor cortex (Bhandari et al. 2016) or alterations to the muscle fibers (i.e. fiber size) (Lexell et al. 1988). Further

investigation of these age-related neuromuscular mechanisms and changes in the hand may provide future avenues and rehabilitation strategies to improve or mitigate age-related declines in hand control.

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# **Chapter 4- Post-operative Management and Rehabilitation Following the Supercharged End-to-Side Anterior Interosseous Nerve to Ulnar Motor Nerve Transfer: A Report of 3 Cases**

## **Introduction**

Aside from carpal tunnel syndrome, ulnar nerve entrapment at the elbow (UNE) is the most prevalent compressive neuropathy (Mondelli et al. 2005). Clinical presentation of ulnar neuropathy often includes clawing of the hand, significant intrinsic muscle weakness, and atrophy (Palmer and Hughes 2010). Sensory complaints from patients may include paresthesia and numbness, mostly in the ulnar digits along with medial elbow pain. Entrapment traction and increased pressure, with a decreased blood supply can lead to epineural ischemia (Tapadia et al. 2010). Likewise, venous return may be affected which can lead to fibrosis and scar tissue formation with resulting intraneural edema. Initial management of mild ulnar neuropathies includes activity modification that avoids fixed elbow flexion postures and direct pressure over the epicondylar groove. The addition of night extension splints, neural mobilization, and hand therapy may help to maintain strength, range of motion (ROM) and prevent clawing (Robertson and Saratsiotis 2005). Several surgical interventions may be performed to treat ulnar neuropathy at the elbow such as decompression (Bartels et al. 2005), ulnar nerve transposition (Caputo and Watson 2000), nerve transfers (Brown et al. 2009) or a combination of these techniques (Jarvie et al. 2018). Overall, the prognosis and recovery from severe ulnar axonopathy are less than ideal in terms of motor functional outcomes (Lan et al. 2019).

A new addition to the treatment options available is the technique of transferring the anterior interosseous nerve (AIN) as a donor nerve to the motor fascicle side of the ulnar nerve in the distal forearm to augment innervation closer to the target muscles. This surgical procedure is known as the supercharged end-to-side (SETS) nerve transfer technique (Barbour et al. 2012). Conceptually, the surgery utilizes the AIN to “supercharge” the motor fascicles of the ulnar nerve, allowing for reinnervation of the hand musculature (Kale et al. 2011; Farber et al. 2013b; Doherty et al. 2017). Initial



animal models have demonstrated increased nerve regeneration, muscle mass, and improved quality of nerve regeneration (Kale et al. 2011; Farber et al. 2013a). Past reports of the SETS AIN to ulnar nerve technique applied to human participants have demonstrated improved functional outcomes such as increased pinch and grip strength, and increased ability to abduct and adduct the affected hand intrinsic musculature (Kale et al. 2011; Barbour et al. 2012; Baltzer et al. 2016; Jarvie et al. 2018; Doherty et al. 2020). Although standard clinical and qualitative nerve conduction studies and EMG procedures have been used to evaluate motor neuron and neuromuscular endplate properties, the use of quantitative EMG to examine neuromuscular changes following SETS procedures have not been reported to date.

Nerve transfer procedures provide promising results for improved patient recovery, but the rehabilitation approaches and protocols specific to these surgical procedures have not been explored extensively. Post-operative rehabilitation programs, usually performed by a hand therapist, were frequently reported as an integral part of the participants' care following the surgery. Aside from standard patient education and traditional hand therapy exercises, a focus on motor re-education has also been incorporated (Barbour et al. 2012; Jarvie et al. 2018). The clinical observation that focus on donor activation has been suggested to maximize functional outcomes of hand rehabilitation after nerve transfer (Kahn and Moore 2016).

The aim of this repeated comparative case study was to describe the responses of three participants to a specific hand therapy program aimed at improving function, following the SETS AIN to ulnar nerve surgery. By describing the outcome of multiple cases, we hope to provide potential explanations for the varied response of the participants. Further, a self-reported outcome measure (Quick Disability of Arm Shoulder and Hand (QuickDASH)) and the addition of neurophysiological measures using decomposition-based quantitative electromyography (DQEMG) have been added to compare their post-operative recovery and neuromuscular health.

## **Case Selection and Description**

### **Sampling**

In a repeated comparative case study, specific patient cases are selected with intent. Patients in this study were recruited from an ongoing clinical trial which prospectively evaluates the SETS AIN to ulnar nerve for compressive ulnar neuropathy at the elbow (UNE) in comparison to a standard ulnar nerve transposition. Exclusion criteria for this study included patients with ulnar neuropathy at multiple anatomic locations along the course of the nerve. Three participants were purposively selected and represented three varying levels of improvement of small, moderate, and large to the surgical and therapeutic interventions as defined by their functional outcome >23 months post surgical intervention. Magnitude of improvement were selected based on their final outcomes from i) patient reported outcome measure (QuickDASH) and ii) clinical assessment performed by the occupational therapist/hand therapist (J.L.S.). Using this approach provides a means of exploring the clinical decision making and potential case factors that may have contributed to personalization of the rehabilitation and the outcomes achieved. Written informed consent was obtained from each participant.

## **Patients**

Overall, three retired older males (> 60 years old) who underwent a SETS AIN to ulnar nerve procedure for severe ulnar neuropathy at the elbow were selected to participate in the current study. Table 1 presents the baseline characteristics and personal/environmental factors of each participant. Similarities between the three participants include their age, sex, occupation status (retired), and the surgical procedure that they received. Differences between the three participants include the mechanism of injury, time from neuropathy to surgery, comorbidities, and social history. Patient C had a unique mechanism of injury where he developed a compression neuropathy secondary to a humeral fracture. Further, Patient C had very few comorbidities (hypertension). In contrast, Patient A was the only participant with a social history of living alone. Patient A also lived in a more remote and rural region, where access to therapy was more challenging. Patient B had a common comorbidity in UNE and was beginning to experience ulnar neuropathy in his contralateral upper extremity. Overall, this may have affected his upper extremity function, as it would have decreased his ability to compensate with his contralateral limb.

## **Evaluative Procedures**

During the rehabilitation sessions, participants underwent a thorough history and physical examination with one occupational therapist/hand therapist, who is also a coauthor to this study (J.L.S.). Examination included screening for red-flags, neurological assessment, strength testing (i.e. MRC muscle scale, grip, pinch) (Bove 2008), and range of motion assessment. Several clinical motor tests were performed to evaluate the participants' hand function. In order to assess dysfunction of the interossei muscles, the Crossed Finger Test and Egawa's Sign were performed (Goldman et al. 2009). Similarly, Froment's sign and Wartenberg's sign were documented to detect for adductor pollicis and hypothenar muscle dysfunction (Goldman et al. 2009), respectively. To evaluate overall finger and hand abduction, finger tracings of maximal hand abduction were performed (Barbour et al. 2012). Total abduction was measured using the distance from tip of the 1<sup>st</sup> digit to tip of the 5<sup>th</sup> digit with the hand flat and in the pronated position on a table (see Figure 5). Hand therapy adherence was assessed by the hand therapist through therapy attendance, subjective evaluation by the therapist (J.L.S.), and self-reporting from the patient through simple and direct questions (Babatunde et al. 2017b).

A physical therapist not involved in the participants' care also evaluated study outcomes (Author P.T.) A patient reported outcome measure was obtained from all three participants as a long-term (>23 months) evaluation of their current upper extremity disability. Quantitative EMG was acquired from two of the participants to evaluate neuromuscular health (Doherty and Stashuk 2003). Patient A did not participate in quantitative EMG testing because it was physically and logistically too demanding for him to attend.

### ***Patient Reported Outcome Measure***

One approach to capture disability as a result of upper extremity dysfunction is using a patient reported outcome measure. The QuickDASH is an efficient outcome measure developed by Beaton et al. (2005) as a short form to the Disability of Arm, Shoulder, and Hand (DASH) (Hudak et al. 1996; Beaton et al. 2005). The QuickDASH has been well validated in several clinical populations such as those with mixed upper

extremity disorders (Gummeson et al. 2006), patients with distal radius fractures (Tsang et al. 2017) and patients undergoing rotator cuff surgery (MacDermid et al. 2015).

