ABSTRACT

Mechanisms Underlying the Flexion Synergy and Hand Dysfunction following Stroke:

Implications for Neuro-prosthetics

Yiyun Lan

The over-a-decade quantitative study of the flexion synergy has provided concrete evidence that the stereotypical movement coupling of shoulder abduction with elbow flexion and wrist/finger flexion (i.e. flexion synergy) significantly affects the ability to perform functional upper extremity movements that are essential for activities of daily living (e.g. reach-to-grasp an object). However, it is still not entirely clear what the underlying mechanisms are responsible for the flexion synergy, and furthermore, how this knowledge can advance the development of effective approaches in regaining functional upper extremity movements, especially those with moderate to severe impairment. In the current research, we will provide new insights in trying to answer these questions with three studies conducted in individuals with chronic hemiparetic stroke.

In the first study, we seek to determine the extent to which the shoulder abduction loading affects the ability to open the hand and grasp an object in individuals with chronic hemiparetic stroke. It is understood that when stroke participants are only abducting the shoulder, the torques and EMG activity of a relaxed hand increase as a function of the load applied to the shoulder. But it is not clear whether voluntary efforts of opening the hand or grasping can overcome the involuntary flexion torque generated due to the flexion synergy.

In the second study, the goal is to find out whether the expression of flexion synergy on the hand is a result from increased shared neural drive to the shoulder abductor and wrist/finger flexors. To achieve this goal, wavelet coherence of EMG signals in the shoulder
abductor and wrist/finger flexors was calculated and compared with the non-flexion synergy muscle pairs and with age-matched able-bodied individuals. It is found that the alpha band (8-13 Hz) flexion synergy muscle coherence in the stroke group is significantly higher than in the able-bodied group, suggesting an increased use of the slow-conducting, polysynaptic motor pathways after stroke (e.g. cortico-reticulo-spinal tract).

In the third study, we explored the possibility of improving the classification accuracy of paretic hand opening, grasping and relaxing in individuals with chronic hemiparetic stroke. Specifically, we demonstrated that the classification accuracies of hand opening, grasping and relaxing decreased in the presence of the flexion synergy. Furthermore, the use of a subject-specific, muscle-specific, coherence-based filter to reduce synergy-induced EMG component can improve the classification accuracy. This approach promises a better classification accuracy of hand movement intent during functional upper extremity activities.

Overall, the work in this dissertation provides valuable insights on movement control of the paretic hand during voluntary hand opening and grasping within the context of flexion synergy, advances our understanding of the underlying neural mechanisms responsible for the expression of the flexion synergy, and demonstrates a novel approach that has the potential to improve classification accuracies of hand movements during functional upper extremity activities. We hope work in this thesis will open new possibilities for clinicians, scientists and engineers to develop and deliver neural machine interfaces for individuals with chronic hemiparetic stroke to regain basic hand function.
ACKNOWLEDGMENT

To my mentors, Drs. Jules Dewald and Jun Yao, I will be forever indebted to you for all the training I received from you to become a Ph.D. Dr. Jules Dewald, you are without a doubt “the beacon” of this trio. The perspective and vision you offer to me prepare me well for the challenges during my Ph.D. study. You are always patient with my mistakes and value my opinions even when I did not know much about science and research. I could not recall how many hours you have dedicated to my writing pieces. As a non-native English speaker and the only English speaker in my family, I could not be prouder for what I have accomplished today, and all of these will not happen without your mentoring. I enjoy very much chatting with you about languages (beyond English) and cultures, and I wish I could also speak 5 languages someday. Dr. Jun Yao, I see you as the “Mom” in the US and I do feel you take care of me as your “3rd son”. In the past couple of years, we see each other more than any of my family members combined. You are the “engine” of this trio, and because of you, I see myself grow both professionally and personally. Thank you for all the hands-on experiences you provided over the years. Your attention to details and commitment to perfection speak louder than words. I am humbled by your dedication and passion to science and research, and I will always remember you and keep learning from you.

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For many families who volunteer to host me for holidays, you make me feel welcome and loved while alone in the States. As Confucius used to say, “How delightful it is to have friends visiting us from afar!” No matter wherever I will be, I will always remember your kindness and your hospitality.
LIST OF ABBREVIATIONS

