ABSTRACT

LUDOVICE, MIRANDA CLAIRE. Understanding the Neuromuscular Control of the Fingers in Children with and without Cerebral Palsy (Under the direction of Dr. Derek Kamper).

Cerebral palsy (CP) is a neurodevelopmental disorder resulting from a non-progressive brain insult or abnormal development prenatally, during infancy, or in early childhood. CP is the most common pediatric motor disorder. Hemiplegic cerebral palsy (HCP), a common subtype, is characterized by impairment on one side of the body. More than half of children with HCP have significant hand impairment, and many have greater impairment in their affected upper limb than their affected lower limb. Hand impairment can lead to substantial disability due to the hand's role in many self-care, social, occupational, and educational tasks. To better understand the source of hand impairment in HCP, we first must understand how neuromuscular control of the hand develops in neurotypical children. In this dissertation, we explored how finger neuromuscular control may be affected by typical childhood development and HCP.

We first performed a literature review of quantitative measures of hand function in children with HCP. We began with a summary of the results of common quantitative measures and assessments of hand function in children and adolescents with HCP. We then examined the extent of methodological variation in these assessments. Finally, we identified areas for further research.

We then quantified voluntary coactivation and the voluntary activation capacity (VAC) during middle finger flexion and extension in both hands of 10 typically developing children (11.1 ± 2.6 years old). Both measures have been shown to vary with age in children but have yet to be quantified in the hand. This characterization was done using surface electromyography, surface muscle stimulation, and a novel set-up for measuring three-dimensional fingertip force. Our VAC values were comparable to values measured in other pediatric upper limb muscles. We

saw that neither hand dominance nor force direction significantly impacted VAC or coactivation at 100% MVC. Direction had a significant impact on coactivation at 40% MVC. We did not see a statistically significant difference in coactivation between the two levels of voluntary force.

We then utilized musculoskeletal modeling to explore how age-related changes in index finger size and strength affect neuromuscular control during childhood development. We created ten models representing the average index fingers of male and female children aged 6 to 10 years old in OpenSim. We employed static optimization to predict the muscle activations required to produce a maximal palmar force with the index finger in two different postures. In the less flexed posture, age affected activation for most muscles, while sex affected all muscles. For the more flexed posture, however, age did not have a significant effect on activation level for most of the muscles. When separated by sex, the male models did have a significant correlation between age and activation for most muscles, while the female models had no significant correlations with age. This may be due to differences in growth rates between males and females.

Finally, we examined how fingertip force direction and neuromuscular control may vary between the paretic (more affected) and non-paretic (less affected) hands in children with HCP. We first measured the three-dimensional index finger force vectors produced during maximal force production in both hands of four children with HCP (9 ± 0.8 years old). Using the previously created age and gender-matched musculoskeletal models, we estimated what muscle activations were required to produce the resulting fingertip force vector. We also performed a sensitivity study on the relationship between muscle activations and the magnitude and direction of the resulting fingertip force vector in our model. The paretic hand force vectors did reveal relatively more shear force than the non-paretic hand, potentially leading to objects slipping from the hand. The muscle activations also varied between the hands.

Understanding the Neuromuscular Control of the Fingers in Children with and without Cerebral Palsy

by
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DEDICATION

To my mother for giving me my love of medicine. To my father for giving me my love of engineering and for his continued support and guidance throughout my academic career. To Jerry for supporting me in every way possible throughout this process.

BIOGRAPHY

Miranda Claire Ludovice received her Bachelor of Science with highest honors in Biomedical Engineering from the Georgia Institute of Technology in May 2017. Throughout her senior year and before entering graduate school, she worked as a research technician in the Agriculture Technology division of the Georgia Tech Research Institute. In August 2017, she began her graduate studies in the Joint Department of Biomedical Engineering at the University of North Carolina Chapel Hill and North Carolina State University. She will complete all requirements for a Ph.D. in Biomedical Engineering in April 2023.

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CHAPTER 1: INTRODUCTION

1.1 Background

Cerebral palsy (CP) is the most common movement disorder in children, with an incidence rate of roughly 3.3 out of every 1000 live births [1,2]. One of the most prevalent subtypes found within this diagnosis is hemiplegic CP (HCP) which predominantly affects one side of the body [3]. Children with HCP may have significant upper extremity impairment, which is often greater than the deficits in the affected lower limb [1]. Within the upper limb, the hand is the most likely segment to be impaired [4]. More than half of children with HCP have significant impairment of motor function of the hand. This hand impairment can lead to substantial disability since the hand is the primary means of interacting with the world.

A major difficulty in studying the differences in neuromuscular control in children with CP is the lack of comparative data from typically developing children. Children experience continuous reshaping of bone, muscle, and soft tissue as they develop. These physiological changes likely impact their neuromuscular control strategies. Additionally, the nervous system itself undergoes dramatic development and plasticity.

These changes are especially profound for the hand. Corticomuscular coherence for the intrinsic hand muscles, the first dorsal interosseous and the abductor pollicis brevis, is greater in adults than children [5]. The morphology of the hand motor cortex itself changes with age [6]. Accordingly, motor control appears to progress over time from the more proximal muscles to more distal muscles with age based on both corticomuscular coherence and comparisons of real-life motor control strategies [5,7].

In addition to the changes in the nervous system, both the size and strength of the hands also increase with age. Hand strength, as measured by the lateral or key pinch [8–13], palmar pinch [9–11], tip pinch [9–13], three-chuck pinch [9,12], or grip force [9,10,12–14], increases with age for children of both sexes. These changes could be due in part to age-related increases in muscle cross-sectional area and hand size, the latter of which impacts the moment arms for musculotendon forces [10,13]. Indeed, studies have also found positive relationships between hand strength measures and hand size [9,10,13]. Changes in strength may also arise from alterations in neural activation. Conversely, changes in muscle and bone morphology impact the musculotendon moment arms which would impact the required muscle activation patterns to achieve a desired task.

Two potential sources of these age-related changes in hand or finger strength, are changes in voluntary muscle activation capacity and coactivation. Voluntary activation capacity (VAC) is a measure of the extent to which a muscle is being activated during maximal voluntary contraction. While few studies have measured the VAC of children's upper limb muscles, the reported results have indicated that children, especially pre-pubescent children, have lower voluntary activation capacity than adults [15,16]. Coactivation is a measure of how much of the antagonist muscle is activated during voluntary activation of the agonist muscle. While some coactivation occurs in most movements, the level of coactivation varies widely depending on the muscle or the movement itself. Some studies have found greater coactivation in children, but others have failed to find a significant difference between adults and children [17]. Evaluations of the difference in coactivation between adults and children are quite limited for upper limb muscles [17–19].

A common task for the hand is to grip and lift objects. To successfully grip and lift an object, the index finger and thumb must produce forces normal to the surface of the object large enough to counteract the object's weight. Without adequate normal force, the object may be dropped, while with excessive force it may be crushed [20]. Typically developing children can scale their grip force to be just above the minimal force required to lift an object without slipping. Children with HCP struggle in coordinating these forces [21] as well as in adapting to different weights [22] and textures of objects [23]. Post-stroke adults have been shown to struggle with controlling the orientation of their fingertip forces of their paretic hands when compared to their non-paretic hands or those of neurologically intact adults [24]. Since post-stroke adults and children with CP have a similar pathophysiology and both populations show similar grip impairments [25], children with HCP likely also struggle to control the orientation of their paretic fingertip forces.

Despite the prevalence of hand impairment in children with HCP, research into the underlying causes of these hand impairments has been limited. This may be due in part to the difficulty in studying children throughout rapid and continuous changes in physiology and muscular control as they grow and develop. Additionally, the hand is challenging to study due to its many degrees-of-freedom, the wide range of tasks it performs, and the many different muscles involved in control of the hand. As these muscles are relatively small and tightly packed, capturing their activity through electromyography (EMG) is difficult, especially in children.

The goal of this dissertation is to first examine neuromuscular control of the fingers in typically developing children and to explore how this control might be altered in children with HCP. We believe these results will add to our current understanding of pediatric development of finger control in children and contribute to future research, therapies, and treatments for children with HCP. In chapter 2, we first present an examination of the current state of research on the quantitative differences in hand strength and function in children with HCP. We examined grip strength, range of motion of the wrist or finger, two-point discrimination, and several clinical evaluations of hand function. In chapter 3, we measured the voluntary activation capacity (VAC) and coactivation during middle finger flexion and extension in typically developing children. In chapter 4, we used musculoskeletal modeling to examine how age-related changes in index finger strength and size impact neuromuscular control. In chapter 5, we measured three-dimensional maximal index finger force vectors in children with HCP to examine how fingertip force direction varies between the paretic and non-paretic hands. We then used age-matched index finger models to examine how these differences in fingertip force and orientation might affect neuromuscular control. In chapter 6, we present opportunities for future research based on the findings in this dissertation.

1.2 Dissertation Outline

1.2.1 Chapter 2: Review of Current Research in Hand Function in Children with Hemiplegic Cerebral Palsy

We performed a scoping review of 131 articles on quantitative measures of hand and finger function in children with HCP. Articles were included which reported quantitative data for children with HCP on grip, range of motion (ROM), two-point discrimination (2PD), Box and Block Test (BBT), Melbourne Assessment of Unilateral Upper Limb Function (MUUL), and the Assisting Hand Assessment (AHA). We began with a summary of the results of common quantitative measures and assessments of hand function in children and adolescents with HCP. We then examined the extent of methodological variation in these assessments. Finally, we identified areas for further research on hand function in children with HCP. Our review provides researchers and clinicians with an overview of quantitative measures of hand function in children with HCP and creates a summary of the current state of research.

1.2.2 Chapter 3: Pediatric Voluntary Activation Capacity and Coactivation in the Hand

We examined voluntary coactivation and the voluntary activation capacity (VAC) in the extensor digitorum communis (EDC) and flexor digitorum superficialis (FDS) muscles during middle finger flexion and extension in ten typically developing children, aged 8-14 years. The aim of this study was to quantify these measures in typically developing children for comparison to both adults and children with motor impairment. We hypothesized that we would not find a statistically significant difference in the VAC or coactivation between the dominant and non-dominant hands or between flexion and extension. Previous studies showed little difference in coactivation or voluntary activation capacity of the finger flexors and extensors in control adult subjects [26,27]. We did not anticipate a difference in VAC or coactivation between the hands because many studies failed to find a difference in hand strength between the hands in children of similar ages [9,11,14]. Neither hand nor force direction had a significant effect on VAC or coactivation at 100% MVC. Only direction had a significant effect on coactivation at 40% MVC.

1.2.3 Chapter 4: The Impact of Finger Length and Posture on Muscle Activation Patterns Using Computer Modeling

We used musculoskeletal modeling to explore the effects of index finger size and finger posture on neuromuscular control. First, we created 10 pediatric finger models in OpenSim 3.3 based on anthropometric data of male and female children aged 6 to 10 years-old [13,28,29]. We used static optimization to estimate the muscle activations required during a maximal palmar index finger press in two different finger postures. Posture 1 had 0° of flexion at the metacarpophalangeal (MCP) joint, 30° of flexion at the proximal interphalangeal (PIP) joint, and 0° of flexion at the distal interphalangeal (DIP) joint. Posture 2 had 0° of flexion at the

MCP joint, 60° of flexion at the PIP joint, and 30° of flexion at the DIP joint. Target index finger forces came from average tip pinch data [13]. We hypothesized that the relative activations would change with model size, but that finger posture would have a greater impact on activation patterns than size alone. As anticipated, posture did profoundly impact the estimated muscle activation patterns. In the more extended posture 1, most of the muscle activation percentages increased with age, while variation in activation patterns with age was much less consistent for posture 2. When separated by sex, male models did have a significant correlation between activation and age for certain muscles, while none of the female models had a relationship between activation and age. These sex-related differences may have been due to differences in the rate of change in finger size versus finger length between the male and female models. Overall, these results imply that the effect of finger size may vary with finger posture and neuromuscular controls may need to adjust based on both size and posture.

1.2.4 Chapter 5: Neuromuscular Control of the Finger in Children with Hemiplegic Cerebral Palsy

We examined the differences in the orientation of the forces measured in both hands of four pediatric subjects with HCP. We did this by measuring the maximal three-dimensional index finger force vector in both hands. We then used musculoskeletal modeling to estimate the muscle activation patterns required to produce those fingertip force vectors. By using modeling, we could control for hand size and posture and estimate the activations of muscles that would be difficult or impossible to acquire using surface electrodes. We hypothesized that the paretic hands would produce a less normally oriented fingertip force vector than the non-paretic hands, and that the estimated muscle activations would vary between both hands. We did find that the orientation of the fingertip force vectors, and the muscle activations patterns varied significantly between the paretic and non-paretic hands.

1.2.5 Chapter 6: Conclusions and Future Opportunities

We discussed the overall results and implications of our experimental and computational modeling work. We also presented opportunities for future *in vivo* and computational research based on this work.

CHAPTER 2: REVIEW OF CURRENT RESEARCH ON HAND FUNCTION IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY

Adapted from J. McCall, M. Ludovice, C. Elliott, and D. Kamper, "Hand Function Development of Children with Hemiplegic Cerebral Palsy: A Scoping Review", *J. Pediatr. Rehabil. Med.*, vol. 15, pp. 211-228, 2022, doi: 10.3233/PRM-200714

2.1 Introduction

Cerebral palsy is the most common movement disorder in children, occurring in roughly 3.3 out of every 1000 live births [1,2]. One of the most prevalent subtypes found within this diagnosis is hemiplegic CP (HCP) which predominantly affects one side of the body [3]. Uvebrant et al.'s retrospective study of 169 children with HCP found that 53% of the children had significantly impaired motor function in their hands. In their own study and three of four similar studies, more children had greater impairment in the affected upper limb versus the affected lower limb than children who had equal impairment or greater lower limb impairment [1]. Within the upper limb, the hand is the most likely segment to be impaired [4]. Hand impairment can lead to substantial disability since the hand is the primary means of interacting with the world. As 96% of all children with CP live into adulthood, chronic hand dysfunction will impact employment, recreational, and social opportunities throughout a person's lifetime [30].

Despite the importance of research into upper limb impairment in HCP, few reviews have focused on the characterization and quantification of these hand deficits. Many of the previous reviews that addressed upper limb impairment neglected the hand altogether. When the hand was included, a finite number of tasks and clinical measures were used. Research has been especially limited in the areas of three-dimensional limb kinematics and bimanual task performance [31,32]. Previous review articles have largely focused on identifying and/or assessing the reliability of clinical assessments of hand impairment rather than empirically measuring these impairments. These reviews also do not report the raw or aggregated results of the clinical measures taken in the reviewed studies [33–35]. To understand the underlying causes of hand dysfunction and to test the effectiveness of therapies in children with HCP, we need a robust collection of quantitative measures of the baseline impairments across many different tasks.

The aim of this scoping review of previously published articles was to fill the existing gap in reviews of hand-specific quantitative research in children with HCP. Rather than focus on a specific task or measure, the goal of this review was to provide a broad overview of existing original literature rather than directly quantified hand function deficits in children with HCP. We began with a summary of the results of common quantitative measures and assessments of hand function in children and adolescents with HCP. We will then examine the extent of methodological variation in these assessments. Finally, we will identify areas for further research on hand function in children with HCP. While both qualitative and quantitative assessments can inform future research and clinical applications, this scoping review was limited to quantitative measures since they enable more direct evaluations of function and provide insights into the underlying causes of these impairments. Our review will provide researchers and clinicians with an overview of quantitative measures of hand function in children with HCP and create a summary of the current state of research.

Table 2.1. Summary of the Inclusion and Exclusion Criteria.

Inclusion Criteria	**Exclusion Criteria**
Hemiplegic cerebral palsy	Not available in the English language
Participant age of 18 years or less	Participants who had upper limb surgery or botulinum injection within six months prior to the study
Sample size of 3 or more	Conference proceeding or review article
Includes one or more of the identified hand function measures	

2.2 Methods

We implemented the following steps to identify studies that met our inclusion criteria. First, we created a search and data inclusion protocol in compliance *a posteriori* with the Joanna Biggs Institute scoping review protocol requirements. The preliminary search was conducted in May and June of 2018 and an updated search was completed in October of 2019. The search terms 'cerebral palsy' and 'hemiplegia', 'hemiparetic', or 'unilateral' were used to capture the desired study population. The term 'hand' was used to isolate studies that measured hand function. A few optional terms were used to describe possible measures that might be used (e.g., 'strength', 'force', 'kinetics', 'EMG', 'activation', 'brain', 'imaging', 'skill', 'function', or 'motor'). These search terms were input into PubMed, PEDro, Web of Science, CINAHL, and SpringerLink.

Table 2.1 outlines our full inclusion and exclusion criteria. Conference proceedings and review articles were excluded to avoid any duplicate data sets. Only articles with at least three subjects under 18 years of age were included. Due to a lack of translation services, only articles written in the English language were considered. No restrictions were placed on the date of publication or study type. Due to their impacts on sensorimotor control, studies where subjects received botulinum toxin treatment or upper limb surgery within six months of the study were excluded, but any available pre-operative data were included.

After collecting all articles that met our search criteria and eliminating duplicate articles, we collated all measures taken and the most common types of measurements were extracted. For clinical assessments that evaluated the same or similar components of hand function, the most common assessment was used. The following measures of hand function were selected: pinch strength, finger forces, grip strength, range of motion (ROM), electromyography (EMG), two-point discrimination (2PD), pegboard tests, Box and Block Test (BBT), Jebsen-Taylor Test of Hand Function (JTTHF), Melbourne Assessment of Unilateral Upper Limb Function (MUUL) [36], and the Assisting Hand Assessment (AHA) [37]. While not every measure from the selected studies was included, preliminary analysis revealed that this set of measures encompassed many common clinical measures and covered a range of elements of sensorimotor development.