### ***Decomposition-based Quantitative Electromyography (DQEMG)***

DQEMG is an efficient approach to capturing several motor unit and neurophysiological variables regarding motor unit health and neuromuscular physiology (Doherty and Stashuk 2003). DQEMG and the Sierra EMG system software (Sierra Inc) were used to collect the quantitative EMG data. The algorithms of DQEMG have been previously discussed (Doherty and Stashuk 2003). Self-adhesive Silver Mactrode electrodes (GE Medical Systems, Milwaukee, WI) were used to detect surface signals with bandpass setting of 5 Hz to 5000 Hz. 25 mm x 30-gauge disposable concentric needle electrodes (TECA elite, CareFusion, Middleton, WI) were used to detect intramuscular needle EMG signals with bandpass settings of 10Hz to 10KHz.

For EMG data collection, each participant's skin was cleansed with isopropyl alcohol before surface electrodes were placed. For the first dorsal interosseus (FDI) and abductor digiti minimi (ADM) muscles, the active electrode was positioned over the muscle belly, whereas the reference electrode was positioned over the 2<sup>nd</sup> and 5<sup>th</sup> metacarpal phalangeal joint line, respectively. The ipsilateral ulnar styloid process was used for the ground electrode placement. A bipolar stimulator was used to elicit a maximum compound muscle action potential (CMAP) by stimulating the ulnar nerve at the wrist. The stimulus intensity was gradually increased until the CMAP negative peak amplitude no longer increased and was determined to be supramaximal (Preston and Shapiro 2012).

A concentric needle was inserted into the muscle belly of the FDI and ADM. For FDI and ADM, the needle electrode was always positioned a minimum of 2 mm away from the active surface electrode. Participants were asked to perform mild isometric finger abduction contractions, while an optimal needle position was determined using the minimal rise times of the MUPs generated. Once an optimal position was obtained, participants were asked to maintain a mild contraction (approximately 15% MVC). Each contraction was held for ~30 seconds. During each contraction, participants received

verbal feedback from the investigator to maintain the desired contraction intensity. Subsequent contractions were performed until a minimum of 20 suitable MUP trains were collected. Contractions were separated by ~30 second breaks or longer if needed by the participant. To capture motor units from various parts of the muscle, the needle was repositioned between contractions.

EMG signals were reviewed offline to screen for the acceptability of MUP trains. Criteria for accepting MUP trains included a minimum of 51 MUPs with consistent and physiological MU firing rate, an inter-discharge interval (IDI) histogram with a Gaussian-shaped main peak, and a coefficient of variation of the IDI of less than 0.3 (Stashuk 1999a). Raster plots were examined visually to determine whether the MUPS were all originating from the same motor unit. Motor unit number estimation (MUNE) for FDI and ADM were calculated by dividing the CMAP negative peak amplitude by the SMUP negative peak amplitude mean (Doherty and Stashuk 2003).

## **Interventions**

All three patients received the same surgical treatment and the SETS AIN to ulnar nerve surgery. The surgical process involved an internal neurolysis to identify the ulnar motor fascicles of the ulnar nerve and confirmed with intraoperative electrical stimulation. The AIN was then harvested and coaptated to the motor fascicles of the ulnar nerve through a neurorrhaphy and end to side procedure in the standard fashion. Further details of the SETS AIN to ulnar nerve procedure have been previously reported (Kale et al. 2011; Barbour et al. 2012). Subsequent surgical care was required for Patient B as he had issues with hand and finger dystonia and finger deformities due to his underlying neurological condition (i.e. Parkinson's disease). Therefore, botulinum toxin injections were applied at approximately 9 months post ulnar nerve surgery.

The formal neuromuscular rehabilitation sessions for all three cases were initiated at approximately 6-8 months post surgery, when reinnervation is first noticed either clinically (MRC 1) and/or through the presence or new MUPs on clinical follow-up EMG studies assessing the FDI, ADM and fourth dorsal interosseous (4DI) muscles. All patients were instructed in active and passive range of motion exercises to ensure that

mobility of the digits would not be compromised. Hand splints were fitted and prescribed to address patient issues with hand contractures (Taylor et al. 2003). Education and treatments regarding edema and scar management were provided in the early months and visualization exercises were begun immediately including activation of the donor nerve. Examples of scar management strategies included the use of silicone gel sheets and desensitization techniques (Mercer 1989).

Formal rehabilitation comprised of exercises to encourage the activation of the donor nerve. Patients were provided with an exercise program that involved the coactivation of donor and recipient muscles (i.e. pronation combined with finger abduction, adduction and intrinsic plus flexion). EMG-biofeedback (NeuroTrac Myoplus 2 Pro) was utilized when reinnervation was found on EMG studies and first noticed (MRC 1 to 2). The rationale of early biofeedback was to facilitate motor relearning and cortical plasticity. Surface, self-adhesive electrodes were placed over recipient muscles while patients performed donor activation exercises. During this phase, the goal of the EMG-biofeedback was to reach a threshold, determined as a percentage of the maximum voluntary contraction (MVC) (i.e. approximately 50% MVC). The goal of using an approximate threshold of ~50% MVC with a sustained isotonic contraction of ~5 seconds was to implement therapeutic exercises that would facilitate optimal challenge and learning (Guadagnoll and Lee 2004). The threshold was gradually increased with the progression of the patients' performance.

Once there were signs of increased innervation both clinically (MRC 3) and through EMG studies (increased number of maturing motor units), EMG-triggered muscle stimulation (ETS) was introduced. The goal of ETS utilization at later stages was to improve strength and endurance, while still encouraging the facilitation of cortical plasticity and learning. Using ETS is beneficial due to a specific feature. The neuromuscular stimulation of the ETS was only triggered by volitional muscle activation up to a threshold. It should also be noted that the biofeedback and ETS device had algorithms that adjusted the muscle activation threshold based on the participants' performance. When participants reached an activation threshold with ease, the algorithm would adjust the threshold to a new EMG activation level. Neuromuscular electrical

stimulation (NMES) was only used in the latter part of the rehabilitation process with the goal of facilitating muscular endurance and capacity. NMES in peripheral nerve rehabilitation is becoming increasingly popular and protocols have even been developed to guide treatments (Asensio-Pinilla et al. 2009).

## **Outcomes**

Patient A, B, and C's demographic information can be found at Table 1. All three patients demonstrated a similar adherence to attending their hand therapy sessions. Progress of clinical performance measurements like grip strength and pinch strength can be observed at Figure 1. Due to Patient A's complications during the rehabilitation and recovery period, several clinical measures like grip strength and pinch strength were not obtained. QuickDASH measures were obtained from all three patients as a long-term evaluation (>23 months) of their function (Figure 2). A higher score represents a greater degree of upper extremity disability experienced by the patient. Normative scores for the DASH (full version) in the general population has been reported to be 10.1 with a standard deviation of 14.7 (Hunsaker et al. 2002). Patient C is less than one standard deviation away from the population norm and Patient B within 2 standard deviation. However, Patient A is approximately 4 standard deviations away from the population norm.

DQEMG was obtained from Patient B and C to examine their neurophysiological and neuromuscular health. Due to Patient B's atrophy of the FDI muscle, DQEMG was only obtained from his ADM (hypothenar) muscle. DQEMG was obtained from both the FDI and ADM for Patient C (Table 4). Due to Patient A's health complications and lack of transportation, we were unable to obtain DQEMG measurements from him. In contrast to Patient B, Patient C's ADM muscle demonstrated greater motor unit counts. Patient C's intramuscular EMG variables like shorter MUP duration and smaller MUP area suggest that overall, his motor units may be smaller. We propose that this may be possibly due to greater recovery of new or immature motor unit numbers (i.e. nascent units). Patient C's ADM muscle demonstrated higher NF jiggle in comparison to Patient B's, suggesting decreased motor unit stability. This may be due to an increase in the number of new or

nascent motor units, which in theory will provide long term benefits as they grow and mature.

Patient A was a gentleman who had a small improvement to the surgical and rehabilitation intervention implemented. Patient A's demographic and pre-surgical history can be found in Table 1. In addition to ulnar neuropathy, his health history indicated issues with gout, depression, and idiopathic Parkinson's Disease. Patient A attended his scheduled rehabilitation sessions but admitted to a low adherence to his rehabilitation exercises, as he only performed them once per week with another therapist. Patient A also had issues with hand tone-related rigidity and contractures due to Parkinsonism. Several splints were applied in attempt to mitigate hand stiffening. The improvement of his fingers' ROM was minimal as observed in Table 2. Even during late stages of rehabilitation, Patient A showed diminishing signs of intrinsic hand function, such as increased ulnar clawing. Throughout Patient A's rehabilitation process, it was challenging to complete the progressions necessary to increase his hand function.