ACT$^{3D}$: Arm Coordination Training 3-Dimensional Robot

ANOVA: analysis of variance

CBST: corticobulbospinal tract

CMSAh: Chedoke-McMaster Stroke Assessment

CRST: corticoreticulospinal tract

CST: corticospinal tract

DTI: diffusion tensor imaging

ECR: extensor carpi radialis

EDC: extensor digitorum communis

EEG: electroencephalogram

EMG: electromyography

FCR: flexor carpi radialis

FDS: flexor digitorum superficialis

FMA: Fugl-Meyer Assessment

mDEL: intermediate deltid

MRI: magnetic resonance imaging

MVT: maximum voluntary torque

N: Newton

Nm: Newton-meter

RST: reticulospinal tract

SABD: shoulder abduction

SD: standard deviation
SE: standard error

TMS: transcranial magnetic stimulation
# TABLE OF CONTENTS

1 INTRODUCTION .................................................................................................................. 17
   1.1 Problem Statement ...................................................................................................... 17
   1.2 Research Goal ........................................................................................................... 18
   1.3 Research Aims ........................................................................................................... 19
   1.4 Dissertation Outline .................................................................................................. 19

2 BACKGROUND ................................................................................................................... 21
   2.1 Etiology of stroke ...................................................................................................... 21
   2.2 Post-stroke Impairment .............................................................................................. 22
   2.3 Quantification of the Flexion Synergy ........................................................................ 25
   2.4 Organization of Motor Neuron Pathways .................................................................. 26
   2.5 Corticospinal pathway .............................................................................................. 27
   2.6 Reticulospinal tract .................................................................................................... 28
   2.7 Rubrospinal tract ....................................................................................................... 30
   2.8 Propriospinal tract ..................................................................................................... 30
   2.9 Vestibulospinal tract .................................................................................................. 31
   2.10 Introduction to Neural Machine Interfaces .............................................................. 31

3 THE IMPACT OF SHOULDER ABDUCTION LOADING ON VOLITIONAL HAND OPENING AND GRASPING IN CHRONIC HEMIPARETIC STROKE .............................................................. 35
   3.1 Abstract ...................................................................................................................... 35
   3.2 Introduction ................................................................................................................ 37
3.3 Methods

3.3.1 Participants

3.3.2 Experimental setup

3.3.3 Experimental Protocol

3.3.4 Data collection and analysis

3.3.5 Statistics

3.4 Results

3.4.1 Hand pentagon area during opening

3.4.2 Grasping force generation

3.5 Discussion

3.5.1 Possible neural mechanisms

3.5.2 Impact of changes in muscle properties at the paretic hand

3.5.3 Clinical implications for recovery of hand function after stroke

3.6 Future studies

4 INCREASED SYNERGISTIC NEURAL DRIVE, AS REVEALED BY EMG/EMG WAVELET COHERENCE, IS RELATED TO HAND IMPAIRMENT IN INDIVIDUALS WITH POST-STROKE FLEXION SYNERGY
4.3.4 Data collection and data analysis ................................................................. 65
4.3.5 Statistics ....................................................................................................... 67
4.4 Results ............................................................................................................. 68
4.5 Discussion ....................................................................................................... 72
  4.5.1 Coherence in the flexors ........................................................................... 74
  4.5.2 Coherence in the α- and β-band ............................................................. 78
  4.5.3 Coherence and post-stroke hand impairment ....................................... 81
  4.5.4 Technique applied to remove cross-talk .............................................. 82

5 REDUCING THE IMPACT OF SHOULDER ABDUCTION LOADING ON THE
CLASSIFICATION OF HAND OPENING AND GRASPING IN INDIVIDUALS WITH POST
STROKE FLEXION SYNERGY ............................................................................. 83
  5.1 Abstract ....................................................................................................... 83
  5.2 Introduction .................................................................................................. 85
  5.3 Methods ....................................................................................................... 87
    5.3.1 Participants ............................................................................................ 87
    5.3.2 Equipment and Setup .......................................................................... 88
    5.3.3 Protocol ................................................................................................. 89
    5.3.4 Data Analysis ........................................................................................ 89
      5.3.4.1 Coherence ....................................................................................... 89
      5.3.4.2 Algorithm ....................................................................................... 90
      5.3.4.3 Dataset and Model Evaluation ....................................................... 92
    5.3.5 Statistics ............................................................................................... 93
  5.4 Results .......................................................................................................... 94
5.5 Discussion ..................................................................................................................................................... 99

5.5.1 Novelty and Main Finding ......................................................................................................................... 99

5.5.2 Impact of Flexion Synergy on Classification Accuracy ................................................................. 102

5.5.3 Variation in significant coherence frequency range ............................................................................ 103

5.5.4 Variation in Classification Improvement .............................................................................................. 104

5.5.5 Scientific Implication and Future Work ................................................................................................. 104

6 CONCLUSION AND FUTURE WORK ........................................................................................................ 106

6.1 Conclusion ................................................................................................................................................. 106

6.2 Future Work .............................................................................................................................................. 109
LIST OF FIGURES

Figure 2.1 Hemorrhagic and ischemic strokes. ................................................................. 22