This dissertation focused on the following subset of quantitative measures: grip strength, range of motion (ROM), two-point discrimination (2PD), the box and block test (BBT), Melbourne Assessment of Unilateral Upper Limb Function (MUUL), Assisting Hand Assessment (AHA). The other measures addressed in the full review article were previously published in another dissertation [38].

The preliminary search of the five databases produced 1,536 unique articles. Two authors independently screened the title and abstract of each article against the inclusion and exclusion criteria (**Table 2.1**). If the abstract alone did not provide sufficient detail, the article's full text was examined. Consensus was required to include or exclude any articles. A total of 1,536 unique articles were collected from the initial database searches. After screening the titles and abstracts based on our inclusion criteria, 1,209 irrelevant articles were excluded, and 327 articles remained. Once the full texts of the 327 articles were reviewed, 195 additional articles were excluded based upon our inclusion and exclusion criteria. This left a final total of 132 articles (**Fig. 2.1**).

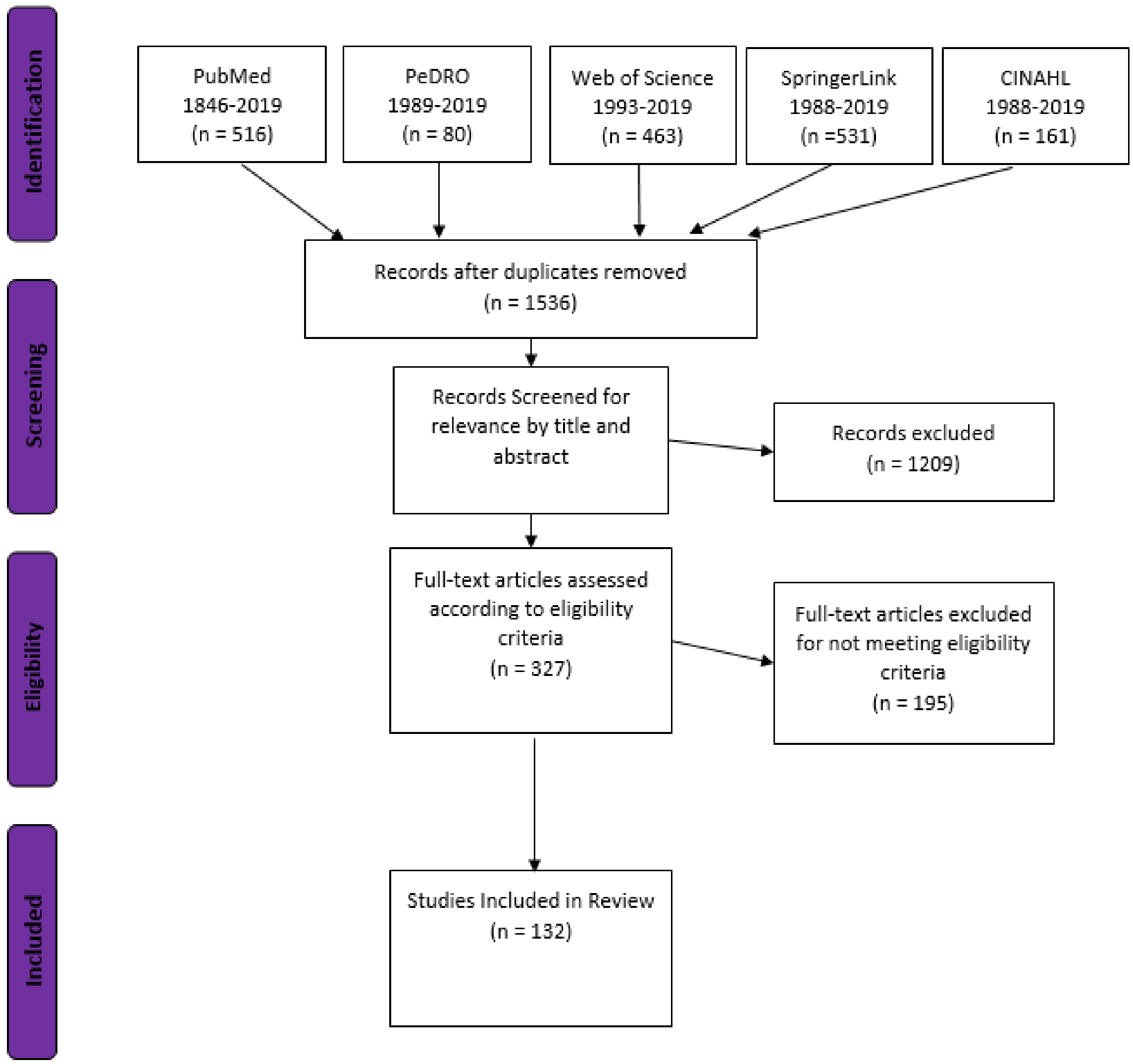

Figure 2.1. PRISMA diagram of article selection. A total of 327 articles were assessed; 131 articles met the desired criteria and were included in this review.

The following areas of focus were identified: quantitative neuromechanics, clinical assessments, and clinical functional evaluations. Articles without data in these categories were excluded. Due to the broad focus of this scoping review, the sources of evidence were not critically appraised. Most of the measures used are common standardized measures that have been previously validated.

The identified quantitative measure(s), participant ages, neurological status, assessment results, and clinical measures of impairment (e.g. MACS, GMFCS or Zancolli scores) were extracted from each article included in the review. Data extraction was divided equally between two authors, but results were reviewed jointly and discussed to arrive at a consensus. For each type of quantitative measurement, the context of use, values for different age groups, the relationship between quantitative measurement values, and the results of relevant clinical evaluations were examined.

Individual study data were collated by participant age, characteristics, and assessment outcomes. Overall mean values for these groups were reported. Some articles only reported average results by group while others reported individual participant data. If any average values included participants that did not meet our inclusion criteria (e.g., adults subjects, different subtypes of CP, etc.), these values were not included. If individual data were provided, then new averages were calculated using only the data from the appropriate participants. All included data values were averaged or charted separately. Mean assessment outcomes were charted against mean ages or MACS score. Data sets were divided by hand, either the dominant or non-dominant hand in TD children or the paretic or non-paretic hand in children with HCP.

2.3 Results

Fourteen articles evaluated and reported maximum grip strength in children with HCP. A total of 12 studies provided quantitative measures of grip strength and age (**Fig. 2.2**). Some studies only provided intraclass correlation coefficients for grip measurements [39]. Overall, children with HCP were found to have a lower maximum grip strength in their paretic hand when compared to their non-paretic hand or either the dominant or non-dominant hands of age-matched TD children [40–51]. Six of the included articles used a handheld dynamometer to measure grip strength. In total, these six studies involved 176 children with HCP and 48 TD children [41,46,47,52–54]. The aggregated data suggest substantial relative deficits in the grip force of the paretic hand. The overall average paretic hand grip was 82 N while the non-paretic hand was more than double at 214 N (**Fig. 2.2A**). The dominant hand of TD participants was 195 N, and the non-dominant hand was 121 N (**Fig. 2.2B**). Some of this difference may be explained by having many more data points for the paretic (n = 12) hand than the non-paretic hand (n = 6) or either hand in TD children (n = 4). Many studies did not include TD children for comparison, and some only reported the paretic hand in children with CP. The aggregated average age was also less for the paretic hand data at 10.6 years old, while the non-paretic hand was 11.5 years old, and the TD subjects were 11.3 years old. The magnitude of the deficit increased with age; the absolute difference at 13 years of age approached 200 N. Values for the non-paretic hand were comparable to the non-dominant hand in TD children (**Fig. 2.2B**).

Five articles measured grip during lifting tasks where participants must create a sufficient normal force with minimal shear forces to counteract gravity and the inertia of the lifted object. Two articles were excluded from **Fig. 2.2** because they only reported an instantaneous peak grip force over a longer period rather than a single grip force during a maximal voluntary contraction [48,53]. When children with HCP lifted an object with their paretic hand, they produced excessive grip force, giving themselves a large safety margin [53,55–57]. Those with HCP also had a slower reaction time when responding to an increasing variable load [58].

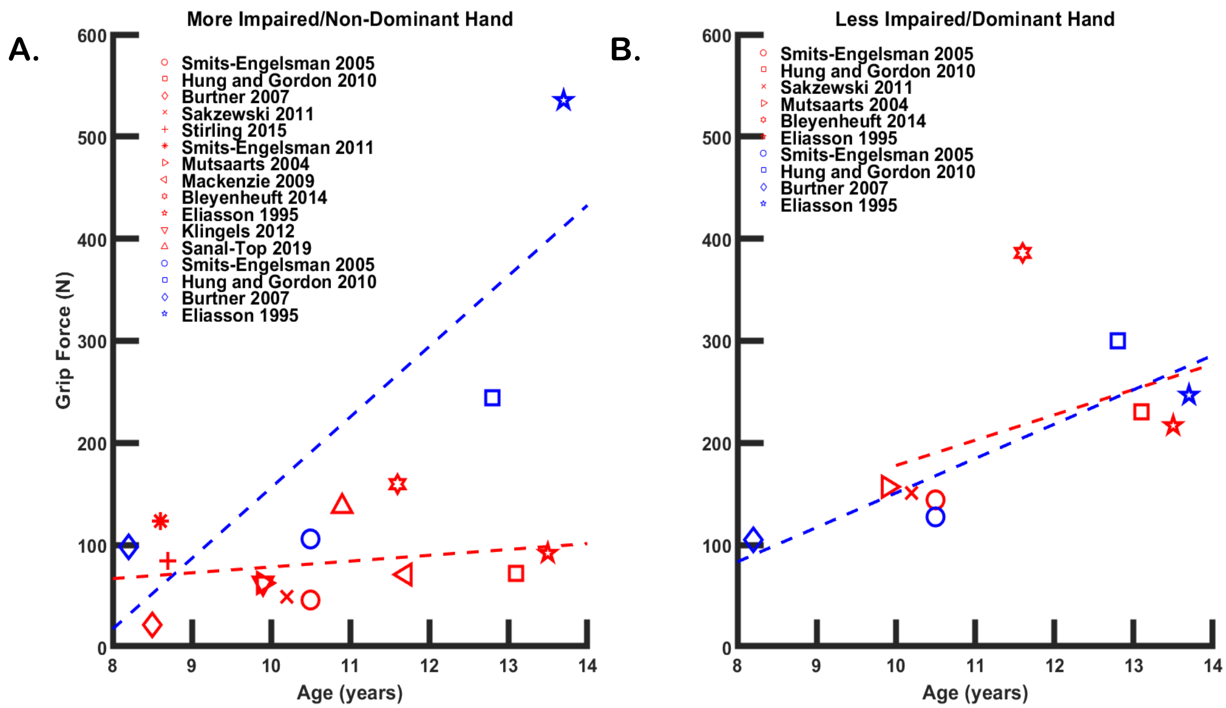

Figure 2.2. Maximum grip strength data aggregated from Twelve Studies. Symbols represent mean data for a given age group for the referenced study. A) Grip force of the non-dominant and paretic hands vs. age. Substantial deficits were present in the paretic hand (Blue: TD non-dominant hand & Red: CP paretic hand). B) Grip force of the dominant and non-paretic hands vs. age (Blue: TD dominant hand & Red: CP non-paretic hand). The legend indicates the references associated with specific data points. Studies reporting data from both the paretic and non-paretic hands may be referenced twice. Trend lines were added to figures to provide a rough visual guide; the trend lines were created by computing a least-squares linear fit to the data.

Eight articles reported data on range of motion (ROM) of the wrist or fingers [43,45,56–61]. Methods used to determine ROM varied across studies, but all eight used a goniometer to measure joint angles. One article examined passive range of motion (PROM) of thumb joints and noted that the PROM of the carpometacarpal joint of the paretic hand was reduced for abduction and extension compared to the non-paretic hand [60].

Passive extension of the fingers of the paretic hand was severely limited when compared to the non-paretic fingers even when the wrist was flexed to aid in extension of the fingers [60]. Klingels et al. reported hyperextension of the proximal and distal interphalangeal joints of the fingers. They found that older children generally exhibited greater upper extremity limitations in the PROM [43]. Five studies of wrist PROM reported normal values for the paretic wrist. These articles reported "no movement limitation" [45] with PROM wrist extension of 67˚–80˚, wrist flexion of 78˚–95˚ [55,56,61], and total wrist PROM of 177˚ [57].

Studies also investigated active range of motion (AROM) in the fingers and wrist. Hyde et al. found a significant negative correlation between AROM of the wrist and the Ashworth score of the finger flexors. Additionally, AROM was generally decreased in individuals who struggled to maintain a consistent isometric force (60% coefficient of variation or higher) [55]. Utley et al. reported wrist ROM achieved during performance of several upper limb tasks [58].

Three articles with a total of 144 participants aged 4.6–7.8 years, reported AROM for the wrist together with either the Manual Ability Classification System (MACS) or Gross Motor Function Classification System (GMFCS) classification [57,62,63]. These articles reported that participants with higher overall function had greater wrist AROM. Participants classified as GMFCS I and either MACS I or II had a mean wrist AROM of 105˚, while participants classified as MACS III had a mean wrist AROM of 22˚. Utley et al. reported maximum active wrist extension, together with Zancolli classification, for 20 children with HCP. Those children classified as Zancolli I could achieve 27˚ of wrist extension beyond the neutral position, while those classified as Zancolli IIB could not extend the wrist beyond 42◦ of wrist flexion relative to the neutral position [62].

Twelve articles reporting two-point discrimination (2PD) data in the fingers were included [64–73]. The tools used to measure 2PD included paper clips [73], monofilaments [74], aesthesiometer [75,76] and a discriminator device [48,77]. The 338 participants with HCP in these articles ranged in age from 4–18 years old. No 2PD data were reported for TD children. Across the aggregated groups of subjects, discrimination was found to be poorer in the paretic fingers, with a mean static 2PD score of 5.5mm as compared to 2.4mm in the non-paretic fingers

[48,66,73,76,77,81,89–92]. No significant relationship between age and 2PD ability was observed for either the paretic or the non-paretic hand. Three of these articles, however, reported that some participants did not give reliably repeatable results for the 2PD tests, potentially due to the difficulty for subjects to communicate their perception. Reliability substantially improved in children older than 8 years of age [64,81,91].

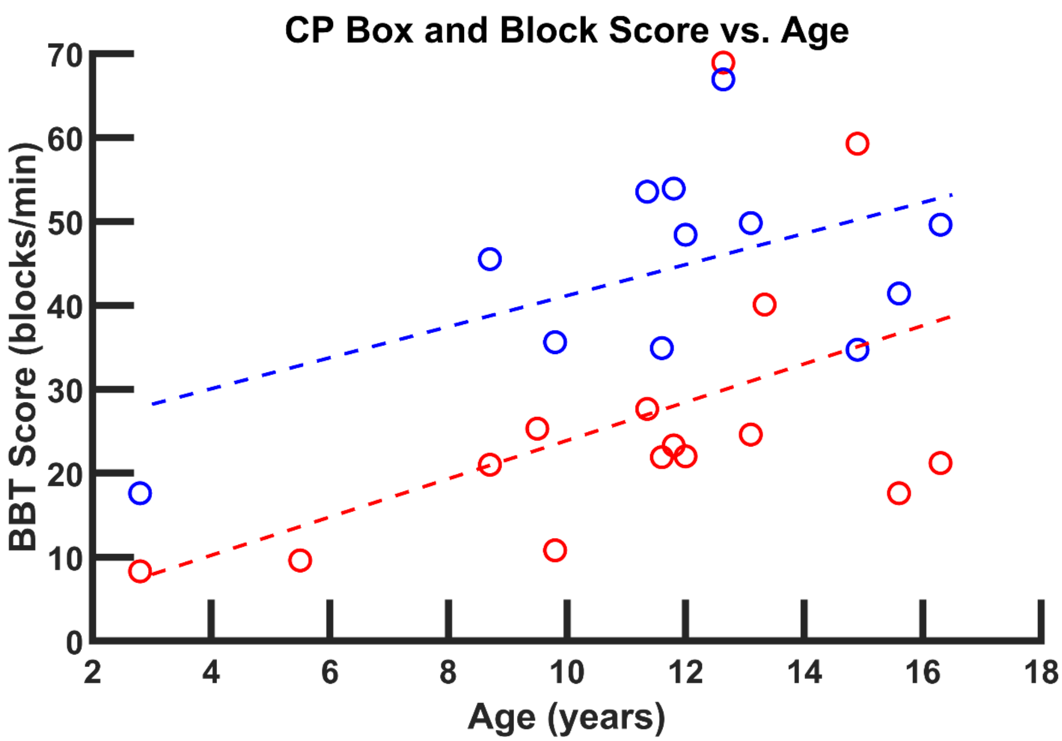

Figure 2.3. BBT Score vs. Age for Data Aggregated from Twelve Studies. Trend lines suggest higher scores in older children for both the paretic and non-paretic hand in children with HCP. Trend lines were added to figures to provide a rough visual guide; the trend lines were created by computing a least-squares linear fit to the data. (Paretic Hand: Red and Non-Paretic hand: Blue). [77–88]

Twelve articles described use of the BBT to evaluate manual dexterity and provided the average BBT score along with participant age (**Fig. 2.3**) [77–88]. Not all studies reported these data which prevented their inclusion in the comparison [93]. The aggregated data from these studies includes outcomes for 375 paretic hands and 319 non-paretic hands in children with HCP (**Fig. 2.3**). The scores for the paretic hand were generally smaller than for the non-paretic hand, indicating reduced dexterity [80,94,95]. Scores for both the paretic and non-paretic hands improved with age. In comparison to the scores for TD children, the HCP participants exhibited substantial deficits. Tomhave et al. found that children with HCP on average moved 24.8 less blocks with their paretic hand than the non-paretic hand. Children with HCP scored significantly below normative values across all age groups for both hands [78]. Holmstrom et al. also found that the paretic hand scored lower than normative data as reported by Mathiowetz et al. [80,96]. In both studies, sensory impairment was correlated with a diminished BBT score. Furthermore, children who had contralateral projections that controlled their affected hand rather than only ipsilateral projections produced higher BBT scores [95].