Patient B had a medium improvement to the surgical and hand therapy interventions. He demonstrated a modest adherence to his home program. One barrier and challenge that was identified by his therapist was his limited ability to understand instructions for his home exercise program. Clinical special tests revealed that Patient B still experienced dysfunction with his adductor pollicis and hypothenar muscles (i.e. positive Froment's and Wartenburg's sign) at 19 months follow-up. Collectively, these deficits made it moderately challenging for Patient B to perform activities of daily living (ADLs) like opening a tight jar and washing his back.

Finally, Patient C had a large improvement and functional increase from the surgical and hand therapy interventions. Patient C demonstrated excellent adherence to his home program and even took the initiative to purchase an NMES device for home use (Allevia 2-in-1 TENS and EMS Unit by ProActive). At his 18 months follow-up, Patient C demonstrated no dysfunctions with his hypothenar muscles or hand intrinsic interossei muscle (i.e. negative Wartenburg's, Cross Finger Test, Egawa's Sign). However, he still



demonstrated a positive Froment's Sign, which he functionally compensated by using his flexor pollicis longus.

**Table 11. Patient Demographic Information**

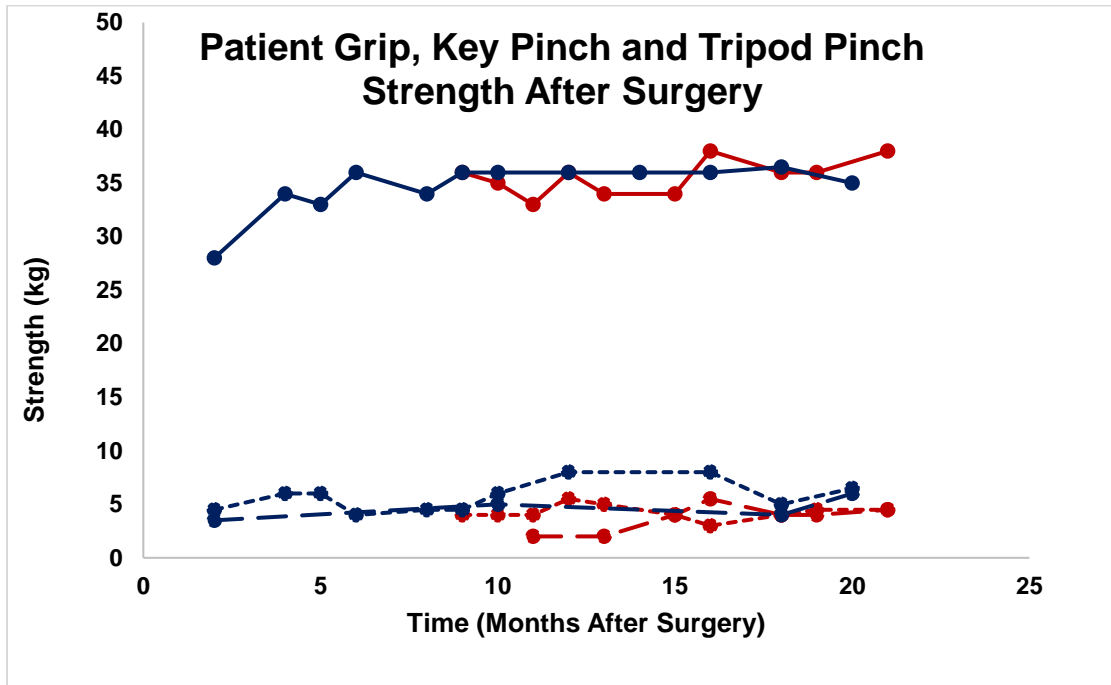
	<b>Patient A</b>	<b>Patient B</b>	<b>Patient C</b>
<b>Age (years old)</b>	76	80	76
<b>Sex</b>	M	M	M
<b>Handedness</b>	R	R	R
<b>Affected Limb</b>	L	R	R
<b>Duration of Symptoms (pre-surgical)</b>	2-3 years before surgery	> 3 years before surgery	~1 year before surgery
<b>Mechanism of Injury</b>	Compressive neuropathy	Compressive neuropathy	Compressive neuropathy secondary to humeral fracture
<b>Comorbidities</b>	Parkinson's Disease, Atrial fibrillation, Dyslipidemia, Depression, Gout	Dyslipidemia, Hypertension, Cerebrovascular Accident (Posterior cerebral artery), Mild Ulnar Neuropathy (Contralateral Hand)	Hypertension
<b>Personal Barriers to Recovery</b>	Age, Previous occupation (television technician), Lives in more rural setting with less access to care	Age, Previous occupation (electrician)	Age
<b>Therapy Attendance (Sessions)</b>	17	18	17
<b>Therapy Adherence</b>	Low	Moderate	High
<b>Social Supports</b>	None reported	Lives with spouse	Lives with spouse
<b>Life Roles</b>	Father	Spouse, father	Spouse, father

**Table 12.** Patient A: Range of motion progress at D4 and D5 of the affected hand

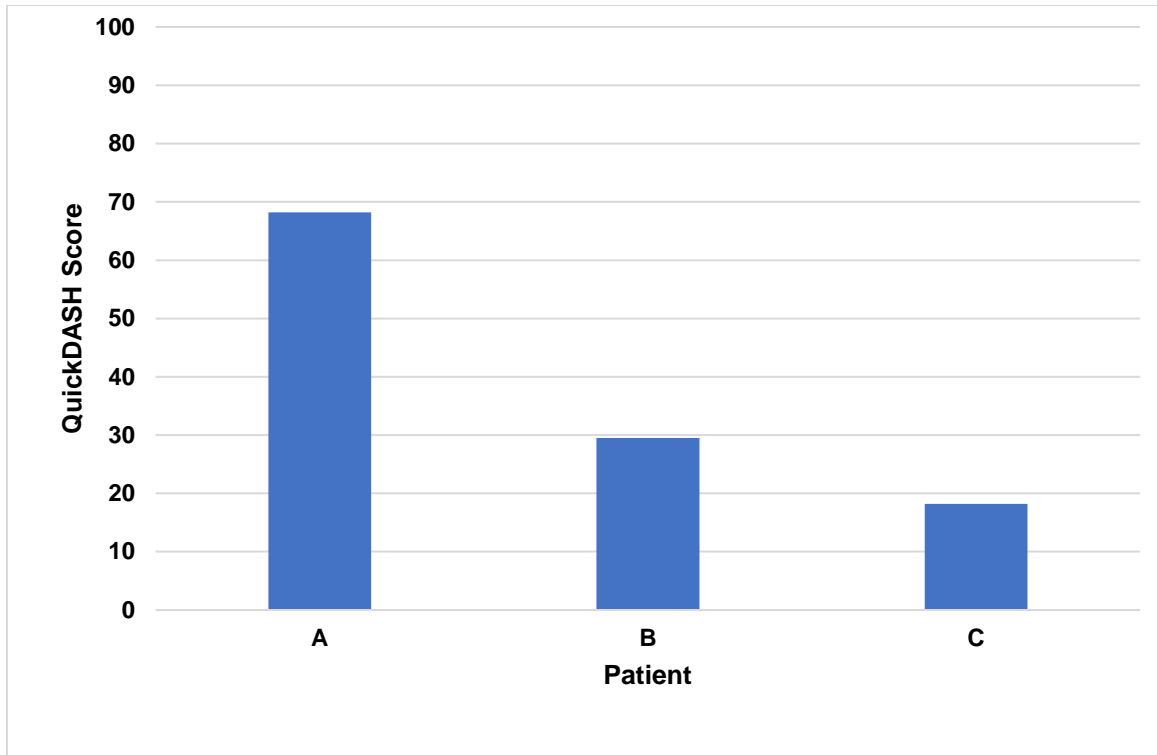
		12 months		16 months	
	Joint	Flexion active ROM (°)	Extension active ROM (°)	Flexion active ROM (°)	Extension active ROM (°)
D4	MCP	0	-80	0	-85
	PIP	-45	-85	-50	-95
	DIP	-10	-55	-15	-55
D5	MCP	0	-85	+ 10	-85
	PIP	-50	-80	-55	-95
	DIP	-10	-45	0	-65

**Table 13.** DQEMG Outcomes from Patient B's Abductor digiti minimi (ADM) muscle and Patient C's ADM and first dorsal interosseus (FDI) muscles at Long-Term Evaluation (> 2 years following SETS AIN to Ulnar Nerve Surgery).