Figure 2.2 Affected brain areas due to stroke. Top: motor and sensory map in central gyrus;
Bottom: blood supply to the cerebral hemispheres. ......................................................... 25

Figure 2.3 Direct and indirect cortical projections (Lemon, 2008). ................................. 28

Figure 2.4 Schematic description for a brain machine interface ........................................ 32

Figure 2.5 Pipeline of classifying hand movements based on the EMG recordings. .......... 33

Figure 2.6 Comparison of several common classification techniques using conventional
classification error ............................................................................................................. 34

Figure 3.1 Experimental Setup ......................................................................................... 40

Figure 3.2 Pentagon area changes .................................................................................... 45

Figure 3.3 Hand Pentagon Area and Grasping Forces during Hand Opening .................... 48

Figure 3.4 Grasping Forces in One Stroke Individual and One Control Individual .......... 49

Figure 3.5 Grasping Forces in Severe Stroke Group, Moderate Stroke Group and Control Group........................................................................................................................................ 51

Figure 4.1 Grasping forces, EMGs and coherence during a hand grasping task ............. 72

Figure 4.2 Coherence difference between stroke and able-bodied group in the α-band.... 73

Figure 4.3 Coherence difference between stroke and able-bodied group in the β-band.... 76

Figure 4.4 Correlation between coherence and synergy-induced hand impairment. ........ 78

Figure 5.1 Experiment setup ............................................................................................. 92

Figure 5.2 Increased SABD loading resulted in a significantly decreased accuracy rate in the
stroke group. ..................................................................................................................... 94
Figure 5.3 Greater alpha-band coherence between mDEL and wrist/finger flexors in the stroke individual. ................................................................. 96

Figure 5.4 Significant frequency range across participants during hand grasping at SABD50... 98

Figure 5.5 The overall classification accuracy improvement after applying the filters at SABD50 in the stroke group. ................................................................................................................. 101
LIST OF TABLES

Table 2.1 Muscle groups in flexion and extension synergies .................................................. 25

Table 2.2 Motor Neuron Pathways .......................................................................................... 27

Table 4.1 Participant demographics ....................................................................................... 63

Table 4.2 Mixed three-way ANOVA: interactions in the α-band ............................................. 69

Table 4.3 Mixed three-way ANOVA: interactions in the β-band ............................................. 69

Table 5.1 Participant demographics ....................................................................................... 88

Table 5.2 EMG features extracted in the time domain .............................................................. 91

Table 5.3 Mixed two-way ANOVA for overall accuracy rate .................................................. 99

Table 5.4 Mixed three-way ANOVA for improvement in the overall accuracy rate ............. 100
1 INTRODUCTION

1.1 Problem Statement

Stroke is a leading cause of serious long-term disability in the United States, affecting approximately 795,000 people per year and leaving more than 50% with some motor deficits (Mozaffarian et al., 2015). In addition to muscle weakness and spasticity, impaired ability in performing functional upper extremity movements that demands independent joint control of the shoulder, elbow and wrist/fingers (e.g. reach-to-grasp) is very common after stroke. Regaining control of basic hand function is one of the most desired functions among individuals with chronic stroke, especially for those with moderate to severe impairment. Therefore, the understanding of the loss of hand function with full consideration of the effect of proximal muscles activation is crucial for development of more effective interventions that seek to rehabilitate the paretic hand.

In the process of motor recovery post stroke, two stereotypical motor behaviors in the upper extremity of the paretic side have been described in clinical practice: flexion synergy and extension synergy. As one of the more commonly exhibited motor behaviors, the flexion synergy is the coupling of shoulder abduction with shoulder extension/external rotation, forearm supination, and elbow, wrist, and finger flexion (Twitchell, 1951; Brunnstrom, 1970). In contrast, the extension synergy is the coupling of shoulder adduction with shoulder flexion/internal rotation, forearm pronation, elbow extension and possibly wrist extension and finger flexion (Brunnstrom, 1970). While extensive research in the past has been conducted to understand the loss of hand function after stroke, few of them has given full consideration of the deleterious effect of the flexion synergy on the hand yet. Even though past work reported progress in mapping the increased involuntary
response of the hand during shoulder abduction (Miller and Dewald, 2012), it falls short in determining post-stroke paretic hand control during functional upper extremity movements where both shoulder and hand movements are actively involved.

1.2 Research Goal

The current study is very much rooted in the groundwork laid by previous research: 1) well established abnormal movement coupling of shoulder abduction with elbow flexion resulting in increased abnormal torque coupling (Dewald et al., 1995) and muscle co-activation patterns (Dewald et al., 2001), a reduced reaching distance (Ellis et al., 2006) and working area (Sukal et al., 2006) when progressively increasing shoulder abduction loading; 2) advancement in our understanding the impact of the flexion synergy on the paretic hand post stroke, including determination of involuntary forearm EMG activity and involuntary muscle torques generated at the paretic wrist and fingers when increasing shoulder abduction loading (Miller and Dewald, 2012).