Eleven different articles reported MUUL scores as a percentage of the total possible score [3,48,71,97–105]. Some studies did not provide comparable pre-intervention values [106,107]. The aggregated data were obtained from a total of 380 children with HCP. Children 9-13 years old tended to have higher relative scores of their paretic hands than children aged 4-8 years old.

A total of 47 articles reported Assisting Hand Assessment (AHA) group scores and the average age of the cohort [43,51,83,84,90,91,95,97,101,103,104,108–135]. Some studies only reported post-intervention values [136]. The AHA measures how well children with unilateral hand impairment use their paretic hand with their non-paretic hand [137]. Across the selected studies, data were collected from a total of 2332 children with HCP. Generally, older children scored higher on the AHA (**Fig. 2.4**).

In general, children with HCP had reduced function in the paretic hand when compared to their non-paretic hand or the dominant or non-dominant hands of TD children. While many of the clinical outcome measures (BBT, MUUL, and AHA) improved with age, children with HPC failed to match the scores of their TD peers. This led to greater relative deficits with increasing age. Both grip force and 2PD showed little improvement with age while PROM did not improve with age. For all available measures, the non-paretic hand performed similarly to the hands of TD children. A total of 196 identified studies had to be excluded from assessment for this review due to lack of reported data, the reporting of only post-intervention data, heterogeneous subject pools (including multiple patient populations), or the inclusion of data from adults with CP.

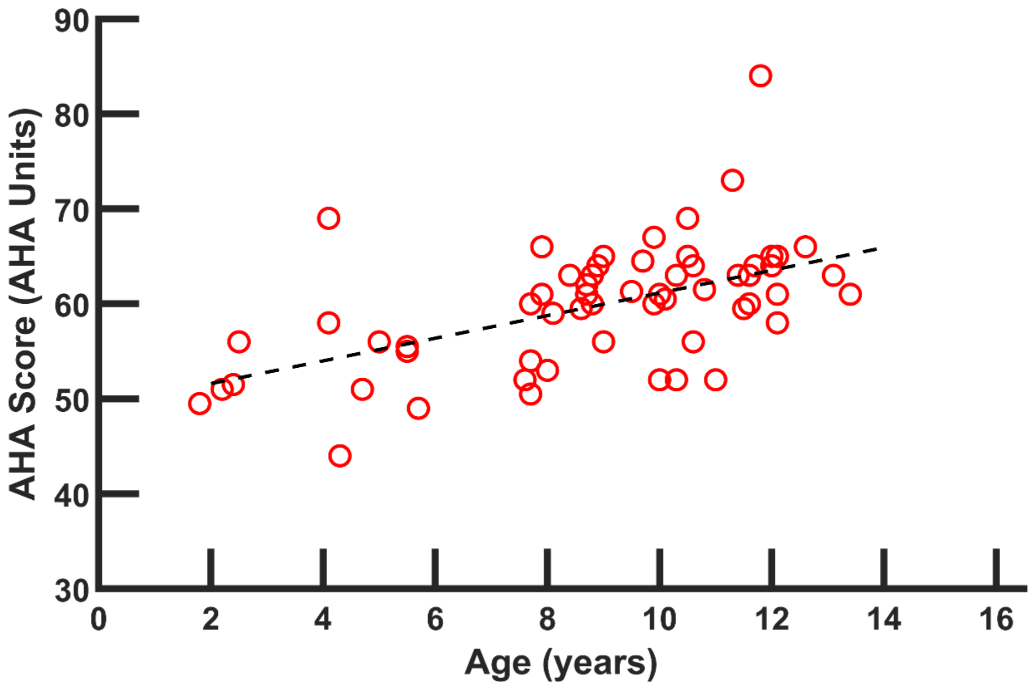

Figure 2.4. Group AHA Scores vs. Average Cohort Age Across Forty-Seven Studies. General trend shows improved AHA scores in older children with HCP. Trend lines were added to figures to provide a rough visual guide; the trend lines were created by computing a least-squares linear fit to the data.[43,51,83,84,90,91,95,97,101,103,104,108–135]

2.4 Discussion

The 131 included articles covered kinetics, kinematics, sensory perception, and functional task performance. In agreement with the findings of a past review article [31], the studies examined in this scoping review showed that children with HCP generally performed worse on upper limb assessment with their paretic hand than their non-paretic hand.

The included articles utilized a wide variety of study designs, including randomized controlled trials, cohort studies, cross-sectional studies, and case series. For 2PD, the equipment used varied significantly between studies. Not all studies provided descriptions of their exact methodology for their reported measures. Previous reviews of upper limb assessments in children with HCP have reported a lack of standardization on methods collection, analysis, or reporting of measurements [31,34]. The protocol for the AHA is standardized, but many studies failed to adhere to the standardized protocol or data format, thereby making comparisons across studies difficult.

Grip strength was the main kinetic measurement identified in the included studies. The included articles were primarily from cross-sectional studies and longitudinal study designs. Measurements were typically made using purely mechanical devices rather than load cells. In general, the paretic side performed worse than the non-paretic hand. This could be due to neuromuscular abnormalities such as the substantially increased sarcomere lengths in spastic wrist muscles [138]. Muscle fiber force generation would suffer with increased sarcomere length. Additionally, infiltration of the muscle with collagen fibers and fat may decrease force-producing capabilities. The infiltration has been associated with a reduced number of muscle satellite cells in individuals with CP [139]. This muscle weakness may also have neurological origins. Xu et al. reported larger EMG signals in the non-paretic wrist muscles than those of the weaker paretic hand and excessive coactivation of the flexors and extensors in the paretic hand which results in reduced net force [140]. Limited activation of agonists and involuntary activation of antagonists could both contribute to observed weakness.

Further studies, particularly involving EMG, are needed to better determine the origin of the profound hand weakness. Presumably, force deficits are even greater for wrist and finger extension, but relatively few studies have examined finger extensor strength, despite the prevalence of finger extensor weakness in children with CP [134]. Only a few articles used load cells to quantify individual fingertip forces [134,141,142]. Potential issues such as finger force individuation or differences in relative weakness across fingers could impact overall grip strength.

Most of the reviewed kinematic analyses focused on active or passive range of motion of the wrist. The included articles were primarily from cross-sectional studies and longitudinal study designs. Results for PROM of the paretic wrist tended to show normal ranges, like those of the non-paretic hand or TD children. The typical PROM and the lack of contractures in the evaluated children may be explained by several factors. Contractures and reduced PROM generally develop over time; four of these articles had participant groups with mean ages of 5 [143], 9 [144,145], and 13 [62]. Due to their younger ages, many of these participants likely had not yet developed significant contractures. Additionally, three of these studies focused on children with mild to moderate hand dysfunction (MACS I, II and III or Zancolli I, IIA, and IIB [62,144,145]. PROM reduction may be greater in children with HCP with greater hand impairment who are less likely to use their paretic hand. Also, children who had undergone hand surgery or botulinum toxin injections in the previous six months were explicitly excluded in two studies, potentially excluding participants who previously had greatly reduced PROM or significant contractures [62,144]. The AROM of the paretic wrist, in contrast, could be quite limited. Greater wrist AROM was associated with higher function (MACS or Zancolli scale) [143,146,147]. Examination of finger and thumb movement was quite limited. Future studies could report on the PROM and/or AROM of the various finger joints since these values may vary from the wrist.

Two-point discrimination was the most common sensory perception measure identified. It was evaluated in 24 articles, including both cross-sectional studies and longitudinal interventions. Comparison of study results across these articles, however, was hampered by the range of equipment and techniques employed to measure 2PD. For example, some studies using moving 2PD where the two points are moved continuously closer to each other across the skin, while other studies used static 2PD where the two points are placed in multiple fixed locations.

In general, studies reported that children with HCP frequently have impaired 2PD ability compared to TD children. Unlike the strength values, however, the 2PD values do not appear to vary much with age for either the paretic or non-paretic hand. It should be noted that participants 6–8 years old may give relatively unreliable results (35% of subjects) and those less than 6 years old may give very unreliable results (44%) [64,77,91]; therefore, 2PD tests may not be appropriate for young children. Future studies would also benefit from a more standardized method of collecting 2PD.

Clinical evaluation of task performance was the most widely reported measure of hand function in children with HCP. These measures were reported primarily in articles based on cross-sectional study designs and longitudinal interventions. Since the BBT uses standardized materials and methods, aggregation of this data was much simpler. General trends showed that older children with HCP typically performed better on the tasks with their paretic hand than younger children with HCP, although scores continued to lag behind those of the non-paretic hand or the hands of TD children.

In contrast to the strength measurements, the deficits of the paretic hand relative to scores of the TD hand tend to decrease with age. Part of the reduction may be attributable to a ceiling effect for time to perform a task or the number of objects that can be moved. The score increases seen with age for these measures may result in part from improved motor control of the arm and the rest of the body rather than improved control of the hand. Interestingly, while the aggregated data largely showed deficits in the paretic hand in BBT scores in comparison with the non-paretic hand, some investigators have reported no difference between performance with the two hands [94]. Further studies examining BBT scores across various ages and skill levels for children with HCP would help to better establish performance outcomes. Other measures may better capture fine manual dexterity. The 9-hole peg test and modified 9-hole peg test focus more specifically on the hand by employing smaller boards that do not require extensive reaching away from the body.

While the review focused on measures that have been shown to have good reliability when aggregating data from different studies (e.g., BBT and grip strength), various techniques may have been used by different investigators. As this was a scoping review, there was no critical appraisal of the included studies. As quality appraisal was not performed, some of the data sets included may be less reliable than others. This risk is mitigated in part by using many common measures with high inter-rater and intra-rater reliability. This is especially true for clinical assessments and functional evaluations. Also, the presentation of aggregated data helps to identify potential outliers.

Unfortunately, it was not possible to include studies written in languages other than English. The exclusion of these articles may limit the applicability of the results in regions where scientific literature is not generally published in English. Most articles identified by the searches, however, were available in English. Only 22 of the 1536 articles were not available in English. Future work would ideally include all articles regardless of language.

2.5 Conclusions

Despite the profound functional role of the hand, sensorimotor characteristics of it have been studied much less than other parts of the upper limb or the lower limbs in children with HCP. The specific impairment mechanisms of the hand are not completely understood, thereby limiting the capacity to create targeted therapies or therapy programs. Data were especially limited for kinematics and kinetics of individual fingers and the thumb. These data are needed to improve therapies and treatments for life-long hand impairment seen in those with CP.

CHAPTER 3: PEDIATRIC VOLUNTARY MUSCLE ACTIVATION CAPACITY AND COACTIVATION IN THE HAND

3.1 Introduction

As children grow and develop, their neuromuscular control strategies must adapt to changes in muscle and bone size. Hand strength, as measured by lateral or key pinch [8–13], palmar pinch [9–11], tip pinch [9–13], tripod or three-chuck pinch [9,12], grip force [9,10,12–14], increases with age for children of both genders from 5 to 18 years of age. Previous studies have noted a positive relationship between hand strength measures and hand anthropometrics as well as between hand strength and BMI [9,10,13]. Since these studies compared children of different age groups, it is hard to separate the effects of these differences from the effect of age. Studies in adults of both sexes though have also found correlations between height, weight, and anthropometric measures of the arm and hand with grip strength and the strength of various types of pinches, indicating that these differences in size may still affect hand strength even when age is controlled for [148–150].

Both handedness and sex could also impact hand strength. Previous studies, however, have failed to find a significant difference in grip strength between the dominant and non-dominant hands in children [9–11,14]. Reported pinch strength results were more mixed. Some studies did not detect a difference in pinch strength between the hands [9–11], while others observed that the dominant hand produced greater pinch force [10,12]. While handedness may not affect hand strength in children, adult subjects exhibited a greater lateral, key, tip, and three-jaw chuck pinch force in the dominant hand compared to the non-dominant hand [150]. Sex-related differences in grip and pinch strength in children vary more widely than hand-related differences. For some studies male subjects had greater hand strength across all ages [9,11,14,151], while other studies only detected greater force production in male subjects in a subset of ages [10,12]. In adult subjects, males show greater grip, tip pinch, key pinch, and palmar pinch forces than females [149,150].

Two potential sources of these age-related changes in hand or finger strength, are changes in voluntary muscle activation capacity and in neuromuscular coordination, particularly coactivation. Voluntary activation capacity (VAC) is a measure of how much of the existing muscle is being activated during maximal voluntary contraction. While few studies have measured VAC in children's upper limb muscles, results have indicated that children, especially pre-pubescent children, have lower VAC than adults. Boys had a significantly lower VAC of the adductor pollicis when compared to men [15]. Male and female pre-pubescent children had reduced VAC of the biceps brachii and brachialis during elbow flexion when compared to post-pubescent children of the same sex [16].

Coactivation is a measure of how much of the antagonist muscle is activated during voluntary activation of the agonist muscle. While some level of coactivation occurs in most movements, the level can vary widely depending on the muscle or the movement itself [17]. A recent systematic review of 25 studies found that most of these studies indicated greater coactivation in children although less than half of these studies reached statistical significance. Studies of multi-joint tasks were more likely to find greater coactivation in children than studies looking at only single joint tasks. Of the 25 studies examined, only three looked at coactivation in the upper limb, including at the elbow and shoulder [17–19].

Given the scant amount of pediatric upper limb data and the vital role of the hand in daily functions, this study aimed to examine muscle activation of the middle finger in typically developing children during isometric force production. We hypothesized that we would not find a statistically significant difference in the VAC or coactivation between the dominant and non-dominant hands since hand strength measures often did not vary between the hands in children [9,11,14]. We also did not anticipate any differences in VAC or coactivation between flexion and extension. Previous studies found little to no difference in coactivation or VAC between the finger flexors and extensors in control adult subjects [26,27].

3.2 Methods

3.2.1 Participants

Typically developing children between the ages of 8-14 years were recruited for this study. Exclusion criteria included any neurological or orthopedic conditions or injuries that affected the hand. Participants were required to provide written assent and parents were required to provide written consent for their child to participate in this study. The protocol was reviewed and approved by the Institutional Review Board of North Carolina State University.

3.2.2 Experimental Protocol

Subjects were seated in a chair with their forearm supported and the elbow flexed at roughly 90º. The thumb and wrist were immobilized with a removable brace (Sammons-Preston, Bolingbrook, IL). Velcro straps were used to lightly secure the forearm to prevent subjects from lifting or twisting the forearm during experimentation. Once the participant was comfortably seated, the locations of the middle finger compartments of the FDS and the EDC muscles were identified through electrical stimulation with a bar electrode (DS7A, Digitimer, Ltd., Letchworth Garden City, UK) After initial palpation, electrode position was adjusted until a single current pulse produced isolated middle finger flexion or extension. Two flexible adhesive electrodes (Valuetrode 1.25” diameter, Axelgaard Fallbrook, CA) were then placed at the stimulation sites located with the bar electrode. Surface electromyography (EMG) electrodes were also secured to the forearm over the EDC and FDS muscles to record muscular activity (Trigno Mini Sensor, Delsys Inc., Natick, MA).

The tip of the middle finger was then connected to a 6 degree-of-freedom (DOF) load cell (Mini40 ATI Automation Apex, NC) affixed to a custom magnetic base that allowed adjustment in position and orientation to accommodate differently sized hands. The fingertip was wrapped in self-adhesive wrap and then encased in a layer of softened thermoplastic material into which screws were inserted prior to the material hardening (**Fig. 3.1**). The screws rigidly connected the finger to the load cell. The load cell was then adjusted in position and

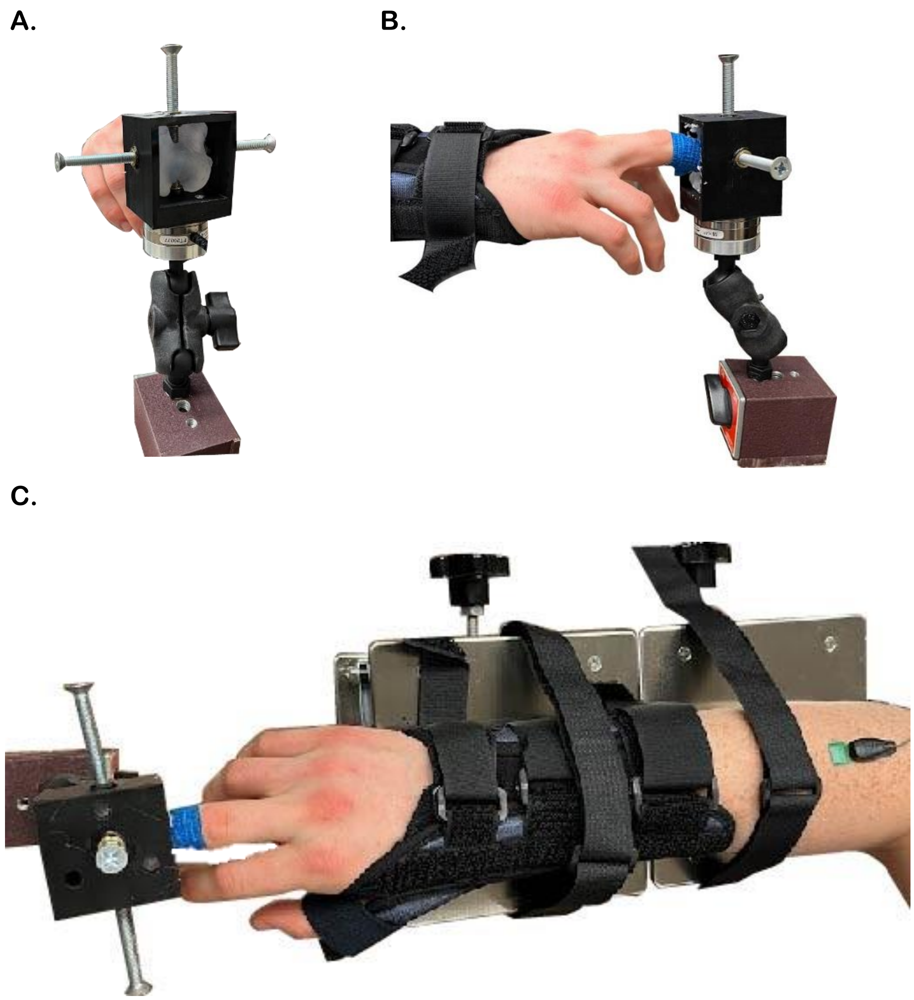

Figure 3.1: Load Cell and Finger Vice Set Up. Depiction of the setup used to measure fingertip force during the experiment. A) Front view of the custom finger vice. B) Side view of the custom finger vice. C) Top view of the full arm supported by adjustable bases while the finger is secured in the vice.

orientation such that the finger was kept in a posture with roughly 0˚ of flexion at the metacarpophalangeal (MCP) joint, 25˚ of flexion at the proximal interphalangeal (PIP) joint, and 10˚ of flexion at the distal interphalangeal (DIP) joint.