	<b>Patient B- ADM</b>	<b>Patient C -ADM</b>	<b>Patient C-FDI</b>
<b>SMUP (<math>\mu</math>V)</b>	42.9	50.4	165.9
<b>CMAP Amplitude (mV)</b>	4	5.5	3
<b>MUNE</b>	93	109	18
<b>MUP Duration (ms)</b>	10.62	7.91	10.67
<b>MUP Area (<math>\mu</math>Vms)</b>	4843.07	2660.28	3695.25
<b>NF Count</b>	2.78	2.75	3.76
<b>NF Jiggle (%)</b>	33.6%	39.52	37.63
<b>NF Jitter (<math>\mu</math>s)</b>	51.33	45.84	78.50



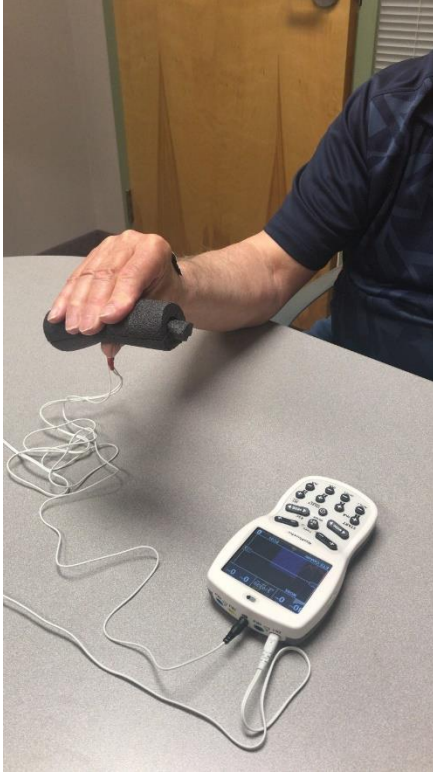
**Figure 4.** Patient grip, key pinch, and tripod pinch strength over time following SETS AIN to Ulnar Nerve Surgery. Patient C is represented by blue. Patient B is represented by red. Grip strength is shown with solid lines, dotted lines represent key pinch strength and dashed lines represent tripod pinch strength.



**Figure 5.** Patient QuickDASH scores at long-term evaluation (> 23 months following SETS AIN to Ulnar Nerve Surgery). Higher scores indicate greater upper extremity disability with a maximum score of 100 and a minimum score of 0.



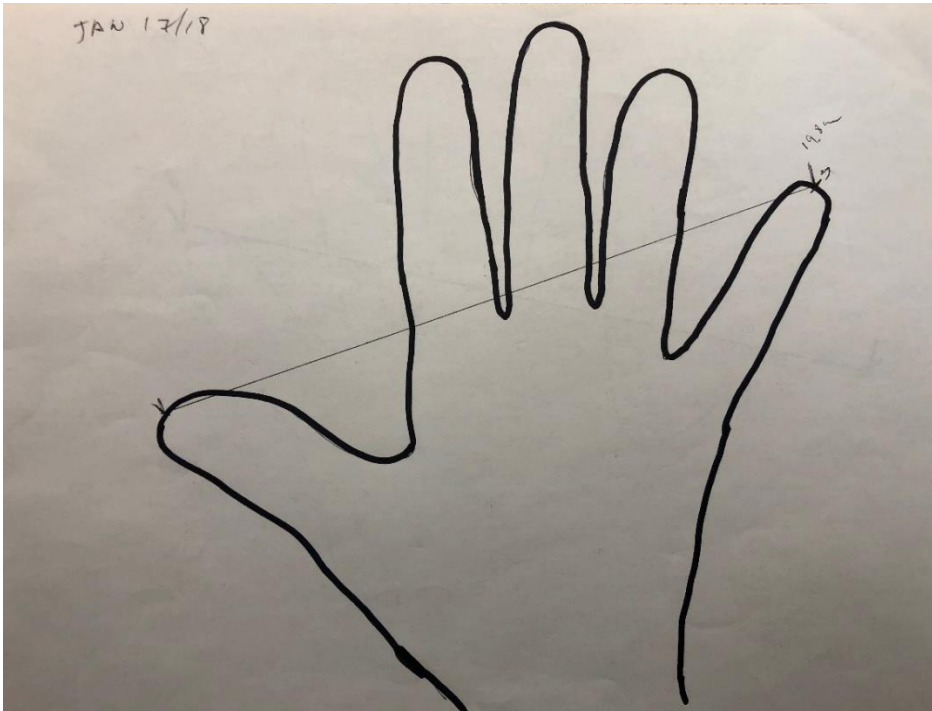
**Figure 6.** An example of a hand therapy session using EMG biofeedback. The electrodes were placed on the intrinsic hand muscles on the dorsal and volar side, excluding the hypothenar eminence. Participant was instructed to practice gravity eliminated donor activation with intrinsic plus flexion.



**Figure 7.** An example of EMG-triggered stimulation (ETS). The electrodes were placed on the intrinsic hand muscles on the dorsal and volar side, excluding the hypothenar eminence. Participant was encouraged to activate the donor nerve while performing resistance against a roll.



A)



B)



**Figure 8.** An example of hand-tracing to measure the participant's total finger abduction (Patient C). Total abduction was measured using the total distance from tip of the 1<sup>st</sup> digit to tip of the 5<sup>th</sup> digit. **A)** ~9 weeks post-operative. Initial hand therapy assessment. Total finger abduction was ~19 cm with very little muscle bulk observed at the hypothenar eminence. **B)** ~43 weeks post-operative. Total finger abduction was ~21.5 cm with substantial increase in muscle bulk at the hypothenar eminence.

## Discussion

Severe ulnar neuropathies frequently do not have optimal long-term functional outcomes. However, innovative surgical and rehabilitation interventions have been developed to improve patient outcomes. The current investigation explored three different patients' response to the SETS AIN to ulnar motor nerve surgery and the subsequent rehabilitation. Three participants were chosen to explore the clinical decision-making and potential mediators that might affect different responses to surgery and rehabilitation. This is important since we know even within clinical trials, when outcomes are improved, that the responses to treatments are variable between patients. For clinicians, it is important to understand the general approach to post-operative management, and the factors that limit or might be leveraged to optimize rehabilitation programs given that patients can be highly variable. Because our purpose was to explore variations in outcomes, we purposely selected patients that demonstrated large, moderate, or small improvements following surgery and rehabilitation. The patient outcomes were demonstrated by their respective QuickDASH scores at a long-term follow-up (>23 months) and from the patients' clinical performance assessed by the hand therapist.

Pre-surgical factors such as comorbidities may have contributed to the patient's response to the interventions. Our investigation uniquely highlights the differences in metabolic and neurological comorbidities observed in the three participants and the potential influence that these comorbidities had on their improvements. Similarly, facilitators and barriers within the rehabilitation process, such as adherence to the proposed rehabilitation program, may have also influenced the patients' observable outcomes. The three participants within this study uniquely allow for us to describe and explore how social and mental health history may influence program adherence. Another unique aspect of this repeated case study was that we were able to perform DQEMG for two of the cases. This provided unique data about the changes that occurred at the level of the motor unit physiology. The participant that demonstrated the most improvements also showed the most substantial increases in MUNE, possibly suggesting a relationship between motor unit reinnervation and functional outcomes. In order to assist in patient prognosis, clinicians should consider patients' pre-existing comorbidities. Cardiovascular