This study continues this line of inquiry by determining the impact of the flexion synergy on the hand with a special emphasis on the quantification of hand kinematic and kinetics during voluntary hand movements while increasing shoulder abduction loading. The overall goal is to quantify the extent to which the flexion synergy constrains the voluntary hand movements post stroke, to understand which underlying mechanisms might possibly drive such influence, and to explore the impact of shoulder abduction on the application of neural machine interface for classification of hand movements for future use of neuroprosthetics in individuals with post-stroke flexion synergy.
In addition to providing insights into the altered motor behaviors of the paretic hand within the context of flexion synergy as well as providing indirect evidence related to the underlying neural mechanisms, this study also explored a scientific based signal preprocessing method to reduce the synergy-induced components in EMG to improve the classification accuracy. This new method may result in a more effective neural machine interface. From the first to the third research aim, the intension is to establish a translational connection between basic science findings and the development of novel clinical interventions and technologies for individuals with chronic hemiparetic stroke.

1.3 Research Aims

To accomplished the research goals stated above, the following three research aims were proposed:

1) To quantify the extent to which shoulder abduction loading alters the paretic hand opening and the control of grasping forces.

2) To quantify EMG-EMG coherence between shoulder abductor and wrist/finger muscles and its relationship with synergy-induced impairment of the paretic hand.

3) To determine the effect of shoulder abduction loading on the accuracy of EMG-based classification of the intent to open, close or relax the paretic hand and whether removal of coherent EMG reduces the classification error rate.

1.4 Dissertation Outline

Chapter 2 consists three parts: part 1 provides background knowledge about the etiology of stroke, post-stroke impairment, and summarizes the organization of motor neural pathways; Part
2 provides an overview of the past literature documenting research work with regards to the expression of flexion synergy, including evidence reported in both animal and human experiments; and Part 3 introduces the concept of neural machine interfaces and reviews its application in humans.

Chapter 3 through 5 address the three research aims, each with separate introduction, results, and discussion sections. Specifically, Chapter 3 details work done to address Aim 1 and has been accepted to be published in the Journal of Neurorehabilitation and Neural Repair as:


Chapter 4 addresses Aim 2 with the goal of quantifying EMG-EMG coherence between shoulder abductor and wrist/fingers muscles in individuals with chronic stroke. The content of this work is now in preparation for submission to the Journal of Neuroscience as:

Lan Y, Yao J, Dewald JPA. “Increased Synergistic Neural Drive, as Revealed by EMG/EMG Wavelet Coherence, is Related to Hand Impairment in Individuals with Post-Stroke Flexion Synergy.” J of Neuroscience.

Chapter 5 covers the efforts made to reduce the impact of shoulder abduction loading on neural machine interface in classifying paretic hand movements. This work has been submitted to the Journal Frontier in Bioengineering and Biotechnology as an invited original manuscript under the topic “Application of Synergies in Human Machine Interfaces”:

2 BACKGROUND

2.1 Etiology of stroke

Stroke is classically characterized as a neurological deficit attributed to an acute brain injury of the central nervous system (CNS) by a vascular cause, broadly categorized as ischemic and intracerebral hemorrhage (ICH) strokes (Figure 2.1). Of all strokes, 87% are ischemic strokes, in which an obstruction occurs within a blood vessel supplying blood to the brain, depriving brain tissue of oxygen and nutrients. The obstruction occurs because of the development of fatty deposits lining the vessel walls, which can be caused by cerebral thrombosis, a blood clot that develops at the clogged part of the vessel, or cerebral embolism, a blood clot that forms at another location in the circulatory system and later travels to a clogged location in the brain. 13% are hemorrhage strokes when a diseased blood vessel within the brain bursts, allowing blood to leak inside the brain. Depending on where the blood vessel ruptures, it can be further categorized as intracerebral hemorrhage and subarachnoid hemorrhage. There are two types of diseased blood vessels, one is called aneurysm, and the other is arteriovenous malformation. An aneurysm is a ballooning of a weakened region of a blood vessel which is likely to rupture and bleeds into the brain if left untreated. An arteriovenous malformation is a tangle of abnormally formed blood vessels connecting arteries and veins in the brain.
Figure 2.1 Hemorrhagic and ischemic strokes.