Once positioned, participants were then asked to produce their maximum voluntary force (MVF) with their middle finger in either flexion or extension, in accordance with methodology employed in a prior study [27]. Continuous force feedback in the intended direction was provided through a on a custom graphical user interface (GUI) (LabView, National Instruments, Austin, TX). Three MVFs were recorded in both the flexion and extension directions.

After recording the MVF, we then examined voluntary muscle activation. The participant was instructed to first produce 40% of their previously recorded MVF in the indicated direction; force feedback was again provided through the GUI. As the subject maintained the target force, a stimulation train (five rectangular 500-μs current pulses at 400V with a 10 ms rest period in between) at 100 Hz was applied to either the FDS during flexion or the EDC during extension [27]. Participants were instructed to maintain the desired force throughout the stimulation period. Stimulation current amplitude was gradually increased over successive trials until the force no longer increased with increased current or the participant expressed discomfort. Once the peak stimulation current was determined, three trials were repeated with this current level. This same procedure was then repeated for a target force of 100% of MVF. Again, visual feedback was provided to encourage maximal contraction. This procedure was repeated such that both force directions (flexion and extension) were examined for both hands (dominant and non-dominant). Flexion trials were completed first since it was more intuitive for the subjects than extension. Dominant and non-dominant hands were tested in a randomized order.

3.2.3 Data Analysis

Force data were first lowpass filtered at 20 Hz with a fourth-order Butterworth filter to remove noise. The MVF was determined by the largest average value observed over a 250-ms window slid across the entire trial. An average was used to reduce the effect of any instantaneous peaks or falls in the voluntary force. At high force outputs, participants might struggle to maintain a steady force and would waver between slightly above or slightly below a given force. An average over a small window would provide a more realistic estimation of the level of force they could sustain rather than capturing an intermittent peak. To determine the maximal stimulated force (MSF), the peak value recorded in the normal direction during the stimulation was calculated. The peak value was used because the stimulation produced a sudden and symmetrical peak. An average value would not reflect the full increase in force induced by stimulation.

The VAC in the instructed direction (VAC_i) was then calculated as the ratio of the MVF in the intended direction to the MSF in the intended direction during the maximal force trials (Eq. 3.1). VAC was calculated for each individual trial and averaged over three trials, yielding a value between 0% (no voluntary activation) and 100% (full voluntary activation).

$$VAC_i = \frac{MVF}{MSF} \cdot 100\% \qquad (3.1)$$

To focus more closely on activation of individual muscles, the VAC was also computed based on the three-dimensional force vector produced by the muscle of interest. This force vector was obtained from the change in force elicited by the stimulation during the 40% MVF trial (Eqs. 3.2-3.4). This directional vector ($\vec{v}_{ds} = \vec{v}_{F_{stim}\ 40\%\ MVC} - \vec{v}_{40\%\ F_{pre-stim}\ 40\%\ MVC}$) was then normalized into a unit vector representing the direction of the change in force induced by stimulation ($\hat{v}_{ds}$). The dot product between $\hat{v}_{ds}$ and the three-dimensional vectors of the MVF ($\vec{v}_{F_{pre-stim_{100\%\ MVC}}}$) and MSF ($\vec{v}_{F_{stim_{100\%\ MVC}}}$) values were then computed to isolate the activation of the muscle of interest. Voluntary activation capacity in the direction of the stimulation (VAC_{ds}) was then computed from these values as follows:

$$d_{MVF} = \vec{v}_{F_{pre-stim_{100\%\ MVC}}} \cdot \hat{v}_{ds} \tag{3.2}$$

$$d_{MSF} = \vec{v}_{F_{stim_{100\%\ MVC}}} \cdot \hat{v}_{ds} \tag{3.3}$$

$$VAC_{ds} = \frac{d_{MVF}}{d_{MSF}} \cdot 100\% \tag{3.4}$$

Calculations were once again completed for each trial and then averaged over three trials. VAC_{ds} values were also capped at 100%.

EMG signals were examined to determine coactivation during voluntary force production. Surface EMG data were bandpass filtered between 20 and 450 Hz prior to being sampled at 2 kHz (Trigno, Delsys). The mean signal value was subtracted from each signal to ensure it was centered at 0V prior to lowpass filtering at 400 Hz with a fourth-order Butterworth filter. The resulting signal was then rectified and lowpass filtered with a fourth-order Butterworth filter with a 20-Hz cut-off frequency to produce an envelope of the EMG amplitude. The envelope was then normalized by the absolute peak envelope value of that muscle across the entire experiment.

Coactivation was computed for flexion trials with FDS as the agonist and for extension trials with EDC as the agonist for 40% MVF and 100% MVF trials. The period prior to stimulation was used for the 40% MVF trials. Mean EMG values for each muscle were determined across a one-second window centered in the period of constant force production. Coactivation values across trials for the same condition were averaged to produce a single set of data for each subject. While there are several methods for calculating coactivation, we chose a method that has been shown to produce more reliable results than methods relying on simply dividing the antagonist signal by the agonist signal [152]. Percent coactivation was calculated as a value between 200% (entirely antagonist activation) and 0% (no coactivation – agonist activation only) according to:

$$\frac{2(EMG_{ANT})}{(EMG_{ANT} + EMG_{AG})} \cdot 100\% \tag{3.5}$$

EMG_{ANT}: normalized activation of the antagonist muscle

EMG_{AG}: normalized activation of the agonist muscle

Statistical analyses were performed to test the stated hypotheses. Data were first tested for normality with a Shapiro-Wilkes test. If the data distribution satisfied the normality assumption, a repeated measures analysis of variance (ANOVA) was employed to examine the fixed effects of the hand (dominant vs. non-dominant), direction (flexion vs. extension), and any interactions between the two as well as the random effects of subjects on VAC and on voluntary coactivation using JMP Pro 16 statistical software (SAS, Cary, NC). For data sets that did not meet the normality criteria, a non-parametric Kruskal-Wallis test was performed. A Pearson's correlation was calculated for both the VAC versus participant age and coactivation versus participant age.

3.3 Results

A total of ten children (5 females and 5 males) participated in this study (**Table 3.1**). Participant ages ranged from 8 to 14 years of age with an average of 11.6 years old. Based on self-reporting, all subjects were right-handed.

We examined the impact of hand and direction on the voluntary activation capacity in the instructed (VAC_i) direction. Overall, average activation levels were high, ranging from 85%-95% of full activation (**Fig. 3.2**). As the null-hypothesis that the distribution of VAC_i in

Table 3.1: Study Participant Demographics

Participants	Sex	Age (years)
TD01	M	14
TD02	F	14
TD03	M	9
TD04	M	14
TD05	F	8
TD06	F	12
TD07	M	8
TD08	F	13
TD09	M	10
TD10	F	9
Mean ± SD	**5 F: 5M**	**11.1 ± 2.6**

the dominant FDS was normal was rejected according to a Shapiro-Wilkes test (W= 0.80, $p<0.05$), a Kruskal-Wallis test was performed. Neither hand (dominant vs. non-dominant) nor direction (flexion vs. extension) had a significant effect on the VAC_i ($p > 0.1$, **Fig. 3.2**), although the activation mean was slightly greater for the EDC than the FDS - dominant EDC: 92.1% (95% CI: 88.9-95.4%), non-dominant EDC: 92.6% (95% CI: 88.9-96.3%), dominant FDS: 91.5% (95% CI: 88.4-94.6%), non-dominant FDS: 90.5% (95% CI: 87.1-93.8%). No significant Pearson's correlation was found between VAC_i and age.

A Kruskal-Wallis test was also performed after finding evidence of non-normality for the distribution of VAC_{ds} in the dominant FDS (W= 0.77, $p<0.05$) and the non-dominant EDC (W= 0.70, $p<0.001$) according to a Shapiro-Wilkes test. Similarly, the VAC in the three-dimensional direction of the stimulation (VAC_{ds}) did not vary significantly with either hand or direction ($p > 0.1$) according to the results of a repeated measures ANOVA (**Fig. 3.2**). VAC_{ds} values were slightly lower than VAC_i activations - dominant EDC: 87.1% (95% CI: 82.1-92%), non-dominant EDC: 88.6% (95% CI: 76.2-101.1%), dominant FDS: 88.8% (95% CI: 83.4-94.3%), non-dominant FDS: 89.3% (95% CI: 84.9-93.6%). No significant Pearson's correlation was found between subject age and either measure of VAC. According to a

Kruskal-Wallis test, no significant difference between the two methods of calculating VAC (VAC_i vs. VAC_{ds}) was detected (p>0.05). Data from subject TD05 were excluded from the analyses for VAC_{ds} in the dominant hand due to inconsistencies in stimulation direction at 40% MVC across trials.

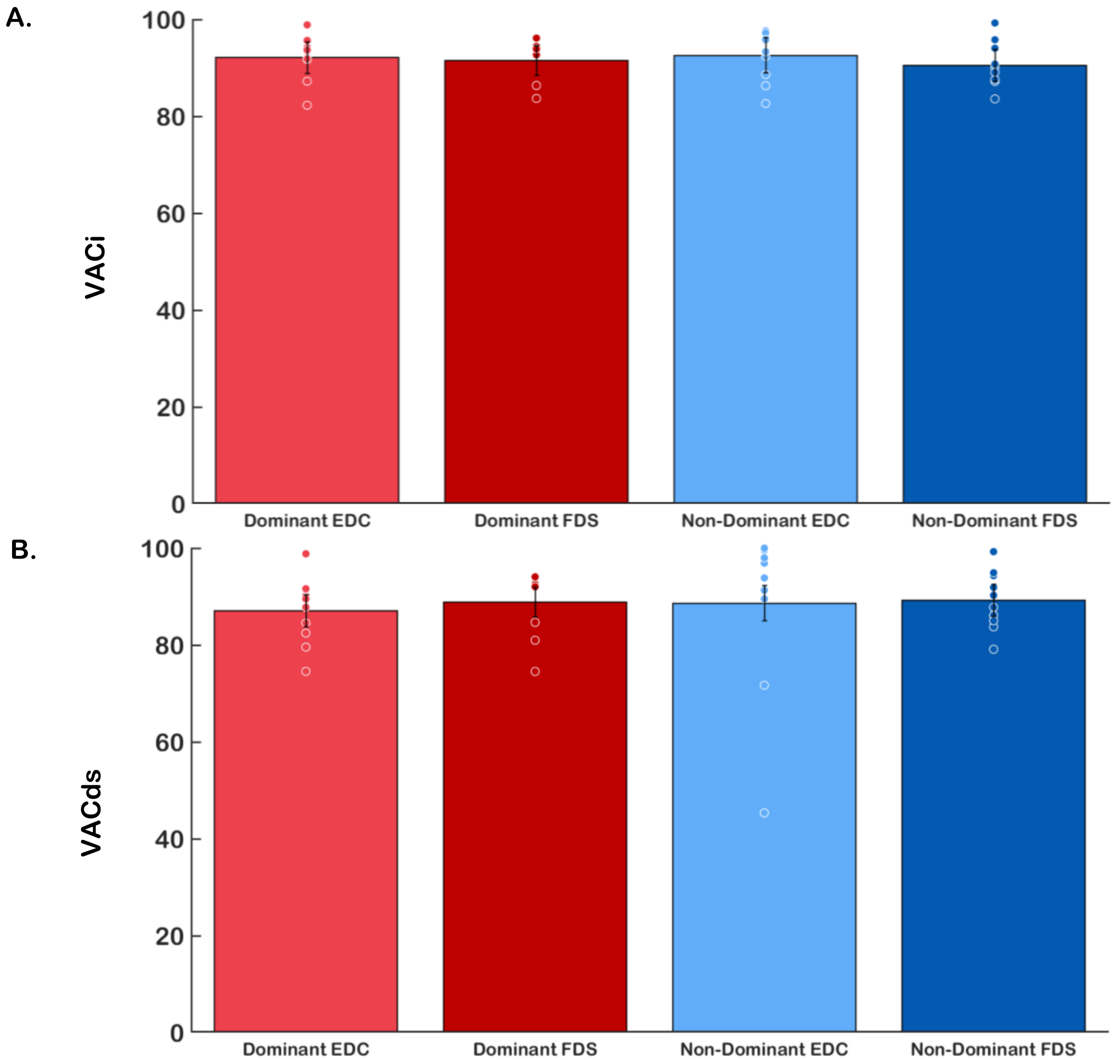

Figure 3.2. Average Voluntary Activation Capacity During Maximal Middle Finger Force. Voluntary activation capacity was calculated in the direction of the intended finger force (A) and along the change in the finger force vector resulting from stimulation (B) during middle finger flexion and extension for both the dominant and non-dominant hands. The bar graph represents the mean value, while individual data points are overlayed. (Light Red: non-dominant extension; Dark Red: dominant hand extension; Light Blue: non-dominant hand flexion; Dark Blue: dominant hand flexion), Error bars represent 95% confidence intervals.

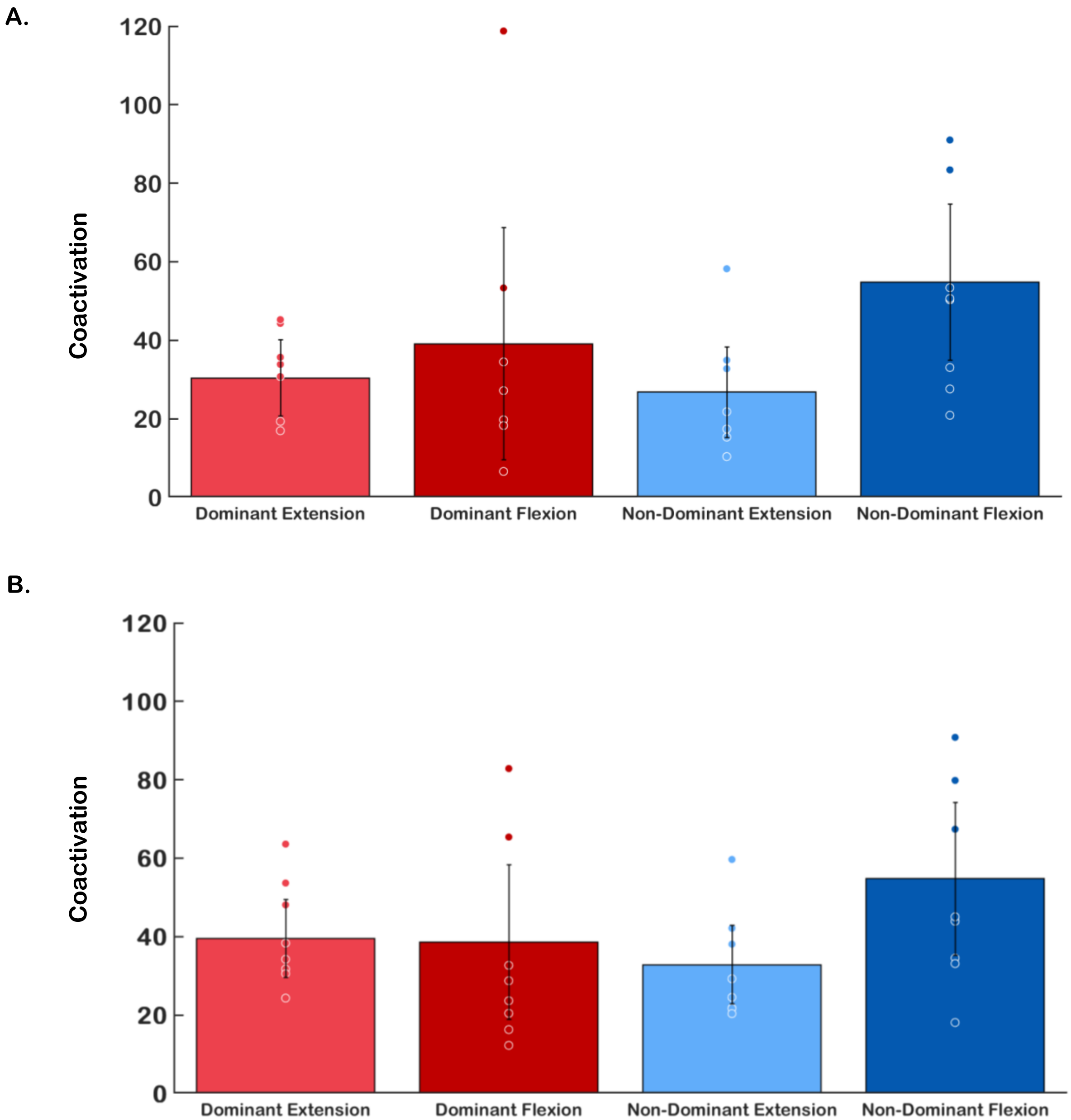

Figure 3.3. Average Voluntary Coactivation During Maximal Middle Finger Force. Coactivation was calculated in the flexor digitorum superficialis and the extensor digitorum communis muscles during 40% of maximal voluntary activation (A) and maximal voluntary activation (B) of the middle finger in the flexion and extension directions in both hands. The bar graph represents the mean value, while individual data points are overlayed. (Light Red: non-dominant extension; Dark Red: dominant hand extension; Light Blue: non-dominant hand flexion; Dark Blue: dominant hand flexion), Error bars represent 95% confidence intervals.