and metabolic factors like hyperlipidemia, obesity and diabetes should be examined. Patients A and B both had pre-existing dyslipidemia prior to surgery. Although not commonly associated with neuropathies, dyslipidemia or hyperlipidemia may have factored to their responses to the interventions. Some experimental studies have shown that hyperlipidemia may have direct neurotoxic effects on peripheral nerves and increased progression of peripheral neuropathy with elevated triglycerides (Vincent et al. 2009). Similar risk factors like hypertension should also be considered. Within our cohort, Patients B and C both had hypertension. Although the mechanism of hypertension on peripheral neuropathies is not as well defined, hypertension has been previously identified as a contributor to specific neuropathies (Tesfaye et al. 2005; Grisold et al. 2017). Possible mechanisms may include hypertension leading to changes in epineurial arteriolar function and endoneurial perfusion (Ponirakis et al. 2019). Targeting metabolic factors like hyperlipidemia and hypertension in neuropathic populations has been recommended previously as a direct form of therapeutic intervention (Vincent et al. 2009). Proposed interventions are typically pharmaceutical in nature. However, adjunct interventions such as aerobic exercise may have potent mediating effects that may augment metabolic factors like hypertension (Naci et al. 2019) and hyperlipidemia (Kelly 2010). In ulnar neuropathy, factors like the onset of symptoms and the timing of surgical interventions may influence patient clinical outcomes. Patient C received his surgical intervention at a relatively earlier time. In contrast, the other participants had a longer wait time prior to their surgical intervention. There are several factors that may influence the timing of surgical interventions including diagnostic and clinical indications for surgery. Typically, early surgical intervention for indicated patients provide the recipient muscles with more receptive and functioning motor endplates for reinnervation (Power et al. 2020). Increased reinnervation of the recipient muscles allows for improved functional outcomes. One recent report has provided specific indications for SETS surgical intervention after the onset and diagnosis of cubital tunnel syndrome. These protocols may provide the opportunity for increases in surgical success and improved functional outcomes (Power et al. 2020).

Neurological conditions that impact the central nervous system (CNS) are critical to evaluate in patients recovering from peripheral neuropathies. Patient B had a previous

cerebrovascular accident (CVA) of his posterior cerebral artery (PCA) approximately 13 years before the onset of his ulnar neuropathy. Following CVAs (greater than 6 months), approximately 60-70% of patients experience impaired hand functions (Feigin et al. 2003). We believe that Patient B's CVA may have left residual cortical sensorimotor dysfunctions leading to his decreased ability to activate and utilize the recipient muscles following surgery (i.e. minimal recovery of FDI). Similarly, Patient A had idiopathic Parkinson's disease (PD), a neurodegenerative movement disorder known to impair central sensorimotor hand circuitry and hand control (Jo et al. 2014; Dubbioso et al. 2019). Patients with PD may present with decreased hand function (Mak et al. 2015), increased hand rigidity (Cantello et al. 1995) and hand contractures (Kyriakides and Langton Hewer 1988) due to motor impairment. One major barrier to Patient A's recovery were hand contractures that developed following the surgery. In the presence of limited hand mobility, Patient A's functional recovery was diminished and likely contributed to his poor outcomes. Understanding the central nervous system's mechanisms and influence on peripheral neuropathies will hopefully allow for future interventions that concurrently influence the peripheral and central nervous system (i.e. Hebbian plasticity) (Tsang et al. 2015).

Psychosocial factors and adherence to the rehabilitation regime should be considered following surgical interventions. Adherence to exercise programs is a critical factor to successful recovery in rehabilitation (Balducci et al. 2006). Patients with better adherence often achieve better outcomes (World Health Organization 2003). Conversely, patients with better physical recovery may be more capable of performing some components of their rehabilitation program. The World Health Organization has provided a framework for understanding adherence that includes considering health care systems, therapy (i.e. exercise), condition, patient, and socioeconomic-related barriers (World Health Organization 2003). All three patients demonstrated similar adherence to attending in-clinic hand therapy sessions but had varying levels of adherence to home programs or abilities to progress their therapy program. Our cases illustrate that several patient factors can influence an individual's ability to accurately (fidelity) and consistently adhere to home exercise programs. Specifically, in our cases, patient factors may include mental health status and social connectivity. For example, Patient A demonstrated low home

exercise adherence throughout his hand therapy. Although he attended weekly sessions with a different local therapist, he admitted to being inconsistent with his home exercises. One contributing factor to his low adherence to exercise may be due to his previous history of depression. Depression reportedly affects exercise adherence (Oliver and Cronan 2002; Jack et al. 2010). Also, Patient A lived by himself, possibly leading to decreased social connectivity which is also known to negatively impact exercise adherence (Milroy 2000; Jack et al. 2010). In contrast, Patient B and C's adherence to hand therapy may have been enhanced due to residing with their spouse and having increased social and familial support (Shaw et al. 1994; Jack et al. 2010). For Patient C, had a high commitment to his rehabilitation, adhering to his traditional hand therapy exercises, and he purchased an NMES device for home use which may have had an additional therapeutic benefit. This was associated with the best improvements in grip strength across time and across the cases.

A variety of factors related to therapist or the health system can also influence adherence. There has been a proposed strategy, specifically targeted towards physiotherapists and occupational therapists to increase patient adherence in musculoskeletal rehabilitation (Babatunde et al. 2017b). Although not all components of the strategy were implemented in our study, like using an objective measurement of adherence, many of these strategies were implemented in the three participants' rehabilitation program. In this comparative case study, we reduced some variation by having similar aged men as patients and the same therapist provide treatment for all three cases. However therapeutic alliance between a therapist and different patients can vary and still be a modifier of adherence. Components of increasing therapeutic alliance may involve patient-therapist interactions that encouraged the formation of individualized treatment plans. These treatment plans involve setting short-term and long-term goals that were agreed upon by the participants and the therapist. For example, Patient C had a specific goal to control his 5<sup>th</sup> digit's finger adduction (i.e. no more positive Wartenberg's sign). The hand therapist developed a home exercise program and smaller goals to scaffold towards Patient C's goal. Mutual contribution in creating goals and treatment plans can increase the patients' sense of connectedness, autonomy, and competence, which are key components of therapeutic alliance and self-determination theory (Kayes

and McPherson 2012; Babatunde et al. 2017a). Further, during their hand therapy sessions, educational and behavioural strategies like providing feedback or providing supervised exercises may have enhanced participant adherence. The hand therapist overseeing their rehabilitation (J.L.S.) used a similar individualized approach for all three participants' treatment plans. It is important to increase clinician's understanding of all the factors that influence adherence via knowledge translation. Knowledge translation interventions have been shown to affect how therapists plan to assess, facilitate and monitor adherence (Babatunde et al. 2017b). Collectively, optimizing barriers and facilitators to their rehabilitation adherence may impact the participants' outcomes and response to surgery and hand therapy.

A novel aspect of our study is the use of DQEMG to obtain MUNE from two of the intrinsic hand muscles (FDI and ADM) in two cases. In comparison to Patient C, Patient B demonstrated lower MUNE, decreased SMUP amplitudes, and decreased CMAP amplitudes in the ADM muscle. Lower estimations of motor units (lower MUNE) in the ADM muscle may indicate less reinnervation and recovery of Patient B's hypothenar muscles in comparison to Patient C. With nerve transfers, one of the goals is to improve the number of axon to endplate connections which is known to maximize functional outcomes (Kale et al. 2011). Likewise, muscles with a greater number of motor units may allow for more fine motor control (Henderson and McCombe 2017). Decreases in motor unit counts have also been associated with decreases in muscle performance such as lower power, torque, and MVC (McKinnon et al. 2015; Gilmore et al. 2017b; Kirk et al. 2018). The smaller SMUP amplitudes observed at Patient B's ADM in comparison to Patient C's may also indicate that Patient B had less collateral reinnervation across muscle fibres. Collateral reinnervation is typically a protective mechanism to continually maintain muscle function and strength (Power et al. 2013). Collateral sprouting of new nerves and muscle fiber atrophy may lead to decreased conduction velocity and result in greater SMUP amplitudes (Stålberg and Sonoo 1994). It is interesting to note that Patient C demonstrated greater NF jiggle, a measure of motor unit instability. Patient C's increased motor unit instability may be indicative of an increased number of nascent motor units which typically demonstrate less stable motor unit potentials (Stålberg and Sonoo 1994; Krarup et al. 2016). Collectively, observing these differences in

neuromuscular health between Patient C and Patient B's ADM may elucidate some possible mechanisms that contributed to the differences in hypothenar function following surgery and rehabilitation. Further, in comparison to a healthy aging population (Tsang et al. 2020), Patient C's FDI showed decreases in MUNE, increased SMUP amplitude, and increased MUP area. Increased SMUP amplitude and MUP area are inversely related to lower motor unit counts due to collateral reinnervation. However, although motor unit counts were substantially lower in Patient C compared to normative older adults, Patient C did not demonstrate functional deficits with his interossei muscle or any significant decreases in motor unit stability.