2.2 Post-stroke Impairment

Stroke is a leading cause of serious long-term disability in the United States, affecting over one half million people per year and leaving more than 50% with some motor deficit (Mozaffarian et al., 2015). Post-stroke impairment varies across individuals depending on the exact damaged regions in the specific cerebral hemisphere. For example, an obstruction occurs to the anterior cerebral artery, which supplies the frontal, pre-frontal and supplementary motor cortex, as well as parts of the primary motor and primary sensory cortex (Figure 2.2), may result in paralysis and/or sensory loss of the foot and leg on the opposite side, or deficits in the gait and stance. The most common obstruction sites often occur within the middle cerebral artery, whose territories of blood supply include a portion of the frontal lobe, lateral surface of the temporal and parietal lobes. The
common clinical syndromes often include motor paralysis and/or sensory loss of the contralateral face and arm, possible aphasia, or neglect syndrome.

In the upper extremity, weakness (Kamper et al., 2006), spasticity (Thibaut et al., 2013), and abnormal muscle synergies (Dewald et al., 1995) are considered the three major motor impairments among individuals with chronic hemiparetic stroke. Abnormal muscle synergy affects approximately 40-60% of the stroke population, especially for individuals with moderate to severe impairment. While monitoring motor recovery process post-stroke, Twitchell observed movement patterns that exhibited stereotypical behaviors realized in the appearance of a tight coupling between adjacent joints in the upper and lower limbs (Twitchell, 1951). Brunnstrom later described these abnormal stereotypical movements as limb “synergies” (Brunnstrom, 1970), the coupling of movements of adjacent joints, and she categorized these in the upper limb as part of either a “flexion synergy” or an “extension synergy” (Table 2.1).
**Figure 2.2** Affected brain areas due to stroke. **Top:** motor and sensory map in central gyrus; **Bottom:** blood supply to the cerebral hemispheres.

<table>
<thead>
<tr>
<th>Table 2.1 Muscle groups in flexion and extension synergies</th>
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<tbody>
<tr>
<td><strong>Flexion synergy</strong></td>
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<tr>
<td>Flexion of the elbow</td>
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<tr>
<td>Supination of the forearm</td>
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<tr>
<td>Abduction of the shoulder</td>
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<tr>
<td>External rotation of the shoulder</td>
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<td>Shoulder girdle retraction and/or elevation</td>
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*Adapted from Brunnstrom et al.*

### 2.3 Quantification of the Flexion Synergy

Twitchell and Brunnstrom’s clinical description of abnormal muscle synergies serves as the foundation for the quantitative study of the expression of flexion synergy on the elbow and wrist/fingers, part of this PhD thesis. A thorough investigation of the spatial patterns of muscle activation in paretic and contralateral elbow and shoulder muscles, generated by different shoulder abduction loading levels, revealed specific muscle coactivation patterns between elbow flexors/shoulder abductors and elbow extensors/shoulder adductors (Dewald et al., 1995). This finding was later reaffirmed by a follow-up study on the multi-joint torque patterns associated with the generation of maximum voluntary torques in four degrees of freedom at the shoulder and elbow (Dewald and Beer, 2001). Functionally, the stereotypical coupling of shoulder abduction with the elbow flexion constrained upper extremity reaching range of motion while progressive increasing shoulder abduction loading (Sukal et al., 2007).

The expression of flexion synergy is also found in the wrist and fingers. For example, considerable forces and EMG activity were generated at the paretic hand during lifting of the paretic arm and progressively increasing shoulder abduction loading (Miller and Dewald, 2012).
Interestingly, it was also noted that maximal reaching resulted in greater finger flexion forces than no reaching, suggesting that elbow extension imposed a similar effect, albeit less in magnitude, on wrist/finger flexion as shoulder abduction on the elbow/wrist and finger flexion.

2.4 Organization of Motor Neuron Pathways

Upper motor neurons in the motor cortex influence the lower motor neurons and local circuit neurons in the spinal cord by two routes: direct cortical projections to the spinal cord and indirect projections to brainstem centers that in turn project to the spinal cord (Table 2.2; Figure 2.3). In an intact nervous system, direct projections from the motor cortex are essential for the fine and fractionated control of the distal parts of the limbs, while indirect projections influence the gross motor control such as posture or balance (Lemon, 2008). The initial evidence for the contrasting functions of the direct and indirect projections from the cortex to the spinal cord comes from experiments conducted by Hans Kuypers in rhesus monkeys (Kuypers, 1981). After surgery that transected the direct pathway at the level of the medulla, the animals showed difficulty performing tasks with the hands, but were able to maintain balance and posture. The monkey was even able to climb the cage but the fine control of the hand was permanently lost.