In addition to looking at VAC, we also calculated coactivation during voluntary middle finger flexion and extension at both 40% of maximal voluntary force and 100% of maximal voluntary force (**Fig. 3.3**). At 40% of the maximal voluntary force, coactivation rates were low, but varied widely - dominant extension: 30.4% (95% CI: 20.7-40.1%), non-dominant extension: 26.8% (95% CI: 15.3-38.3%), dominant flexion: 41.5% (95% CI: 11.9-71.0%), non-dominant flexion: 54.9% (95% CI: 35.0-74.7%). According to the results of a repeated measures ANOVA, direction (flexion vs. extension) had a significant effect on coactivation ($p < 0.05$); in contrast, neither hand (dominant vs. non-dominant) nor the hand-direction interaction ($p > 0.1$) had a significant effect on coactivation. Due to equipment malfunction we were unable to capture EMG data from the dominant hand of subject TD01 during the 40% MVC trials.

At the full maximal voluntary force, coactivation rates were like those observed at 40% MVC - dominant extension: 39.4% (95% CI: 29.5-49.4%), non-dominant extension: 32.8% (95% CI: 22.9-42.8%), dominant flexion: 38.6% (95% CI: 18.9-58.4%), and non-dominant flexion: 54.7% (95% CI: 35.2-74.2%). The repeated measures ANOVA revealed that none of the independent variables had a significant effect on the voluntary coactivation during maximal voluntary contraction ($p > 0.10$). No significant correlation was found between voluntary coactivation at maximal voluntary contraction and age. Due to equipment malfunction we were unable to capture EMG data from subject TD07.

3.4 Discussion

Like prior studies of upper extremity muscle activation in children, we observed high levels of voluntary activation. The average VAC_i was greater than 90% for both muscles in both hands, and the average VAC_{ds} was greater than 87% across all conditions. A prior study reported similar a voluntary activation value of 85% for the adductor pollicis thumb muscle in boys of a similar age (11.6 ± 0.1 years) to the participants of this study. The VAC of the biceps brachii and brachialis during maximal forearm flexion were found to be 73% for pre-pubescent males (9.8 ± 0.5 years old) and 67% for pre-pubescent females (9.8 ± 0.6 years old). These lower values may arise from larger, more proximal muscles being tested or from the relatively younger age of the participants, although we did not see an influence of age on VAC in our study. We also did not see any significant effects of hand (dominant vs. non-dominant) or force direction (flexion vs. extension) on the VAC in our participants.

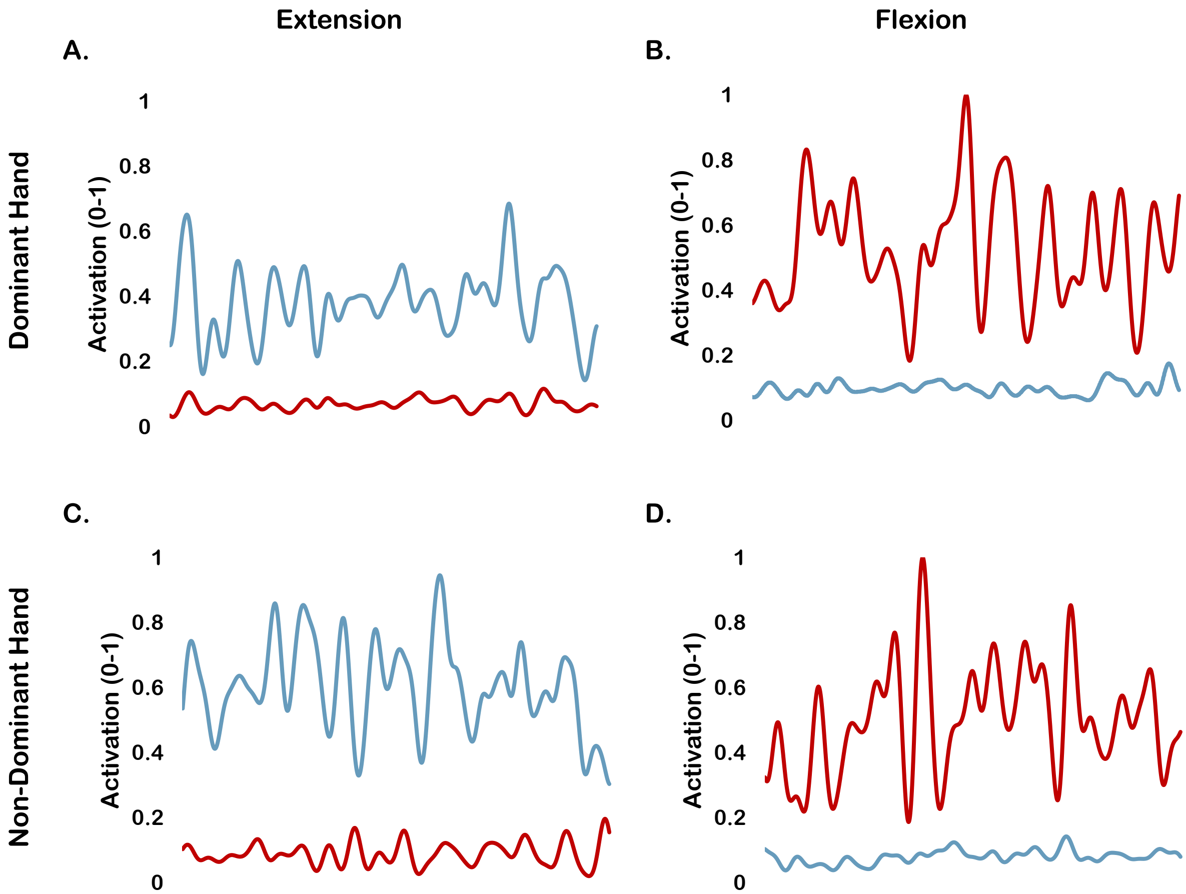

Figure 3.4. Representative EMG Trace. Electromyography (EMG) one-second samples from single maximal contractions. A) MVC trial of the dominant EDC. B) MVC trial of the dominant FDS. C) MVC trial of the non-dominant EDC. D) MVC trial of the non-dominant FDS. Data taken from subject TD14. (Blue: EDC, Red: FDS).

Coactivation during voluntary force production was observed during generation of fingertip force in both flexion and extension. Average values ranged from roughly 25%-55%. We only saw a significant difference in coactivation between flexion and extension at 40% of the maximal force. We did not see any significant differences in coactivation between the dominant and non-dominant hand or between flexion and extension at 100% of the maximal force. While we did see an increase in coactivation with increased force, the difference was not statistically significant. Coactivation tended to be greater during flexion, but the variance was so great that differences were not significant. At 40% of the MVC, coactivation ranged from 6.6 to 118.8%, while at 100% MVC, coactivation ranged from 12.3 to 90.8%. Since each subject's coactivation values are the averages from three different trials, it is less likely that these values are from a single unrepresentative or abnormal trial.

These differences could be due to natural differences in muscles of the elbow and those of the hand. Sensor placement may also explain these differences in coactivation values. During our study, the EMG electrodes could not be placed in the center of the muscle belly due to the reduced arm size of pediatric subjects and the placement of the stimulation electrode. This could also explain differences in normalized activation between the hands since electrodes were placed separately on each arm.

Very few studies have reported coactivation values for upper limb muscles in healthy children. Studies of the elbow muscles reported lower coactivation values than we measured in the FDS and EDC muscles. The average coactivation of the triceps brachii during maximal elbow flexion was found to be 59 ± 44% boys (9.6 ± 1.6 years) [19] and 30 ± 12% in girls (9.1 ± 1.4 years) [18]. Coactivation of the biceps brachii during elbow extension was 9 ± 6% in boys [19]. Our values were like those seen the triceps of both male and female subjects, but our values were generally greater than those seen in the biceps of male subjects. Some of these differences could be due to the different calculation methods used by these studies. Coactivation was reported as the ratio of a given muscle's activation when acting as the antagonist to the activation of the same muscle when it is acting as an agonist during a maximal contraction rather than comparing the activations of two different muscles during the same motion. Coactivation of the triceps brachii was calculated as the EMG amplitude of the triceps during elbow flexion divided by its EMG amplitude during elbow extension, while coactivation of the biceps brachii was calculated as the EMG amplitude of the biceps during elbow extension divided by its EMG amplitude during elbow flexion [18,19].

The generalizability of the results of our study may have been limited by several factors, especially with a smaller sample size. First stimulation may not have been at supramaximal levels as we made sure not to exceed the individual comfort levels of each participant. Since the stimulation was a very novel sensation, younger children especially may have been reticent to experience higher currents. This may have contributed to the lack of an impact of age on maximum voluntary activation in our study; a prior study did report greater VAC in pubescent children than pre-pubescent children [16]. Still, we did observe substantial stimulation peaks at 40% MVC and the same stimulation levels are expected to be even more excitatory at 100% MVC due to the corresponding muscle shift closer to the stimulating electrodes. The lack of influence of age may also have resulted from the relatively low number of subjects at different ages. Finally, we only provided feedback in the intended direction rather than all three dimensions of the fingertip force vector, as we anticipated that younger subjects would struggle to comprehend and respond to biofeedback in three dimensions. Thus, the shear forces created during each trial could vary widely as the finger vice ensured that the finger could not slip and subjects were not penalized for producing shear forces.

3.5 Conclusions

VAC values were similar across the dominant and non-dominant hands and between flexion and extension. The children seemed equally adept at activating FDS or EDC, although creation of the extension force seemed to require greater concentration and mental effort.

We did observe a wide variation in coactivations including one subject whose antagonist activation exceeded their agonist activation during dominant flexion. While these may have been due to the limitations in our study design, coactivation value may vary as children develop their motor control. The VAC and coactivation values we measured in typically developing children can serve as a basis for future comparisons to children with HCP, whom we expect will have lower VAC and increased coactivation.

CHAPTER 4: THE IMPACT OF FINGER LENGTH AND POSTURE ON MUSCLE ACTIVATION PATTERNS USING COMPUTER MODELING

4.1 Introduction

Children experience continuous reshaping of bone, muscle, and soft tissue as they develop. These physiological changes impact the performance of daily tasks. Additionally, the nervous system undergoes dramatic development and plasticity. For example, conduction velocity increases in both the ascending and descending corticospinal tracts as children age [5].

These changes are especially profound for the hand. Corticomuscular coherence for intrinsic hand muscles, such as the first dorsal interosseous and the abductor pollicis brevis, is greater in adults than children [5]. The morphology of the hand motor cortex itself also changes with age [6]. Accordingly, motor control appears to progress over time from the more proximal muscles to more distal muscles, as evidenced by improvements in accuracy and smoothness of upper limb movements with age [5,7]. When comparing rhythmic reaching tasks between children (5-10 years old) and adults, researchers found that motor control strategies did vary between children and adults with older children being more like adults. Adult subjects had the most optimal motor control strategy and had the least variability within their age group. Both the rhythm accuracy and motion smoothness increased distally with age from the upper arm to the forearm to the hand [7].

The nervous and musculoskeletal systems work together to produce movement and force. Hand strength, measured by the lateral or key pinch [8–13], palmar pinch [9–11], tip pinch [9–13], three-chuck pinch [9,12], or grip force [9,10,12–14], increases with age for children of both sexes. These changes could be due in part to age-related increases in muscle cross sectional area and hand size, the latter of which impacts moment arms for musculotendon forces and thus joint torque production [10,13]. Indeed, studies have found positive relationships between hand strength measures and hand size [9,10,13]. Changes in strength may also arise from alterations in neural activation. Conversely, changes in muscle and bone morphology may necessitate the use of different muscle activation patterns to achieve a desired task.

The goal of this study was to examine the impacts of changes in index finger size, muscle size, and posture on the muscle activation patterns needed to produce a maximal finger palmar pinch. In this study, we used a musculoskeletal model of the index finger to estimate the muscle activation patterns used to create the pinch force. The model was scaled according to hand bone length in children of different ages. Static optimization was used to calculate the muscle activations required to produce the desired force. We hypothesized that the relative muscle activation levels would change with age and to a different extent for each muscle.

4.2 Methods

Table 4.1: Scale Factors to Create Pediatric Index Finger Models [13].

Age (years)	Male Scale Factor	Female Scale Factor	Male Fingertip Force (N)	Female Fingertip Force (N)
6	0.715	0.693	13.734	12.753
7	0.754	0.726	15.696	13.2435
8	0.782	0.759	17.658	13.734
9	0.820	0.793	17.658	16.677
10	0.831	0.843	19.62	17.1675

We first created 10 pediatric hand models in OpenSim 3.3 based on anthropometric data of male and female children aged 6 to 10 years [13,28,29]. We used static optimization to estimate the muscle activations required during a maximal palmar index finger press in two different finger postures. Target index finger forces were half of the average tip pinch force [13]. Previous research has shown that the thumb and index finger produce equal and opposite forces during tip pinch [153]. The calculated activations were then put into a forward model and the resulting fingertip forces were compared to the desired forces. Fingertip forces were measured via the force between a small sphere rigidly attached to the most distal index phalanx and a surrounding hollow spherical contact mesh [28].

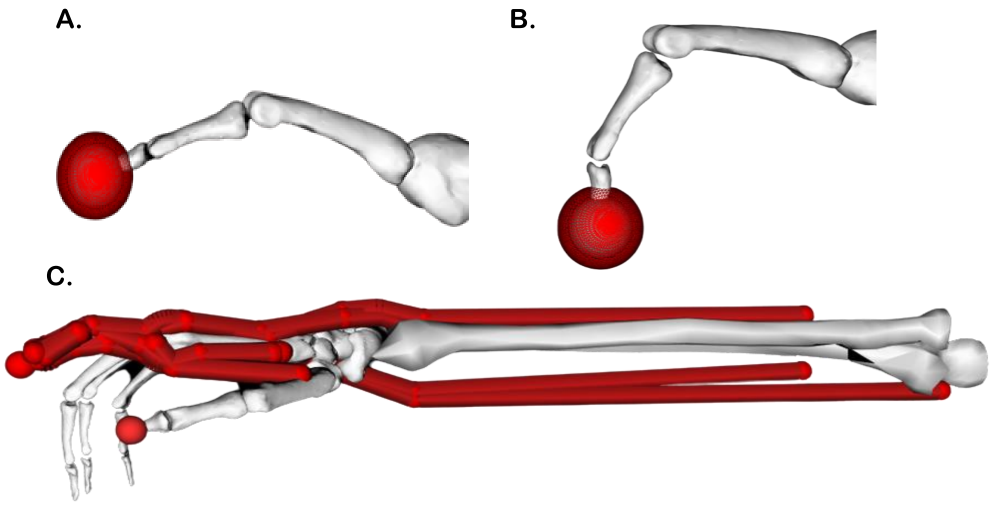

Figure 4.1. Full Index Finger Model in Both Finger Postures. The index finger of the model in posture 1 (A) and posture 2 (B). C) The full OpenSim model with the relevant muscles. The outer contact sphere used to measure fingertip force can be seen on the distal most index finger phalanx.

To create the models, we utilized an existing OpenSim 3.3 index finger model (**Fig. 4.1**) comprised of eight muscle compartments: flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), the medial and lateral heads of the first dorsal interosseous (FDI m and FDI l, respectively), extensor digitorum communis (EDC), extensor indicis (EI), and the first lumbrical (LUM) [28,29]. Literature values of the average index finger lengths for male and female children aged 6 to 10-years-old (n = 461) were used to uniformly scale the proximal, intermediate, and distal phalanges of the index finger [13]. This resulted in 10 pediatric index finger models representing male and female children from 6 to 10 years old. Scale factors (**Table 4.1**) were calculated as the ratio of the wrist to index fingertip for the pediatric subjects [13] relative to this length for the adult model [154]. The maximum isometric forces of each muscle were also adjusted by the same scale factor.