Although these cases highlight clinical decision-making issues in a novel surgical approach to treating severe ulnar neuropathy, we acknowledge the study's limitations. Our current cases do not represent all recovery trajectories or all their possible mediators. Further, although comparative case studies provide a platform for discussing clinical reasoning around differences in outcomes, the associations we observed can only be hypothesized, since causation cannot be inferred from the study design. We believe that it would be beneficial for future investigations with larger sample sizes to explore the effectiveness of structured rehabilitation regimes following nerve transfers.

Emerging evidence suggests that SETS AIN to ulnar nerve is a useful surgical solution for a difficult clinical problem. Given the severity of the pathology in patients who are candidates for this procedure, we expect that normal nerve function and restoration of all physical capacity is not a realistic expectation. This study highlights that pre-surgical neurological and metabolic comorbidities, and the timing of surgical intervention may impact recovery. It also illustrates that adherence barriers and facilitators (i.e. social connectivity) are critical issues that should be considered in customizing hand therapy, as they may ultimately influence patient outcomes. Our study has also provided an opportunity to observe the associations with hand functional outcomes with neurophysiological measures and neuromuscular health (DQEMG). It is important for future quantitative studies to explore surgical outcomes, predictors, and their relationship to nerve functioning. Qualitative studies may inform our understanding of how to best optimize adherence and rehabilitation in this new surgical procedure.

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## Chapter 5- General Discussion

### Overview of Thesis

The overall aim of this thesis was to contribute to the basic science knowledge and associated clinical applications relating to intrinsic hand neuromuscular physiology by studying people with and without ulnar neuropathy, considering the effects of age, and a surgical intervention. Decomposition-based quantitative EMG (DQEMG) was utilized to measure motor unit physiology. A relatively novel electrophysiological indicator near-fibre (NF) jiggle, a specific quantitative EMG measure of motor unit stability was examined across the different studies. The first project within the thesis addressed test-retest reliability of NF jiggle in the intrinsic hand muscles. DQEMG was then used to describe age-related changes in intrinsic hand neuromuscular physiology in typical young, middle, and older aged adults. To explore clinical applications of peripheral nerve functioning in rehabilitation, a repeated case study design was used to examine the clinical trajectory of hand rehabilitation and function and associated hand intrinsic motor unit physiology following a nerve transfer surgical procedure in patients with severe cubital tunnel syndrome. Specifically, the following studies were conducted:

The purpose of the first investigation (Chapter 2) of the thesis was to analyze the test-retest reliability of NF jiggle in the ulnar nerve innervated intrinsic hand muscles of healthy subjects. NF jiggle showed good test-retest reliability in the first dorsal interosseous (FDI), abductor digiti minimi (ADM) and fourth dorsal interosseus (4DI) muscles examined using intra-class correlation coefficient (ICC) values. Based on the ICCs, standard error of measurements (SEM) and minimal detectable change (MDC) were also established for NF jiggle. The Bland Altman plots also demonstrated small systematic bias with test-retest measurements of NF jiggle in the intrinsic hand muscles. Overall, NF Jiggle demonstrates good test-retest reliability with low measurement error in contrast to traditional jiggle.

The aim of second investigation (Chapter 3) was to compare the neuromuscular physiology of a typical aging population in the intrinsic hand muscles. Multivariate

analysis of variance (MANOVA) and discriminant function analysis (DFA) were performed on the surface and intramuscular EMG measures to identify age-related differences in motor unit physiology. With aging, we observed decreases in motor unit number estimation (MUNE) and increases in NF jiggle and motor unit potential (MUP) area in the intrinsic hand muscles. Although the effect size was not as large when comparing between middle aged and younger adults, some differences in motor unit physiology were observed for measurements of NF jiggle and MUP area in the intrinsic hand muscles. Using a multivariate approach allowed for age-related differences and the relationship between the variables to be further elucidated. This study may potentially provide future prognostic predictors of age-related changes to hand neuromuscular physiology.

My third investigation (Chapter 4) was a repeated comparative case report to describe the responses, functional outcomes, and neuromuscular physiology of three participants following a nerve transfer surgery. The surgical process was known as a supercharged end-to-side (SETS) anterior interosseus nerve (AIN) to ulnar nerve transfer surgery to treat severe ulnar neuropathy and we describe the subsequent rehabilitation and hand therapy program that followed. Comparison of the cases suggested that comorbidities, time from neuropathy to surgical intervention and psychosocial influences on rehabilitation adherence influenced the functional outcomes and improvements following the surgery and rehabilitation. The participant with the best functional outcomes also demonstrated the greatest number of motor units using MUNE and altered motor unit stability of the intrinsic hand muscles. This investigation suggests that NF jiggle may be increased following the SETS AIN to ulnar nerve technique due to the presence of nascent units or novel axonal reinnervation of the target muscle.

Overall, the initial investigations of the thesis aimed to enrich the findings in the subsequent studies. The initial investigation (Chapter 2) established the reliability of DQEMG, specifically NF jiggle, in the intrinsic hand muscles. Although reliability has been reported previously regarding DQEMG variables (Boe et al. 2006, 2010; Calder et al. 2008; Ives and Doherty 2012), it is important to examine psychometric properties in each specific context. For this thesis, the context was examining motor unit physiology of

the intrinsic hand muscles. Establishing good reliability of the measure NF jiggle allowed for this measure of motor unit stability to be utilized in an aging and clinical population as seen in Chapter 3 and Chapter 4. The second investigation (Chapter 3) examined the intrinsic hand motor unit physiology of a typical aging population. Although motor unit physiology and DQEMG have been examined in an aging population previously (Hourigan et al. 2015; McKinnon et al. 2015; Gilmore et al. 2017b), there have been no reports of intrinsic hand neuromuscular physiology studied collectively and systematically. Further, using a multi-variate approach in examining quantitative EMG provided new avenues and methods for examining predictive or prognostic factors of age-related neuromuscular changes. Identifying specific age-related changes such as decreases in MUNE or increases in NF jiggle, is important as this provided normative data to examine clinical populations. Chapter 4 of the thesis was able to further examine clinical and physiological markers that may be associated with ulnar neuropathy and the SETS AIN to ulnar motor nerve surgery.

### **Implications of Thesis Findings**

The current thesis has implications for clinicians such as physiotherapists, occupational therapists, and physicians. Specifically, this work impacts clinicians who assess and treat individuals who have alterations in their intrinsic hand muscle physiology (i.e. ulnar neuropathy). Establishing reliability of a measurement method is critical, particularly if the instrument will be used for future clinical evaluation and prognostic purposes. Examining for systematic measurement biases informs the limitations of measurement tools like NF jiggle and DQEMG. Likewise, examining age-related changes in hand neuromuscular physiology may inform assessments, interventions and clinical decision making to account for these alterations. One of the goals of the current findings is that it will help inform future treatment approaches to augment or mitigate pathological neuromuscular alterations in the hand muscles. Finally, the repeated case report provides descriptive trajectories of the recovery processes following a SETS AIN to ulnar motor nerve surgery. The current thesis provides preliminary findings that may inform possible prognostic factors that are facilitators and barriers to improving functional outcomes following nerve transfer and the subsequent rehabilitation. Findings from the thesis may

provide insight for clinicians to be better able to consider comorbid factors and facilitators to program adherence.

This research also has methodological and neurophysiological implications for investigators who examine muscle physiology as it extends upon the research previous quantitative EMG reports. Aside from determining test-retest reliability specific to the context of the intrinsic hand muscles, we provide additional approaches to examining measurement bias such as the usage of Bland-Altman plots. These plots were utilized to identify agreement and systematic measurement error amongst the test and retest session. Additionally, the current thesis contributes to the methodology of analyzing neuromuscular variables associated with aging, specifically to the hands. I examined DQEMG variables using a multivariate modelling approach. Generating these analyses provides the possibility of creating more powerful predictive or prognostic models for age-related or pathological alterations in neuromuscular physiology. With respects to neurophysiology, we have confirmed and extended upon the age-related changes found previously. Likewise, we extend our findings explore alterations to neuromuscular physiology in middle-aged adults (40-60-years old) which has not been frequently explored. Finally, the SETS AIN to ulnar motor nerve is a relatively novel surgical intervention and most models explaining the physiological mechanisms are typically observed in animals (Kale et al. 2011). The current thesis provides some preliminary insight regarding the MUNE and motor unit stability of the hypothesized nascent units present following nerve transfers.