The subsequent section aims to provide a brief overview of the anatomy and function of motor pathways from motor cortex to the spinal cord and put together a list of important findings from past literature about how these motor pathways might function after stroke. The goal is not to provide a comprehensive cover of these motor pathways but rather to set the stage for the studies that will be introduced in Chapter 3-5.
2.5 Corticospinal pathway

Axons of pyramidal cells in the cortical layer V pass through the internal capsule and then descend to the brainstem level, and give birth to two types of corticospinal tracts, depending on whether the fibers decussate or not (Figure 2.3). At the caudal end of the medulla, about 80% to 90% of these fibers cross the midline to the other side and enter the dorso-lateral columns of the spinal cord as the lateral corticospinal pathway. The remaining fibers enter the spinal cord without crossing and form the medial corticospinal tract. The medial corticospinal tract terminates on either side via spinal cord commissure and remains in the ventral-medial columns of the spinal cord (Purves, 2004).

The lateral corticospinal tract comprises the direct cortical projection and is essential for fine and fractionated distal joint control of the limb. In contrast, the medial corticospinal tract influences the axial and proximal muscles and helps with maintaining body postures and balance. After a stroke, the corticospinal tract of the ipsilesional hemisphere is largely interrupted. A typical sign is the great loss of hand dexterity (Kuypers, 1981). It has been shown that post-stroke motor function is correlated with the corticospinal tract damage (Maraka et al., 2014) and the post-stroke potential for recovery is determined by the functional integrity of the corticospinal tracts (Stinear et al., 2007).

<table>
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<tr>
<th>Table 2.2 Motor Neuron Pathways</th>
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<tr>
<td><strong>Direct Cortical Projection</strong></td>
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<td>Lateral corticospinal tract</td>
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Figure 2.3 Direct and indirect cortical projections (Lemon, 2008).
Left: corticospinal projections are shown in blue, which includes the lateral corticospinal tract terminating contralaterally in the dorsolateral intermediate zone (red area) and the medial corticospinal tract terminating bilaterally in the ventromedial intermediate zone (green area). Blue region with small black circles indicate motoneurons innervating the arm and hand. Right: Group A fibers include reticulospinal, tectospinal, vestibulospinal tract. Group B fibers include rubrospinal tract. These brainstem pathways receive significant cortical projections (black).

2.6 Reticulospinal tract

Reticulospinal tract originates from ponto-medullary reticular formation and relays neural pulses from the corticobulbar tract to the motor neurons of the spinal cord. Corticobulbar tract originates from the cortical layer V and travels in parallel with the corticospinal tract, but only terminates at the level of brainstem and gives rise to the bulbospinal pathway including reticulospinal tract. Reticular formation is known as small clusters of neurons that are scattered
among the diffuse fibers that course through the tegmentum. Reticulospinal tract terminates primarily in the medial parts of the gray matter where they influence the local circuit neurons that coordinate axial and proximal limb muscles. The reticulospinal system is involved both in the control of locomotion and of the anticipatory postural changes needed to support these movements (Drew et al. 2004). Noted that reticulospinal tract also extended its axons to distal muscles of the limb such as the hand (Baker, 2015). New evidence found in primate monkeys showed that stimulation of the ponto-medullary reticular formation neurons resulted in facilitation of ipsilateral flexors while suppressing ipsilateral extensors on the paretic hand (Soteropoulos et al., 2012; Riddle and Baker, 2010). In monkeys that had recovered from a unilateral lesion of the pyramidal tract, corticoreticular input to forearm flexors and intrinsic hand muscles is significantly increased (Riddle et al., 2009; Baker et al., 2015).

The reticulospinal tract remains intact after most supraspinal strokes. Although the ipsilesional corticoreticular tract is interrupted along with the corticospinal tract, the contralesional corticoreticular tract projects bilaterally and allows motor commands to descend from the motor cortex to the reticular formation. It has been suggested that reticulospinal tract is able to rely neural commands to the distal joints and therefore has the potential to rehabilitate the hand after stroke (Baker, 2015). It was also reported that the fiber volume of the corticoreticular projection in the unaffected hemisphere seems to be related to walking ability in patients with chronic stroke (Jang, 2012). However, it is still largely unknown what role the cortico-reticulo-spinal tract plays after stroke.
2.7 Rubrospinal tract

Another brainstem structure, the red nucleus, also contributes upper motor neuron pathways to the spinal cord and gives rise to rubrospinal tract (Kennedy, 1990). Rubrospinal tract descends contralaterally in the dorsolateral funiculus and terminates in the lateral regions of the ventral horn and intermediate zone. In humans, the red nucleus is limited to the cervical level and do not project to the rest of the spinal cord (Lemon, 2008; Purves, 2004). Functionally, it shows similar impact as the reticulospinal tract as facilitating flexion-biased movements in the elbow and wrist (Lemon, 2008). The termination cervical area in turn gives rise to short propriospinal neurons.