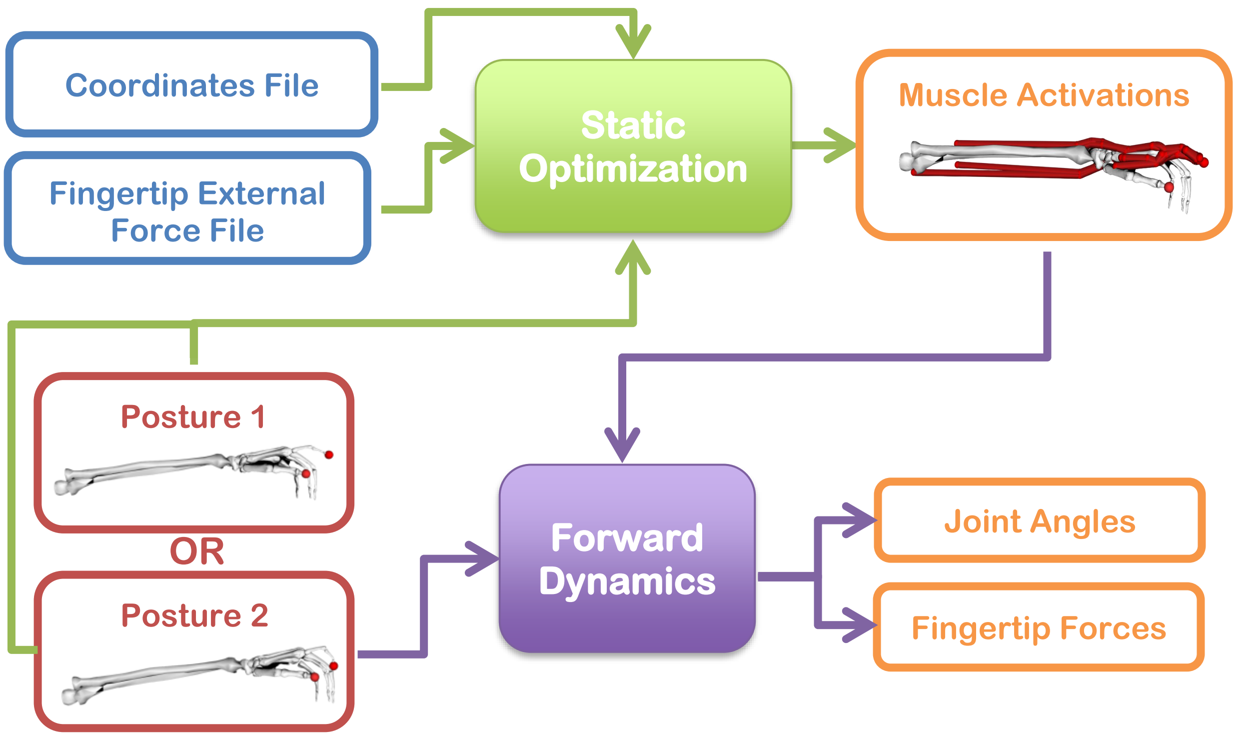

Figure 4.2. Simulation Workflow in OpenSim 3.3. (Blue: motion (.mot) files, Red: model (.osim) files, Orange: state (.sto) files, Green: static optimization workflow, Purple: forward dynamics workflow).

We then used the static optimization procedure within OpenSim to estimate the muscle activations required to create the maximal palmar index finger force, estimated from the palmer pinch data reported for 6 to10-year-old children [13]. Estimates were performed for two different finger postures involving the proximal and distal interphalangeal (PIP, DIP) joints: posture 1 (30˚,0˚) and posture 2 (60˚, 30˚). These postures were chosen to allow comparison with data collected with intramuscular electrodes in adults [155]. The calculated activations were then put into a forward dynamic simulation to verify that the estimated activations patterns created the desired isometric fingertip forces. These three-dimensional fingertip forces in the simulation were measured via the force between a small low-mass sphere rigidly attached to the distal phalanx of the index finger and a surrounding hollow spherical contact mesh [28]. A multiple linear regression was performed to compare the effects of both sex and age on the calculated muscle activations for each muscle. This was performed for each posture. We also ran a forward simulation with the youngest model's activations put into the oldest model and vice versa for both males and females.

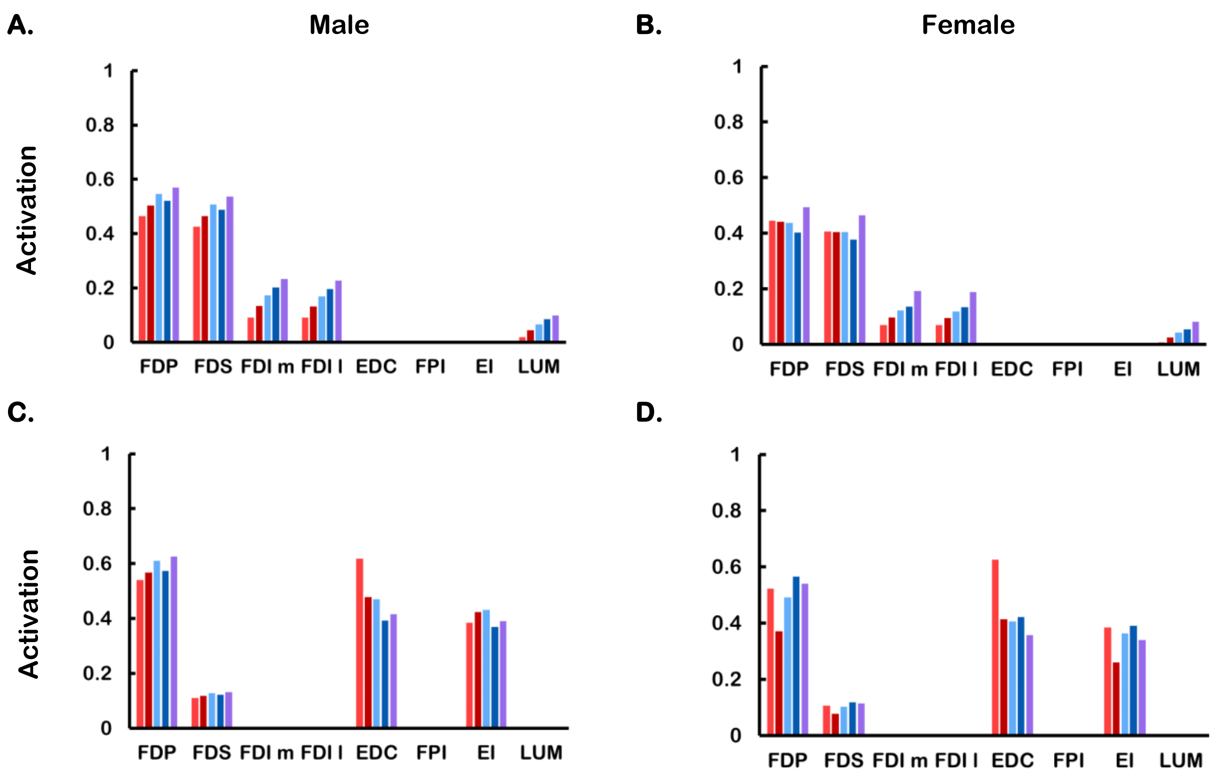

Figure 4.3. Muscle Activations Change with Age of Model and Finger Posture. Muscle activations calculated by static optimization during maximal index finger flexion. A) Male models in posture 1. B) Female models in posture 1. C) Male models in posture 2. D) Female models in posture 2. (6-year-old model: Light Red, 7-year-old model: Dark Red, 8-year-old model: Light Blue, 9-year-old model: Dark Blue, and Light Purple: 10-year-old model).

4.3 Results

The static optimization procedure produced an estimated muscle activation pattern for each model at both postures. The forward dynamics simulations performed with these estimated muscle activations generated fingertip forces that closely matched the desired values, with simulated force vectors lying within 4.7˚ of the desired force vectors in posture 1 and within 6.8˚ in posture 2. The calculated activations did maintain the desired postures during forward simulations. The MCP joint angles stayed within 0.0092˚ for posture 1 and within 0.032˚for posture 2. The PIP angle stayed within 0.078˚for posture 1 and 0.12˚ for posture 2, and the DIP angle stayed within 0.35˚ in posture 1 and within 0.33˚ in posture 2.

The estimated activation patterns were highly dependent upon posture. To create the desired palmar force in the extended posture (posture 1), FDP, FDS and FDI were the primary muscles activated; EDC, EI, and FPI activations were negligible. For the more flexed posture (posture 2), FDP remained at a similar level, but FDS dropped to less than half the activation in posture 1, EDC and EI activations increased from almost zero to more than 30% activation (**Fig. 4.3**). The LUM also decreased from posture 1 to posture 2.

For posture 1, a multiple regression showed that sex had a significant effect on activation level for all muscles ($p < 0.05$). Sex of the model was represented by differences in both model size and the target index fingertip force. The male finger models had greater activations than the female finger models for all muscles except EDC and EI. Age also had a significant effect for FDS, FDI m, FDI l, EDC, FPI, EI and the LUM (**Fig. 4.4**). The interaction between sex and age did not have a significant effect on any muscle ($p > 0.1$). Across both sexes, the LUM, FDI m, FDI l, and FPI had strongest correlations ($R^2 > 0.95$) with age followed by the EDC and EI ($R^2 > 0.86$) (**Tables 4.2 & 4.3**). Relative muscle activation increased with age. Qualitatively, the FDI m, FDI l, and LUM appear to be following a similar activation pattern that scales linearly with age for both sexes (**Fig. 4.3**), as evidenced by the similar slopes between age and activation for both sexes. The slopes for LUM, FDI m, and FDI l varied by only 10-20% between the males and females. For posture 2, multiple linear regression analysis on the combined male and female data set revealed a statistically significant relationship only between the EDC activation and age ($p < 0.01$) (**Fig. 4.4**). EDC activation tended to decrease with age, but this relationship was only significant for the male models. Qualitatively, the activation patterns do not vary much with age

(**Fig. 4.3**). When separated by sex, the female models had no significant relationships between activation and age, while the male models had significant correlations between activation and age for the FDP, FDS, EDC, EI, and LUM.

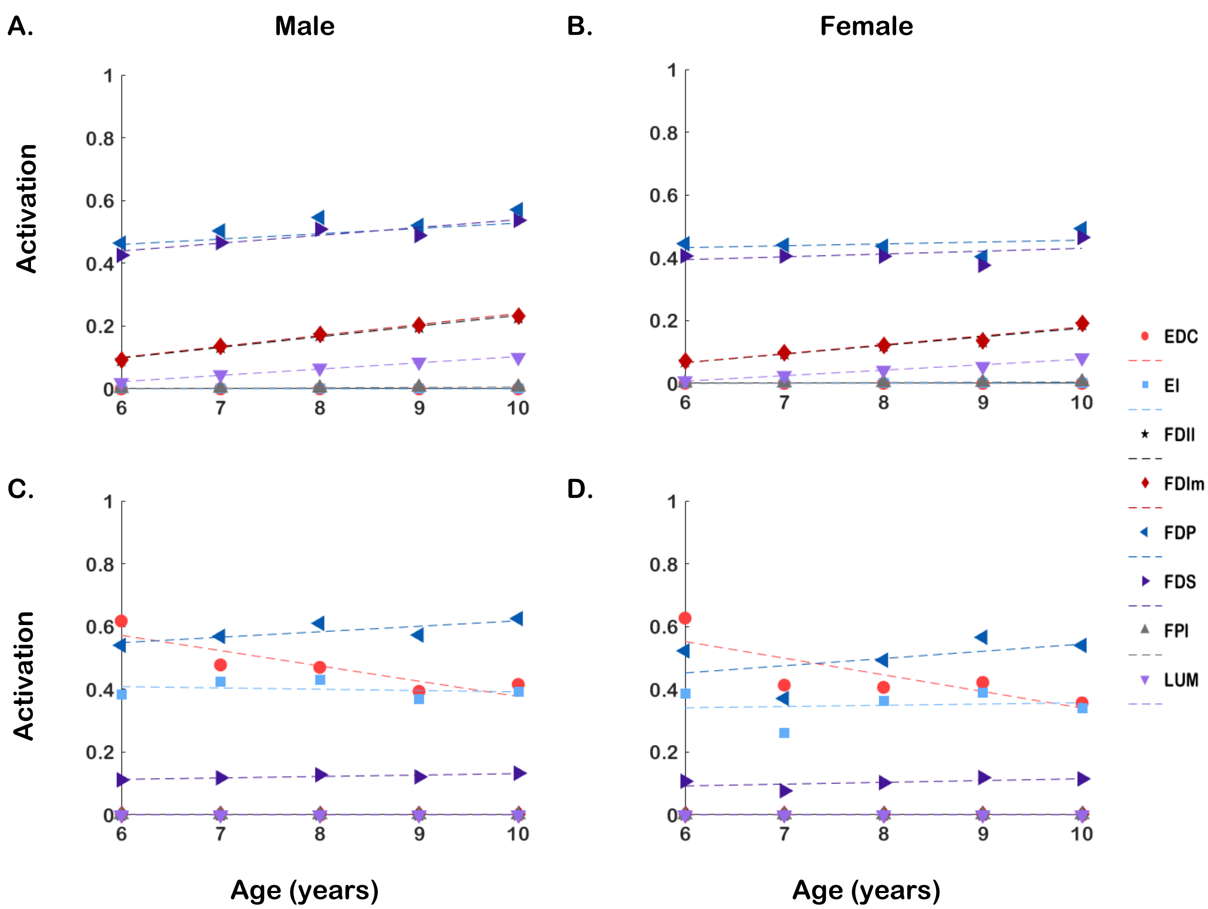

Figure 4.4 Correlations Between Muscle Activations and Age Vary with Sex and Posture. Calculated muscle activations vs. representative age of the model. A) Male models in posture 1. B) Female models in posture 1. C) Male models in posture 2. D) Female models in posture 2. (Dark Blue Left-Facing Triangle: FDP; Dark Purple Right-Racing Triangle: FDS, Dark Red Diamond: FDI m, Black Star: FDI l, Light Red Circle: EDC, Grey Upright Triangle: FPI, Light Blue Square: EI, and Light Purple Downward Triangle: LUM). Lines represent simple linear regression.

The slope between activation and age for the FDP was the same in male models in both postures ($p < 0.05$). The FDS slope decreased by 81.6% between posture 1 and posture 2. The magnitude of the slope for EDC and EI increased greatly from posture 1 to posture 2, but the slopes remained negative. The LUM slope decreased substantially in posture 2.

Table 4.2: Results of Linear Regression of Male Models.

	Posture 1			Posture 2		
Muscle	**R^2**	**Slope**	**p-value**	**R^2**	**Slope**	**p-value**
FDP	0.75	0.017	$p < 0.05$	0.65	0.017	$p < 0.01$
FDS	0.84	0.025	$p < 0.05$	0.76	0.0046	$p < 0.01$
FDI m	0.99	0.035	$p < 0.001$	0.71	$3x10^{-7}$	NS
FDI l	0.99	0.034	$p < 0.001$	0.72	$3x10^{-7}$	NS
EDC	0.92	$-4x10^{-6}$	$p < 0.05$	0.78	-0.049	$p < 0.05$
FPI	0.96	0.0013	$p < 0.05$	0.74	$1.3x10^{-6}$	NS
EI	0.86	$-5x10^{-6}$	$p < 0.05$	0.063	-0.0042	$p < 0.05$
LUM	0.99	0.020	$p < 0.001$	0.78	$4.9x10^{-7}$	$p < 0.05$

Table 4.3: Results of Linear Regression of Female Models.

	Posture 1			Posture 2		
Muscle	**R^2**	**Slope**	**p-value**	**R^2**	**Slope**	**p-value**
FDP	0.084	0.0059	$p < 0.05$	0.23	0.023	NS
FDS	0.19	0.0089	$p < 0.05$	0.30	0.0057	NS
FDI m	0.95	0.028	$p < 0.005$	0.45	$3.1x10^{-7}$	NS
FDI l	0.95	0.027	$p < 0.005$	0.47	$3.2x10^{-7}$	NS
EDC	0.86	$-3x10^{-6}$	$p < 0.05$	0.64	-0.053	NS
FPI	0.97	0.0010	$p < 0.01$	0.44	$1.5x10^{-6}$	NS
EI	0.94	$-5x10^{-6}$	$p < 0.01$	0.013	0.0039	NS
LUM	0.98	0.018	$p < 0.005$	0.60	$5.5x10^{-7}$	NS

Swapping the activation patterns between the 6-year-old models and the 10-year-old models produce changes in the output index finger force. For the 6-year-old male model with the 10-year-old activations, we saw an increase in palmar force from the original model's output of 13.4 N to 15.6 N and a greater increase in shear force. The angle between the intended purely palmar force and the actual force also increased by roughly 10° from 3.7˚ to 13.6 ˚ with the 10-year-old activations. For the 10-year-old male with the 6-year-old activation patterns, the palmar force went from 19.1 N to 16.4 N and the force vector angle increased from 5.0˚ to 17.1˚ with respect to the palmar direction. The female 6-year-old model's palmar force increased from 12.4 N to 15.1 N with the 10-year-old activation pattern and the force vector angle increased from 3.3˚ to 14.4˚ with respect to the palmar direction. The female 10-year-old's palmar force decreased from 16.8 N to 13.8 N with the 6-year-old's activation pattern and the fingertip force angle increased from 4.5˚ to 18.5˚.

The sex related differences we saw in the simulated muscle activation patterns were likely due to differences in the rate of finger growth compared to finger strength between the male and female models. According to the regression analyses, the male and female models differed in the relationship between the scale factor and the fingertip force. Male models had a greater slope and stronger relationship between the scale factor and the fingertip force (slope = 44.8, $R^2 = 0.91$, $p < 0.05$) than the female models (slope = 33.2, $R^2 = 0.88$, $p < 0.05$).

4.4 Discussion

As expected, posture profoundly impacted the estimated muscle activation patterns (**Fig. 4.3**). In agreement with adult experimental data [155], the FDS activation decreased, and the activations of the EDC and EI substantially increased with the greater joint flexion in posture 2. Thus, high activation of the extrinsic extensors was necessary to create a palmar flexion force in this posture. The agreement with experimental results, albeit in adults, increases confidence in the simulation results. In the more extended posture 1, the relationship between size and muscle activation was more apparent for the intrinsic muscles, whose activation levels increased linearly with age for both heads of the FDI, the FPI and LUM for both genders [14].

Generally, variation in activation patterns with age was much less consistent for posture 2, possibly due to the limited involvement of the intrinsic muscles. When separated by sex, male models did have a significant correlation between activation of the FDP, FDS, EDC, EI, and LUM with age, while none of the female models had a relationship between activation and age. This implies that the effect of variations in muscle bone size may vary with finger posture.

The sex related differences were likely due to differences in muscle mass between the male and female subjects in the original anthropometric study. The relationship between finger length, as represented by scaling factor, and maximum fingertip force differed between male and female models. This difference suggests that muscle physiological cross-sectional area was greater for males than females for a given finger length. As muscles and length were scaled equivalently in our models, relatively greater muscle activation would be needed in male models to produce the greater forces.