## **Limitations**

Several limitations should be addressed in the current thesis. In the first investigation of the thesis (Chapter 2), the sample could not be considered a normative population since the study was examining NF jiggle in a relatively younger age group and did not identify reliability across the age span. As seen with Chapter 3 of the thesis, age-related changes to neuromuscular properties are present in the intrinsic hand muscles. Further, Chapter 2 only examined test-retest reliability by one rater. Neuromuscular conditions are frequently treated by multiple clinicians; it would be important for future



investigations to measure the inter-rater reliability of NF jiggle. Finally, for Chapter 2, only NF jiggle reliability was determined, other psychometric properties of DQEMG within the intrinsic hand muscles were not evaluated within the investigation.

For the second manuscript of the thesis (Chapter 3), one limitation was having motor unit counts that were in discrepancy with previous investigations of hand muscles (Feinstein et al. 1955; Doherty and Stashuk 2003; Bromberg 2020) and there were no formal measurements of intrinsic muscular performance (i.e. grip strength, dexterity). Although previous reports have noted decreases in muscular performances associated with decreased MUNE or increases in NF jiggle (McKinnon et al. 2015), it is still valuable to investigate any functional deficits that may relate with changes in intrinsic hand neuromuscular physiology. Likewise, another limitation to our study is the lack of a subgroup for “very old” adult (>80 years old) who are known to demonstrate greater alterations in motor unit properties (McNeil et al. 2005).

Finally, for Chapter 4 of the thesis, I acknowledge the study’s limitations as a case report. Although the case report highlighted the unique trajectories of three patients and their respective improvements (small, medium, large) following the interventions, the investigation does not represent the full spectrum of recovery trajectories. Further, as a case report, the associations observed in the specific cases can only be hypothesized.

Overall limitations to this thesis include methodological limitations such as DQEMG being the primary approach to examine the neuromuscular physiology within the intrinsic hand muscles. There are several approaches to evaluating neuromuscular properties such as imaging (Sinclair et al. 2010), muscles biopsies (Lai et al. 2010), and motor control performance measurements (Li et al. 2004). However, utilizing DQEMG provides unique insight regarding the motor unit physiology and neuromuscular quality from an objective standpoint (Power et al. 2014).

## **Recommendations for Future Directions**

There are many valuable and worthwhile opportunities for future investigations regarding hand neuromuscular physiology. The following recommendations are by no

means exhaustive of the possible future endeavors. Novel investigations may expand upon my findings of the test-retest reliability of NF jiggle in an intra-rater reliability setting. Additional psychometric properties that may be beneficial to investigate include NF jiggle's responsiveness to change; particularly if NF jiggle is used clinically to evaluate alterations in motor unit stability.

Future studies may be added to further explore age-related neuromuscular changes in the hand muscles. Examining performance measurements alongside DQEMG may provide additional insight with regards to how the neuromuscular alterations may influence hand function and performance. Measurements like pinch strength, grip strength, or single finger movements are known to decline with aging (Ranganathan et al. 2001), but have not been examined alongside DQEMG and motor unit physiology mechanisms. Also, examining hand neuromuscular alterations in very old adults may expand upon the current understanding of sarcopenia that have been previously reported within this demographic (McNeil et al. 2005; Gilmore et al. 2018). Aside from examining hand neuromuscular alterations, future work may build upon my thesis and utilize a multivariate approach to explore quantitative EMG variables with a similar framework. Frequently, most investigations use multiple physiological variables to explore viable mechanisms, but analyze the variables using univariate models. Utilizing a multivariate approach to examine alterations in motor unit physiology may provide additional models that inform neuromuscular health in pathological populations such as persons with diabetic peripheral neuropathy, amyotrophic lateral sclerosis, sciatica, or sarcopenia.

The SETS AIN to ulnar motor nerve is a relatively novel surgical intervention. Future studies using a larger population with a cross sectional or longitudinal approach whilst examining motor unit physiology (via DQEMG) would be worthwhile. Further insight regarding the mechanisms of recovery may provide avenues of future treatment and rehabilitation approaches to augment and improve functional outcomes. Another recommendation would be to further explore the efficacy of rehabilitation protocols following nerve transfer surgeries, as these approaches have recently been developed. Protocols like the Birmingham Protocol or another similar structured protocol have been

proposed to improve functional outcomes (Hill et al. 2019; Sturma et al. 2019). Future investigations may explore the efficacy and mechanisms by which these protocols may influence patients' recovery following nerve transfers.

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## **Philemon Tsang- Curriculum Vitae**

PhD Candidate  
Health and Rehabilitation Sciences  
Western University  
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### **EDUCATION**

- 2014 - Present      PhD in Health and Rehabilitation Science  
Thesis Supervisor: Dr. Joy MacDermid  
Thesis title: Quantification and comparison of nerve recovery  
after nerve injury in patients with ulnar neuropathy  
Western University, London, Ontario
- 2016 - 2018      Master of Physical Therapy  
Western University, London, Ontario
- 2014      Masters of Science  
Thesis Supervisor: Dr. Aimee J. Nelson  
Thesis title: TMS for the Investigation of Somatosensory Afferent  
Input on Hand Control  
McMaster University, Hamilton, Ontario
- 2012      Bachelor of Science (Honours Kinesiology)  
University of Waterloo, Waterloo, Ontario

### **ADDITIONAL EDUCATION**

- 2018      Applied Motivational Interviewing and Coaching (Level I)
- 2018      Soft Tissue Release Training Workshop
- 2018      Mulligan Concept Lower Quadrant
- 2015      Western TSC- Teaching in the Canadian Classroom
- 2011      Standard First Aid and CPR-C, Lifesaving Society
- 2010      Ontario's Driver Licence, G-Class
- 2006      National Lifeguard Services, Lifesaving Society
- 2006      Grade 10 Piano with Honours, Royal Conservatory of Music

### **EMPLOYMENT**

**October 2019- Present – Registered Physiotherapist**  
Family Physiotherapy Centre of London, London, ON  
Community Health Centre and Outpatient Clinic

**Apr 2018 – May 2018 – Student Physiotherapist**  
Physiotherapy Alliance, Stratford, ON  
Outpatient Clinic

**Mar 2018 – Apr 2018 – Student Physiotherapist**  
CBI Health Centre- Sarnia, Sarnia, ON  
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**Nov 2017 – Dec 2017 – Student Physiotherapist**  
St. Joseph's Healthcare- Parkwood Institute , London, ON  
Neurotrauma Rehabilitation, Outpatient Rehabilitation

**Jun 2017 – July 2017 – Student Physiotherapist**  
London Health Sciences Centre, London, ON  
Intensive Care Unit, University Hospital

**Jan 2015 – May 2016 – Teaching Assistant**  
Western University, London, ON  
Occupational Therapy, Health and Rehabilitation Science

**Apr 2012 – Aug 2012 – Research Assistant**  
Sunnybrook Hospital, Toronto, ON  
Cognitive Neurology, Heart and Stroke Foundation

**Sept 2012 – Sept 2014 – Teaching Assistant**  
McMaster University, Hamilton ON  
Kinesiology Department

*Courses:*

- Neural Control of Human Movement (KIN 3E03)
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- Human Anatomy and Physiology I (KIN 1AA3/ 1YY3)
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**April 2012 – Aug 2012 – Research Assistant**  
Sunnybrook Hospital, Toronto, ON  
Cognitive Neurology, Heart and Stroke Foundation

**May 2011 – Aug 2011 – Research Assistant**  
University of Waterloo, Waterloo, ON  
Kinesiology Department, Clinical Neuroscience  
Neurophysiology in Sensorimotor Control