2.8 Propriospinal tract

The propriospinal system is a collection of short and long nerve fibers that interconnect various segments of spinal cord and is important in forearm movements in cats such as during reaching for targets (Alstermark et al., 1984). The long propriospinal fibers originate from the ventromedial part of the intermediate zone and link separated cervical and lumbar enlargement. The short propriospinal fibers extend fewer segments of the spinal cord than the long propriospinal fibers. In macaque monkeys, after a complete corticospinal lesion in C5, the ability to reach and grasp the target remained (Sasaki et al., 2004). In humans, it has been shown that non-monosynaptic excitation of wrist flexors might be mediated via C3-C4 propriospinal system (Malmgren et al., 1998). It is not unlikely that propriospinal system could rely motor commands in a post-stroke brain in a way similar to the reticulospinal tract, but it is not clear how it influences the motor control with regards to the upper extremity.
2.9 Vestibulospinal tract

Vestibulospinal tract originates from the vestibular nuclei and descends to the spinal cord motoneurons that control axial and proximal muscles. Vestibular nuclei receive sensory information from the semicircular canals and the otolith organs that help to position the head. Vestibulospinal tract also has two routes. Vestibulospinal fibers that terminate in the medial region of the spinal cord are called medial vestibulospinal tract, which projects to motoneurons that innervate the axial muscles. Other fibers that terminate more laterally are collectively named lateral vestibulospinal tract, which are essential for control of the proximal muscles. The major function of vestibulospinal tract is to maintain head and eye coordination, posture and balance, and position of the limbs (Martini, 2010).

A few studies reported that post-stroke spasticity might be related to the hyperexcitability of vestibulospinal tract (Miller et al., 2014; Li and Francisco, 2015), but no evidence has shown that the vestibulospinal tract contributes to the expression of post-stroke flexion synergy.

2.10 Introduction to Neural Machine Interfaces

Neural machine interfaces, or brain machine interfaces, are the application of re-routing movement-related signals around damaged parts of the nervous system to aid paralyzed patients for the purpose to regain the lost functions. The application of neural machine interfaces has been reported in restoring damaged hearing, sight and movement. The most common movement-related signals include but not limited to bio-signals recorded from the scalp (EEG) or muscles (EMG). In recent years, significant progress for restoring movement has been made in the application of neural machine interfaces in individuals with disabilities. For example, John Donoghue’s group from Brown University implanted 96 electrodes into the cortex of a patient with a C3 tetraplegia.
After the implantation, the patient was successfully able to move a cursor on a screen to issue commands (Hochberg et al., 2006). Another example is the Targeted Reinnervation developed by Dr. Todd Kuiken from Rehabilitation Institute of Chicago. Targeted reinnervation allows amputees to control an artificial limb and regain a sense of feedback with the implementation of nerve transplantations and pattern recognition of bio-signals (Kuiken et al., 2007; Zhou et al., 2005). Figure 2.4 shows a schematic description for a brain machine interface demonstrating how to use EEG signals to decode commands for controlling an artificial limb (Rothschild, 2010).

![Figure 2.4 Schematic description for a brain machine interface](image)

Figure 2.4 Schematic description for a brain machine interface (adapted from Rothschild, 2010).

Figure 2.5 illustrates the process of using EMG recordings to classify different hand movements. Step 3 depicts when the features of the pre-processed signals are extracted. Usually
these features are chosen to best represent the original signals. Ideally, features should be independent from each other and capture the different aspects of the original signals. Time-domain features such as amplitude (Hudgins et al., 1993, Oskoei and Hu, 2007, Zhou et al., 2007), the frequency domain- (Merletti et al., 1997, Li et al., 2014), and the time-frequency domain- features (Englehart et al., 1999, Zhou et al., 2009, Nurhazimah et al., 2016) have been broadly investigated for the efficiency in the classification of movements. Englehart and Hudgins also suggested optimizing parameters for feature extraction such as window length, window overlap and increment to produce models with low bias and variances (Englehart and Hudgins, 2003, Scheme et al., 2011). Following feature extraction, classifiers are usually built to classify different movements based on the features provided. Earlier work by Scheme et al. has demonstrated the effectiveness of different classifiers in detecting movements (Figure 2.6).

![Figure 2.5 Pipeline of classifying hand movements based on the EMG recordings.](image)

Application of neural machine interfaces to the stroke population has been making steady progress. For instance, high classification rates of classifying multiple hand movements have been reported using high-density electrode recordings in a group of individuals with chronic stroke (Zhang et al., 2012). However, the post-stroke motor impairments such as weakness, spasticity, and abnormal muscle synergies significantly affect the accurate recognition of movement patterns.
In one study investigating the classification accuracies of six different hand movements, Sang et al. reported that individuals who are highly impaired have a lower classification rate than the ones who are less impaired (Sang et al., 2011). With bipolar EMG recordings, it was found that lifting shoulder with progressively greater levels of shoulder abduction loading resulted in great reduction in classification accuracies (Lan et al., 2013). Shoulder abduction loading also had a negative impact on the classification of hand opening with EEG recordings in individuals with stroke (Yao et al., 2016).