When we swapped the activations between the 6-year-old models and the 10-year-old models in posture 1, we did see changes in the output index finger force. The activation patterns from the 10-year-old models led to increased palmar force in the younger models, while the older models produced less palmar force with the younger model's activations. Both swapped outputs produced fingertip force vectors with increased shear forces. This does indicate that the activations did need to change to still produce a palmar force in posture 1.

There are limitations to the interpretation and generalizability of our results. We used average hand kinematic measurements to create our model for each age and gender combination. To produce results accurate enough to predict differences between individuals, we would need subject-specific models rather than those based on average hand and force measurements [156,157]. We do know that static optimization may not produce activations that align with experimental EMG values and the difference in activation varies by muscle [158,159]. A study looking at normal gait in adults found that the root mean square error between the experimental and simulated activations ranged from 0.264 and 0.465 when using static optimization on subject-specific models [158]. In addition, *in vivo* EMG measurements vary widely between subjects based on equipment, electrode placement, and other factors.

Since static optimization simply minimizes the sum of the square of each individual muscle activation, some of these results may not be as reflective of physiological activation. Although, these results do indicate that a change in activation would be needed to accommodate differences in muscle moment arms and maximum isometric force even if those changes vary in human subjects. We also used literature values rather than creating personalized models based on more precise finger and hand measurements. More precise alterations could be made to the maximum isometric forces of each muscle by taking body weight, forearm circumference, or ultrasound measurements of muscle cross sectional area.

4.5 Conclusions

We were able to use static optimization in OpenSim to estimate activation patterns in the index finger for isometric force generation. The changes in muscle activation patterns between the two postures were like those measured experimentally, thereby providing support for the use of our methods to estimate activity in muscles that are difficult to measure with surface EMG. The estimated values showed an impact of age, especially for the more extended finger posture. Failure to alter the pattern with age in the simulations led to poorer outcomes in terms of fingertip force and direction. This suggests that individuals may need to adjust muscle activation patterns as they grow to perform a given task, although the changes are smaller than those required to adapt to a new finger posture.

Future studies are needed to examine the impact of posture across a wider range of finger postures. These simulations could also be applied to a different or wider range of children. Younger or older children may have differences in growth rates, strength, and/or neuromuscular control mechanisms. Future *in vivo* or simulation studies could also examine the impact of finger size on muscle activations in other fingers or in other directions of force production. Additionally, future studies could repeat these simulations using personalized models and collecting corresponding *in vivo* activations for comparison. Similar techniques could also be used to explore diseases or conditions that affect neuromuscular control such as cerebral palsy, muscular dystrophy, pediatric stroke, or injuries to the nervous system.

CHAPTER 5: FINGERTIP FORCE ORIENTATION AND NEUROMUSCULAR CONTROL IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY

5.1 Introduction

Occurring in roughly 3.3 out of every 1000 live births [1,2], cerebral palsy (CP) is the most common movement disorder in children. One of the most prevalent subtypes found within this diagnosis is hemiplegic cerebral palsy (HCP) which predominantly affects one side of the body [3]. In children with HCP, the upper limb is more likely to be affected [160]. Within the upper limb, incidence of impairment is often greatest in the hand. A retrospective study of 169 children with HCP found that 53% of the children had significantly impaired motor function in their hands [4]. Hand impairment can lead to substantial disability due to the hand's vital role in many self-care, social, occupational, and educational tasks. As 96% of all children with CP live into adulthood, this chronic hand dysfunction will impact employment, recreational, and social opportunities throughout a person's lifetime [30].

A common task for the hand is the grasp and transport of objects. To lift a given object, the index finger and thumb must produce forces normal to the surface of the object to generate frictional forces that counteract the object's weight. Without adequate normal force, the object may be dropped, and with excessive force, it may be crushed [20]. Typically developing children can scale their grip force to be just above the minimal force required to lift the object without it slipping. Children with HCP, however, struggle in coordinating these forces [21], as well as in adapting to different object weights [22] and textures [23]. Post-stroke adults have been shown to produce fingertip forces that deviate considerably from normal to the object's surface during grip when compared to their non-paretic hand or those of neurologically intact adults [24]. Since grip impairments are similar between post-stroke adults and children with CP [25], children with HCP likely also struggle to properly direct their fingertip forces during grip.

Despite the prevalence of hand impairment in children with HCP, research into the underlying causes of these hand impairments has been limited. This may be due in part to the difficulty in studying children throughout their rapid and continuous changes in physiology and muscular control as they grow and develop. Additionally, the hand is challenging to study due to its many degrees-of-freedom, the wide range of tasks it performs, and numerous muscles involved in control of the hand. As the hand muscles are relatively small and tightly packed, capturing their activity through electromyography (EMG) is difficult, especially in children.

The overall goal of this study was to explore the differences in both index fingertip force direction and muscle activation patterns between the paretic and non-paretic hands of children with HCP. First, we examined the differences in the orientation of the forces measured in pediatric subjects with HCP. Fingertip forces were measured experimentally while musculoskeletal modeling was used to estimate the corresponding muscle activations. By using modeling, we could control for hand size and posture while we estimated the activations of muscles that would be difficult or impossible to record in a child through non-invasive techniques. We hypothesized that the paretic hand would produce a less normally oriented fingertip force than the non-paretic hand. We also anticipated that the paretic hand would have smaller overall muscle activations.

5.2 Methods

5.2.1 Participants

Children with HCP between the ages of 8-14 years old were recruited for this study. Exclusion criteria included additional neurological or orthopedic injuries that affected the hand

and botulinum injections or surgeries within the previous 6 months. Participant and parental consent were obtained in accordance with the stipulations of the University of North Carolina at Chapel Hill Institutional Review Board, which approved this study.

5.2.2 Experimental Protocol

Each participant completed a single experimental session during which they created isometric force with their fingertips. The participant was seated in a chair with back support; the seat height was adjusted so that the forearm rested comfortably in pronation on foam blocks. The forearm was positioned at the side of the body at chest height. The fingertips rested on individual six degree-of-freedom load cells (Nano17, ATI Industrial Automation, Apex, NC) affixed to a two-sided adjustable ball-and-socket joint (RAM Mount Seattle, WA) attached to a magnetic base (Noga Engineering & Technology, Shlomi, Israel). The height, angle, and location of each load cell could be adjusted to accommodate different hand shapes and sizes. The wrist was supported in a neutral posture with respect to flexion/extension by a firm foam block underneath the forearm and the palm. The finger was positioned in a relaxed posture of roughly 0˚ of metacarpal (MCP) flexion, 30˚ of proximal interphalangeal (PIP) flexion, and 0˚ of distal interphalangeal (DIP) flexion.

For a given trial, the subject was instructed to produce their maximal force with the index fingertip in the palmar direction (normal to the surface of the load cell). The subject was asked to maintain that maximal force for at least two seconds. Subjects were guided via verbal encouragement and visual feedback of their force production on a custom graphical user interface (GUI) in LabVIEW (National Instruments, Austin, TX). This procedure was repeated three times with a rest period in between each trial. The participant performed the task with both the paretic and non-paretic hands.

5.2.3 Data Analysis

Force data were digitally lowpass filtered at 20 Hz with a fourth-order Butterworth filter to remove noise. Each force trial was searched for the location of the maximal palmar force averaged over a one-second window. The average three-dimensional force vector was computed across this window. The trial with the greatest average palmar force was selected as the fingertip force vector for that hand.

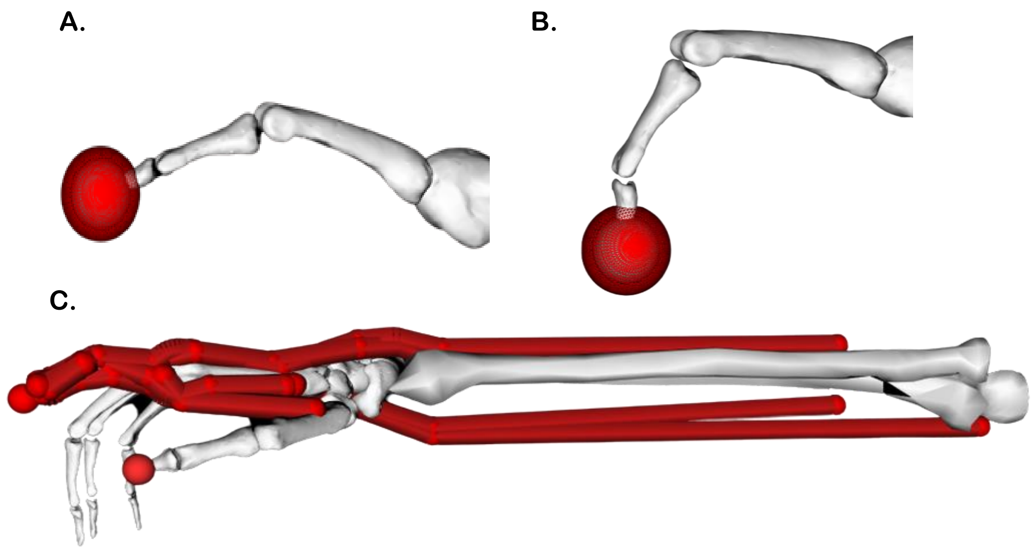

Figure 5.1. Index Finger Model. A) The index finger of the model with the force detecting contact sphere in posture 1. B) The index finger of the model in posture 2. C) The full OpenSim model with all the index finger muscle compartments.

5.2.4 Estimation of Muscle Activations

We had previously created 10 pediatric models representing the average index finger of children aged 6-10 based on hand measures from literature in OpenSim (ver. 3.3) (**Fig. 5.1**) [13,29]. To create these models, the three index finger phalanges were scaled uniformly by the ratio of the pediatric index-to-wrist length [13] to this same measure in the adult data used to make the original model [28,154]. The maximum isometric force of each muscle was also scaled by the same ratio. The model contained eight muscle compartments: the flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), medial and lateral heads of the first dorsal interosseous (FDI m and FDI l, respectively), extensor digitorum communis (EDC), extensor indicis (EI), and the first lumbrical (LUM) [28,29].

The corresponding age and sex-matched model was used to represent each study participant (i.e. the average 9-year-old female model was used for subject CP1). Each model was tested with an index finger posture of (MCP, PIP, DIP) of (0˚,30˚,0˚). The static optimization procedure within OpenSim was then used to estimate the muscle activations necessary to create the recorded 3D finger force vector in the given posture. For our simulations, we constrained the force-length-velocity properties of the muscles and found the muscle activation set that minimized the sum of the square of each individual muscle activation. Due to the repeated measure design, we used a repeated measures mixed model analysis (JMP Pro 16, SAS, Cary, NC) to assess the effects of the hand and muscle on activations.

The validity of each solution was checked by running a forward dynamics simulation to verify that the calculated muscle activation could produce the desired fingertip force in the given posture. The forward dynamics simulation used the muscle activation patterns obtained from the static optimization procedure. This specific index finger model has been adapted to measure isometric fingertip forces, a procedure that is not innate to OpenSim [28]. Namely, the model has a low-mass sphere that is rigidly attached to the distal phalanx of the index finger. During forward dynamic simulations, a hollow spherical contact mesh encapsulated the index finger sphere. Fingertip force was measured as the contact forces produced by the fingertip sphere on a surrounding contact mesh via a joint reaction analysis.

We also employed forward dynamics simulations to perform a sensitivity analysis of the impact of activation of each muscle on the fingertip force generated to examine the potential impact of aberrant activation, as many occur in children with HCP. For this initial exploration, we used the model and estimated activation patterns for the non-paretic hand of subject CP4. Activation levels of individual muscles were increased or decreased in increments of 25% of the original activation while all other muscles were held at the original activation level derived from static optimization. This was repeated for each muscle. FDP and FDS were tested from 25% to 125% of the original activation, while both heads of the FDI and the LUM were tested from 50% to 150% (150% was out of range from the FDP and FDS). Due to their very small activation values the EDC, EI, and FPI were not included in the sensitivity study.

5.3 Results

Table 5.1: Study Participant Data

Participants	Sex	Age (years)	Paretic Hand
CP01	F	9	R
CP02	M	8	R
CP03	F	10	L
CP04	M	9	R
Mean ± SD	**2 F: 2M**	**9 ± 0.82**	**1L:3R**

Four children (2 males and 2 females) with HCP completed the experimental protocol (**Table 5.1**). Their ages ranged from 8-10 years. Three had right-sided paresis while one had left-sided paresis.

Fingertip forces of the non-paretic hand during production of maximal palmar force were: 0.91 N in the ulnar direction (95% CI: 3.27 N ulnar to 1.46 N radial), 1.96 N in the distal direction (95% CI: 7.77 N distal to 3.85 N proximal), and 14.6 N in the palmar direction (95% CI: 1.91 N to 27.35 N palmar). Across the paretic hands, the mean forces were 0.71 N in the ulnar direction (95% CI: 4.97 N ulnar to 3.56 N radial), 0.056 N in the distal direction (95% CI: 4.39 N distal to 4.28 N proximal), and 4.29 N in the palmar direction (95% CI: 9.40 N palmar to 0.83 N dorsal) (**Fig. 5.2**). A paired t-test found no significant difference in mean force in the radial-ulnar or the proximal-distal direction ($p > 0.1$) between the hands, while a significant difference was seen in the dorsal-palmar direction ($p < 0.05$).

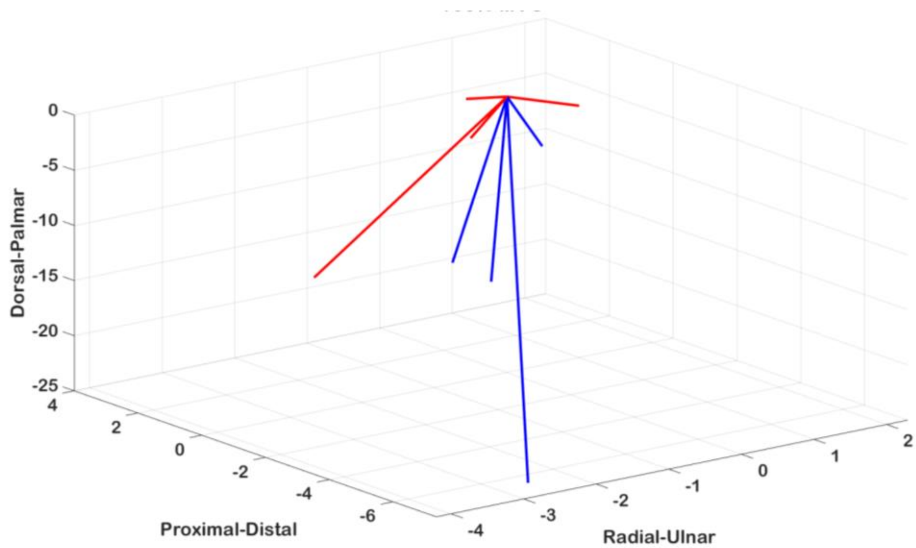

Figure 5.2. Subjects Created More Relative Shear Force with their Paretic Hands. Three-dimensional graph of the individual force vectors produced by the participants during the experimental phase. (Paretic Hand: Red and Non-Paretic Hand: Blue).

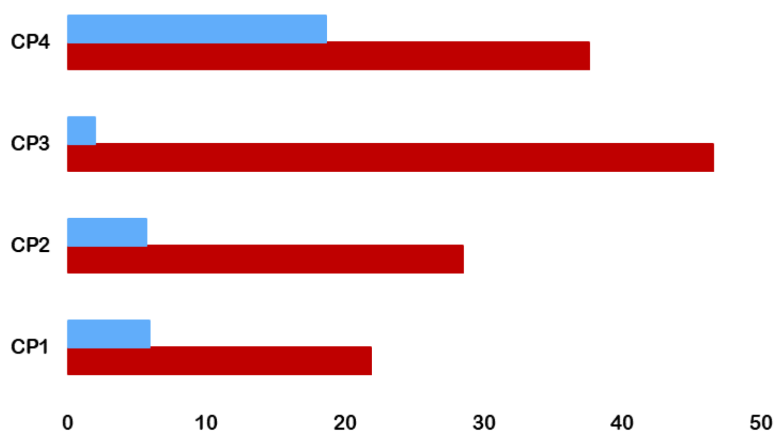

Figure 5.3. The Paretic Fingertip Force Deviated More from the Palmar Direction. The angle taken between a purely palmar force and the actual fingertip force vector for each subject. (Paretic Hand: Dark Red and Non-Paretic Hand: Light Blue).

In general, the relative amount of shear force was much greater in the paretic index finger. To account for the differences in force generating capacity between the hands, we calculated the solid angle between a theoretical purely palmar force and the actual force vector. This angle describes the ratio of the shear force to the normal force, an important quantity for determining whether the fingertip will slip from the object's surface. On average the paretic fingertip force vector was 33.6 ± 10.8˚ from the purely palmar vector, and the non-paretic fingertip force vector was 8 ± 7.3˚ from the purely palmar vector (**Fig. 5.3**). According to a paired t-test, there was a significant difference between the paretic and non-paretic hands ($p < 0.05$).

Each of the static optimization simulations converged on a muscle activation pattern. The forward dynamics simulations confirmed that the static optimization procedure produced viable muscle activation patterns. In the paretic hand, the joint angles stayed within 0.1˚ at the MCP, 0.54˚ at the PIP, 1.4˚ at the DIP of the desired joint angles. The difference in force between the input force and the force created by the calculated simulations was within 1.1 N in the radial/ulnar direction, 1.3 N in the proximal/distal direction, and 0.33 N in the dorsal/palmar direction. In the non-paretic hand, the joint angles stayed within 0.1˚ in the MCP, 0.24˚ in the PIP, and 0.6˚ in the DIP of the desired joint angles. The simulated force was within 1.2 N in the radial/ulnar direction, 1.2 N in the proximal/distal direction, and 0.80 N in the dorsal/palmar direction.