**Sept 2009 – December 2009 – Math/Science Tutor**  
Centennial College, Toronto, ON

**Jan 2009 – April 2009 – Physiotherapy Assistant**  
Carlan Physiotherapy, Toronto, ON

### **PEER-REVIEWED PUBLICATIONS**

1. **Tsang P**, MacDermid J, Eventov M, Miller T, Doherty T, Ross D, Doherty C. Test-retest reliability of near-fibre jiggle in the ulnar intrinsic hand muscles. *Journal of Electromyography and Kinesiology*. 49, 102349. Accepted December 1, 2019.
2. **Tsang P**, Walton D, Grewal R, MacDermid J. Validation of the QuickDASH and DASH in Patients With Distal Radius Fractures Through Agreement Analysis. *Archives of physical medicine and rehabilitation*. 98 (6), 1217-1222. Accepted June 1, 2017.
3. **Tsang P**, Bailey AZ, Nelson AJ. Rapid-Rate Paired Associative Stimulation over the Primary Somatosensory Cortex. *PloS one*. 10(3). Accepted September 23, 2015.
4. **Tsang P**, Jacobs MF, Lee KGH, Asmussen MJ, Zapallow CM, Nelson AJ “Continuous theta-burst stimulation over primary somatosensory cortex modulates short-latency afferent inhibition”, *Clinical Neurophysiology*. Accepted February 21, 2014. [CLINPH-D-13-7282R1]
5. Jacobs MF, **Tsang P**, Lee KGH, Asmussen MJ, Zapallow CM, Nelson AJ “[30 Hz Theta-burst Stimulation Over Primary Somatosensory Cortex Modulates Corticospinal Output to the Hand](#)”, *Brain Stimulation*. Accepted December 15, 2013. (In Press) [[j.brs.2013.12.009](#)]
6. Zapallow CM, Jacobs MF, Lee KGH, Asmussen MJ, **Tsang P**, Nelson AJ “Continuous theta-burst stimulation over the primary somatosensory cortex modulates interhemispheric inhibition”, *NeuroReport*. 24 (7), 394-398.
7. Jacobs MF, Zapallow CM, **Tsang P**, Lee KGH, Asmussen MJ, Nelson AJ “Current direction specificity of continuous theta-burst stimulation in modulating human motor cortex excitability when applied to somatosensory cortex”, *NeuroReport*. 23 (6), 927-931.
8. Premji A, Zapallow CM, **Tsang P**, Tang R, Jacobs MF, Nelson AJ “Influence of area 5 on interhemispheric inhibition”, *NeuroReport* 22 (18), 974-978.

## **CONFERENCE PRESENTATIONS (\*presenter)**

1. **Tsang P**, \*Bobos P, MacDermid J, Miller TA, Doherty TJ, Ross D. “Assessment of age-related differences in decomposition-based quantitative electromyography in the first dorsal interosseous (FDI) and abductor digiti minimi (ADM) muscles”, International Federation of Societies for Hand Therapy (IFSHT Congress 2019), Berlin, Germany, June 2019 (Poster)
2. \***Tsang P**, MacDermid J, Miller TA, Doherty TJ, Ross D. “Assessment of age-related differences in decomposition-based quantitative electromyography in the first dorsal interosseous (FDI) and abductor digiti minimi (ADM) muscles”, World Congress of Physical Therapy (2019 Meeting), Geneva, Switzerland, May 2019 (Poster)
3. \***Tsang P**, Eventov M, Miller TA, Doherty TJ, Doherty CD, MacDermid J. “Test-Retest Reliability of Decomposition-based Quantitative EMG Near Fibre Jiggle in the Ulnar Intrinsic Hand Muscles”, American Congress of Rehabilitation Medicine (2018 Annual Conference), Dallas TX, USA, Oct 2018 (Poster)
4. \***Tsang P**, Eventov M, Miller TA, Doherty TJ, Doherty CD, MacDermid J. “Test-Retest Reliability of Decomposition-based Quantitative EMG Near Fibre Jiggle in the Ulnar Intrinsic Hand Muscles”, Canadian Bone and Joint Conference 2018, London, Canada, May 2018 (Poster)
5. \***Tsang P**, Walton D, Grewal R, MacDermid J. “Validation of the QuickDASH and DASH in Patients With Distal Radius Fractures Through Agreement Analysis”, InterACTION Conference (Ontario Physiotherapy Association), Toronto, Canada, March 2017 (Poster)
6. \* **Tsang P**, Walton D, Grewal R, MacDermid J. “Validation of the QuickDASH and DASH in Patients With Distal Radius Fractures Through Agreement Analysis”, Canadian Bone and Joint Conference 2016, London, Canada, April 2016 (Poster)
7. \***Tsang P**, Jacobs MF, Lee KGH, Zapallow CM, Asmussen MJ, Nelson AJ "Effects of 30Hz continuous theta-burst stimulation over primary somatosensory cortex on short-latency afferent inhibition", Society for Neuroscience Annual Meeting, San Diego, USA, November 2013 (Poster)
8. \***Tsang P**, Jacobs MF, Lee KGH, Zapallow CM, Asmussen MJ, Nelson AJ "Investigating the effects of modified 30Hz cTBS applied over primary somatosensory cortex (SI)", Exercise and Neuroscience Group, Oshawa, Canada, June 2013 (Oral Presentation)
9. \***Tsang P**, Jacobs MF, Lee KGH, Zapallow CM, Asmussen MJ, Nelson AJ "Investigating the effects of modified 30Hz cTBS applied over primary somatosensory cortex (SI)", Southern Ontario Neuroscience Association, Waterloo, Canada, May 2013 (Poster)



10. \*Asmussen MJ, Zapallow CM, Jacobs MF, Lee KGH, **Tsang P**, Nelson AJ. “Changes in short-latency afferent inhibition during movement preparation”, Canadian Association for Neuroscience, Toronto, Canada, May 2013 (poster presentation)
11. \*Asmussen MJ, Zapallow CM, Jacobs MF, Lee KGH, **Tsang P**, Nelson AJ. “Non-selective change in short latency afferent inhibition during movement preparation”, Progress in Motor Control, Montreal, Canada, July 2013 (poster presentation)
12. \*Asmussen MJ, Zapallow CM, Jacobs MF, Lee KGH, **Tsang P**, Nelson AJ. “Task and Muscle specific effects of short-latency afferent inhibition”, Society for Neuroscience, San Diego, USA, November 2013 (poster presentation)
13. Zapallow CM, Asmussen MJ, \***Tsang P**, Jacobs MF, Lee KGH, Nelson AJ. “Influence of primary somatosensory cortex on interhemispheric inhibition”, Southern Ontario Neuroscience Association, Waterloo, Canada, May 2013 (poster presentation)
14. \*Zapallow CM, Asmussen MJ, **Tsang P**, Jacobs MF, Lee KGH, Nelson AJ. “Influence of primary somatosensory cortex on interhemispheric inhibition”, Canadian Association for Neuroscience, Toronto, Canada, May 2013 (poster presentation)
15. \*Jacobs MF, **Tsang P**, Lee KGH, Asmussen MJ, Zapallow CM, Nelson AJ. “Effect of 30 Hz continuous theta-burst stimulation on hand motor circuitry when applied over the primary somatosensory cortex”, Southern Ontario Motor Behaviour Symposium, Toronto, Canada, May 2013 (poster presentation)
16. \*Jacobs MF, **Tsang P**, Lee KGH, Asmussen MJ, Zapallow CM, Nelson AJ. “Effect of 30 Hz continuous theta-burst stimulation on intracortical circuitry of the primary motor cortex in humans”, Southern Ontario Neuroscience Association, Waterloo, Canada, May 2013 (poster presentation)
17. \*Jacobs MF, **Tsang P**, Lee KGH, Asmussen MJ, Zapallow CM, Nelson AJ. “The effects of 30 Hz continuous theta-burst stimulation on human primary somatosensory cortex”, Canadian Association for Neuroscience, Toronto, Canada, May 2013 (poster presentation)
18. \*Jacobs MF, **Tsang P**, Lee KGH, Asmussen MJ, Zapallow CM, Nelson AJ. “The influence of primary somatosensory cortex on hand motor circuitry”, Exercise and Neuroscience Group, Oshawa, Canada, June 2013 (oral presentation)
19. \*Lee KGH, **Tsang P**, Jacobs MF, Zapallow CM, Asmussen MJ, Nelson AJ “The investigation of 30 Hz continuous theta-burst stimulation over the primary somatosensory cortex on tactile perception”, Canadian Association for Neuroscience, Toronto Canada, May 2013 (poster presentation)

## **SCHOLARSHIPS**

2016 – 2019	CIHR Canada Graduate Scholarship - Doctoral (\$90000)
2016 – 2018	Western Doctoral Excellence Research Award (\$10000)
2007	Merit Scholarship, University of Waterloo (\$1000)