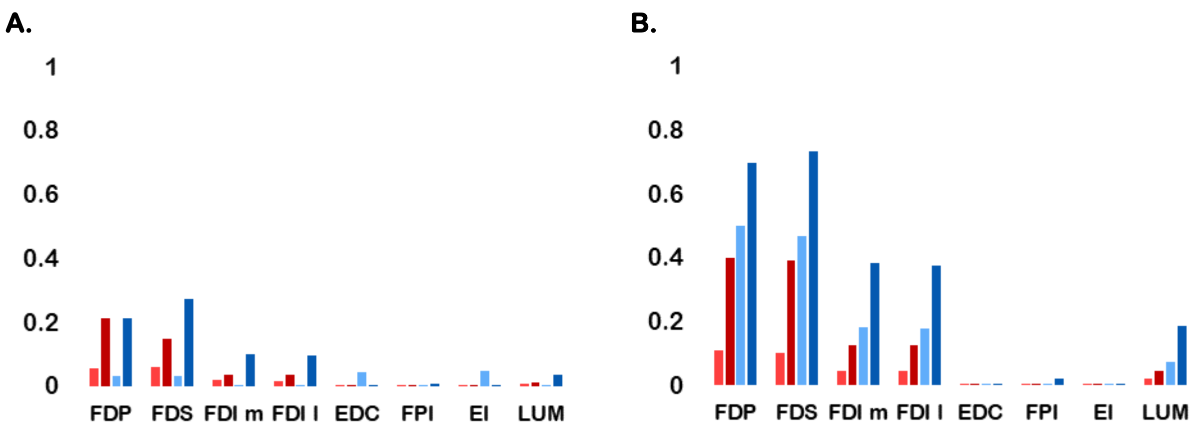

Figure 5.4. Changes in Muscle Activations Between the Paretic and Non-Paretic Hands. Muscle activations calculated by static optimization during maximal index finger flexion. A) Paretic Hands B) Non-Paretic Hands. (Light Red: Subject CP1, Dark Red: Subject CP2, Light Blue: Subject CP3, and Dark Blue: Subject CP4).

For the estimated muscle activation values, we observed a difference in the activations between the paretic and non-paretic hands (**Fig. 5.4**). The average activations for the non-paretic hand were 0.43 ± 0.24 for the FDP, 0.42 ± 0.26 for the FDS, 0.19 ± 0.14 for the FDI m, 0.18 ± 0.14 for the FDI l, 5.5x10-5 ± 5.1x10-5 for the EDC, 0.008 ± 0.009 for the FPI, 5.9x10-5 ± 5.5x10-5 for the EI, and 0.081 ± 0.072 for the LUM. The average activations for the paretic hand were 0.13 ± 0.10 for the FDP, 0.13 ± 0.11 for the FDS, 0.038 ± 0.043 for the FDI m, 0.038 ± 0.042 for the FDI l, 0.011 ± 0.021 for the EDC, 0.0039 ± 0.0027 for the FPI, 0.012 ± 0.023 for the EI, and 0.014 ± 0.016 for the LUM. Muscle ($p < 0.0001$), hand ($p < 0.0001$), and interaction of the hand and muscle ($p < 0.005$) all had significant impacts on activation (**Fig. 5.5**).

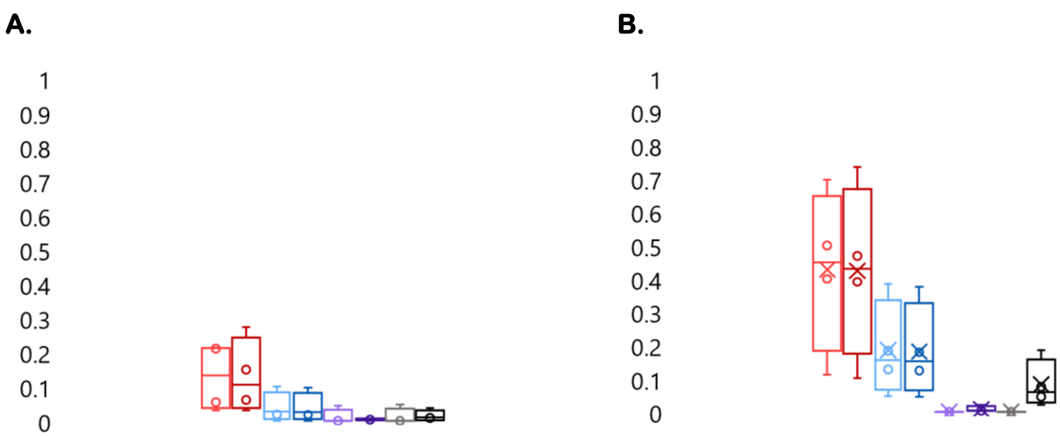

Figure 5.5. Box and Whisker Plots of Muscle Activations in the Paretic vs. the Non-Paretic Hands. Muscle activations calculated by static optimization during maximal index finger flexion. A) Paretic Hands B) Non-Paretic Hands. (FDP: Light Red, FDS: Dark Red, FDI m: Light Blue, FDI l: Dark Blue, EDC: Light Purple, FPI: Dark Purple, EI: Grey, and LUM: Black).

The results of our sensitivity test did show that increasing the activation of the FDP increased force in the palmar direction since it flexes the MCP, PIP, and DIP joints of the index finger simultaneously (**Fig. 5.6**). Surprisingly, the FDS, FDI, and LUM activations had very limited impact on the magnitude of the palmar force created. Changes in the activation of the FDP relative to the FDS led to the introduction of substantial shear forces. Increases in the LUM activation led to increased force in the ulnar and distal directions.

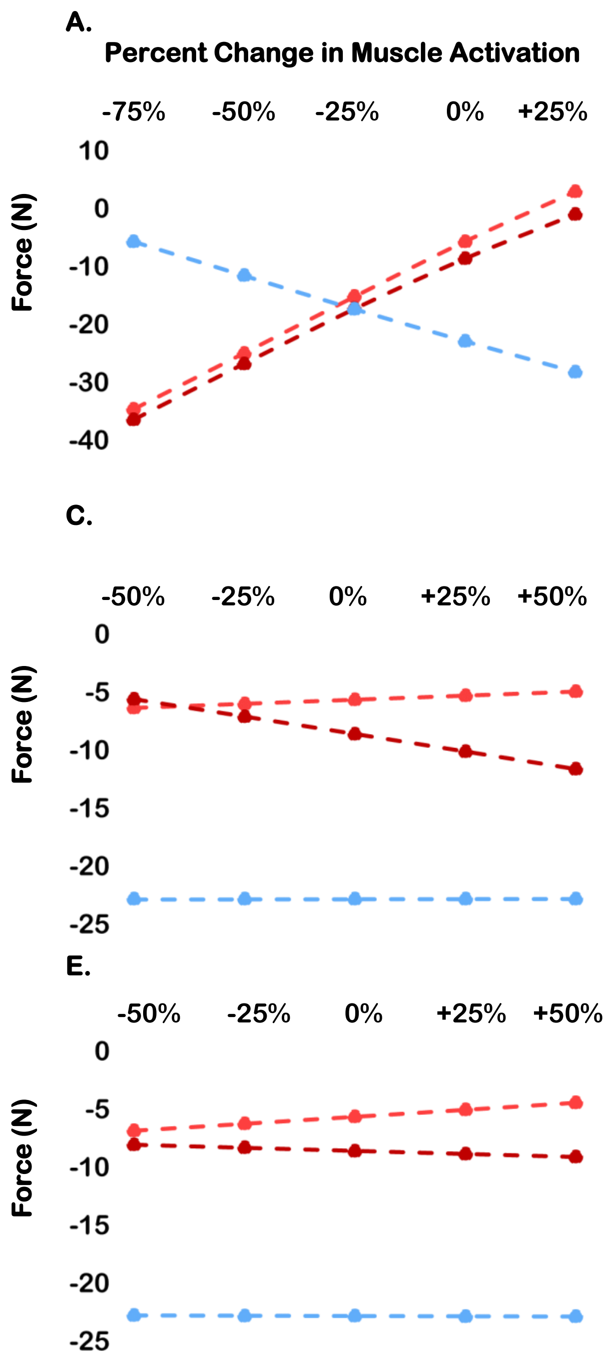

Figure 5.6. Results of a Sensitivity Study on the Impact of Muscle Activation on Fingertip Force. Correlations between activations of individual muscles and fingertip force in all three directions. A) FDP B) FDS C) FDI L D) FDI M E) LUM. (Line color: Light Red - Radial(+)/Ulnar(-) force, Dark Red - Proximal(+)/Distal(-) force, & Light Blue - Dorsal(+)/Palmar(-) force.).

5.4 Discussion

We found that force generation in the paretic hand was considerably reduced compared to force generation in the non-paretic hand in children with HCP. Particularly, the maximum palmar fingertip force in the paretic hand was only 30% of the value for the non-paretic hand. In a review of several studies, the average paretic hand grip force in children with HCP was about 30% of the average non-dominant grip force seen in typically developing children [161]. Younger children (average age of 6.5 years) with HCP produced flexion force with the index and middle fingers of the paretic hand that was equivalent to only 23% of the force generated with the non-paretic hand while older children (average age of 12.5 years) with HCP produced 56% of the non-paretic hand force with the paretic hand [161]. These force deficits restrict the mass of objects that can be grasped as a sufficient normal force must be created to generate the frictional force to resist gravity as the object is raised.

This situation is exacerbated by the excessive amount of shear force created relative to the normal force. This ratio was significantly increased in the paretic hand as evidenced by the greater solid angle with respect to the palmar direction. To prevent slip between an object and the fingers, the solid angle must stay below the arctangent of the static coefficient of friction between the finger and the object [24]. For example, for a frictional coefficient of one, slip would be expected when the solid angle exceeds 45°. While the mean shear forces in the paretic hand were fairly small, this was due to the variation across subjects. The measured forces in the radial-ulnar direction ranged from 4.21 N in the ulnar direction to 2.29 N in the radial direction and from 3.54 N in the distal direction to 2.96 N in the proximal direction for the paretic hand. In comparison, forces in the palmar direction varied from 0.85 to 7.15 N. Thus, the shear force solid angle averaged over 33° in the paretic hand across subjects.

Modeling and static optimization revealed that the activation patterns were estimated to have differed between the hands as well. In general, muscle activations were lower in the paretic hands. The alterations were especially apparent in the intrinsic muscles. The largest difference was in the LUM where the average paretic activation was 17% of non-paretic hand activation. For the FDI m and FDI l, the paretic activations were around 21% of the non-paretic activations. Precise control of intrinsic muscles may be especially affected due to the dependence on corticospinal pathways which are likely to be impacted by the brain injury associated with CP [162]. The FDI and LUM muscles help to direct fingertip forces [155];the limited relative activation estimated by the simulations could result in greater relative shear force and potential slippage of an object during grasp.

According to the sensitivity analysis, FDP had the greatest impact on palmar force magnitude for the tested finger posture. Increased FDP activation was associated with increased palmar force. We also saw a slight increase in radial force with increases in the FDI activation as we would expect with the MCP joint positioned in neutral flexion/extension. Although, we did not see increases in the palmar forces with greater FDS activation. We observed a surprising relationship for both FDS and FDP between activation level and proximal/distal force and radial/ulnar force. Increasing FDP activation led to the fingertip force being directed to a greater extent in the radial and proximal directions while increasing FDS activation had the opposite effect. The original adult model was less accurate in matching experimental data for the ulnar-radial than for other directions [28]. It is possible that these off-axis sensitivities resulted from aberrations in the model.

We did have several limitations to this study. Firstly, we used anthropomorphic measures to create our models rather than participant specific models. Studies of the thumb and shoulder have found that while models scaled by anthropometric data can reflect population-level differences, patient-specific models are more accurate at reflecting a specific patient's physiology [156,157]. We also used the same model for both the paretic and non-paretic hands when there may be differences in muscle size and strength between the hands. We would not necessarily expect static optimization to produce activations that were identical to physiological activation patterns. Additionally, we would expect patients with HCP to have non-ideal control strategies. The goal of these simulations was to see how differences in fingertip force vectors between the paretic and non-paretic hands might change the required muscle control strategies rather than to exactly predict individual muscle control strategies.

5.5 Conclusions

We found that both the magnitude and the direction of the fingertip force in the paretic hand was altered with respect to the non-paretic hand. Profound weakness in force generation normal to the fingertip could impair grasp, while the misdirection of the force could lead to object slippage. The simulations suggest limited force arising from FDP and FDS in the paretic hand, due either to reduced voluntary activation or muscle atrophy, especially reduced contributions from intrinsic muscles. Fingertip force generation seems to be an important target for therapy in HCP, with an emphasis on modulating muscle activation patterns to control force direction.

Future studies could provide more pediatric simulation data for the hand and finger muscles in both children with and without CP. Currently, there are few *in vivo* or computational studies that report finger muscle activations in either neurotypical children or those with CP. This study could also be repeated with subject-specific models. In addition, tools such as the

Calibrated EMG-Informed Neuromuscular Modeling Toolbox could be implemented to produce activations more accurate to children with CP.

CHAPTER 6: CONCLUSIONS AND FUTURE WORK

6.1 Conclusions

This dissertation presents novel research into pediatric neuromuscular control in children with and without HCP. This work contributes to our current understanding of pediatric development of motor control of the fingers. Additionally, we provide insights into the variations in finger neuromuscular control in children with HCP that will contribute to future research, therapies, and treatments for hand dysfunction in children with HCP.

In chapter 2, we reviewed the current state of research of quantitative measures of hand strength and function in children with HCP. Most studies were either cross-sectional or longitudinal studies. We found a lack of studies that examined sensorimotor characteristics of the hand in children with HCP. Data were especially limited for kinematics and kinetics of individual fingers and the thumb. Without more research into these mechanisms of impairment, clinicians may be limited in available treatment options for hand dysfunction in children with HCP.

In general, grip strength was reduced in the paretic hand when compared to the non-paretic hand. The passive range of motion (PROM) of the paretic wrist was like that of the non-paretic wrist or of the wrist of typically developing (TD) children. The active range of motion (AROM) of the paretic wrist, in contrast, was more limited. Additionally, studies reported that children with HCP had sensory deficits, evidenced by an impaired two-point discrimination capacity. Unlike the strength values, however, two-point discrimination did not appear to vary much with age for either the paretic or non-paretic hand for the ages assessed. We did see improvements in the Box-and-Block Test (BBT) performance on the paretic side with increased age, but children with CP still performed worse with their paretic hand than with their non-paretic hand or in comparison to TD peers of the same age.

In chapter 3, we measured the voluntary activation capacity (VAC) and coactivation during middle finger flexion and extension in typically developing children. We found no statistically significant differences in either measure of VAC or in coactivation at 100% MVC between the dominant and non-dominant hand or between flexion and extension. We did find that direction had a significant effect on coactivation at 40% MVC. We did observe a wide variation in coactivations, including some subjects with very high antagonist activation in either one or both hands. While these large variations may have been due to the limitations in our study design, alternatively, coactivation value may vary as motor control of the hand develops. These results can serve as a basis for comparison with values obtained from children with HCP or other pediatric neurological disorders.

In chapter 4, we used musculoskeletal modeling to examine how age-related changes in index finger strength and size impact neuromuscular control. We accomplished this by creating 10 pediatric index finger models that represented male and female children between 6 and 10 years of age. We tested all models in two different hand postures to also assess the impact of posture on muscle activation. We did find a relationship between index finger length and some muscle activations in the more extended finger posture, but not in the more flexed posture. While we only tested two postures, this does indicate that posture can greatly affect neuromuscular control of the finger. Although our results do not necessarily reflect actual individual physiological activations, we did find that muscle activations must change in response to changes in muscle strength and moment arm due to childhood growth and development.

In chapter 5, we measured three-dimensional maximal index finger force vectors in children with HCP to examine how fingertip force direction varies between the paretic and non-paretic hands. We then used age-matched index finger models to examine how changes in fingertip force and orientation between the hands of children with HCP change neuromuscular control. We did find that children with HCP struggle to control the orientation of their fingertip forces in their paretic hand, potentially leading to difficulties in manipulating and transporting objects. We also found that these differences are likely due to different neuromuscular control activation patterns. Our results suggest that training fingertip force orientation could help to improve grip and lift tasks in children with HCP.

6.2 Future Work

Generally, there is a lack of research into the sensorimotor function of the hands in both healthy children and those with HCP. When studies do examine the upper limb, they tend to focus on the elbow or wrist. Very few studies look at the hand or individual fingers outside of standard grip and pinch measures. To our knowledge, no studies have reported values for voluntary activation capacity (VAC) or coactivation in any of the muscles that control the hand or fingers in either healthy children or children with HCP. Data on what muscle activations look like in children during various finger and hand tasks are also lacking.

In chapter 3, we measured VAC and coactivation of the FDS and EDC during middle finger flexion and extension in TD children. Future studies are needed to evaluate these metrics in children with HCP. VAC and coactivation could also be measured in other upper limb muscles.

In chapter 4, we found that finger posture, size, and strength did impact the necessary muscle activation patterns needed to perform a task. This work could be improved by using personalized pediatric models. The maximum isometric force could be scaled by body weight or forearm size to accommodate for different growth rates between hand size and muscle strength. Future *in vivo* or musculoskeletal modeling studies could be performed to look at muscle activations in children of various ages during various finger or hand tasks. Similar techniques could also be used to explore diseases or conditions that affect neuromuscular control such as cerebral palsy, muscular dystrophy, pediatric stroke, or nervous system injury. Musculoskeletal modeling would also benefit from studies of normative values for muscle activations in TD children during various hand and finger tasks.

Our work in chapter 5 could be expanded by providing children with HCP feedback on all three directions of force rather than just in the intended direction. This study could also be expanded to look at other fingers or combination of fingers and muscles in the hand and arms. Future studies could also compare children of different ages to see how these values change during growth and development. Researchers could examine if training fingertip muscle orientation improved performance in grip and lift tasks in children with HCP.

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