Figure 2.6 Comparison of several common classification techniques using conventional classification error. Results represent the average over 11 classes of motion collected from 10 able-bodied subjects. The error bars show the standard deviation across subjects.
3 THE IMPACT OF SHOULDER ABDUCTION LOADING ON VOLITIONAL HAND OPENING AND GRASPING IN CHRONIC HEMIPARETIC STROKE

3.1 Abstract

Background. Up to 60% of individuals with moderate to severe chronic hemiparetic stroke experience excessive involuntary wrist/finger flexion that constrains functional hand movements including hand opening. It’s not known how stroke-induced brain injury impacts volitional hand opening and grasping forces as a result of the expression of abnormal coupling between shoulder abduction and wrist/finger flexion or the flexion synergy. Objective. The goal of this study is to understand how shoulder abduction loading affects volitional hand opening and grasping forces in individuals with moderate to severe chronic hemiparetic stroke. Methods. Thirty-six individuals (stroke: 26; control: 10) were recruited for this study. Each participant was instructed to perform maximal hand opening and grasping forces while the arm was either fully supported or lifted with a weight equal to 25% or 50% of the participant’s maximal shoulder abduction torque. Hand pentagon area, defined as the area formed by the tips of thumb and fingers, was calculated during hand opening. Forces were recorded during grasping. Results. In individuals with moderate stroke, increasing shoulder abduction loading reduced the ability to maximally open the hand. In individuals with severe stroke, who were not able to open the hand, grasping forces were generated and increased with shoulder abduction loading. Stroke individuals also showed a reduced ability to control volitional grasping forces due to the enhanced expression of flexion synergy.
Conclusions. Shoulder abduction loading reduced the ability to volitionally open the hand and control grasping forces after stroke. Neural mechanisms and clinical implications of these findings are discussed.
3.2 Introduction

A majority of individuals with stroke report impaired upper extremity function, particularly of the hand, as a major problem (Broeks et al., 2015). In addition to wrist and finger weakness being greater for extensors compared to flexors (Kamper et al., 2003; Kamper et al., 2006) and a significant loss of finger individuation (Lang and Schieber, 2003; Lang and Schieber, 2004; Raghavan et al., 2006), lifting of the paretic arm results in abnormal involuntary coupling with wrist and finger flexion. This abnormal coupling is proportional to the amount of lifting or shoulder abduction (Miller and Dewald, 2012) and is commonly referred to as the “flexion synergy” (Brunnstrom, 1970). A review of past studies shows that the paretic hand poststroke has been mostly studied in isolation, that is, with the arm fully supported against gravity (Kamper et al., 2003; Kamper et al., 2006; Lang and Schieber, 2003; Lang and Schieber, 2004), thus neglecting the deleterious effects of flexion synergy on hand function. Even though more recently the effect of the flexion synergy was considered during lifting and reaching (Miller and Dewald, 2012), it was studied with the paretic hand relaxed. Failure to study hand dysfunction within the context of proximal joint demands has impeded the progression of the field in its attempts to discern the mechanisms responsible for hand dysfunction and subsequently develop more effective targeted rehabilitation interventions. The goal of this study is therefore to determine, for the first time, the effect of the expression of the flexion synergy on volitional hand function, examined by measuring the effect of various levels of shoulder abduction loading on hand opening and grasping. This should advance our understanding on how the paretic hand function is impacted by proximal joint demands poststroke. Our findings are that individuals with moderate to severe chronic hemiparetic stroke showed a reduced ability to volitionally open the paretic hand with increased shoulder abduction loading, quantified by a decreased hand pentagon area. The ability to control volitional
grasping forces was also reduced with increased shoulder abduction loading. Note that neither of these effects were found in control participants. The underlying neural mechanisms and clinical implications of these findings are discussed. Parts of this work have been previously published in a conference proceeding (Lan et al., 2014).

3.3 Methods

3.3.1 Participants

A total of 36 individuals (stroke, 26; control, 10) participated in this study. Participant demographics are listed in Table 1. Control participants were age-matched to the stroke participants and reported no history of cerebral vascular accidents. Stroke participants were selected from the Clinical Neuroscience Research Registry that is housed in the Rehabilitation Institute of Chicago, as well as from individuals residing in the Chicago area who wished to participate in the study. Qualified stroke participants met the following inclusion criteria: (1) sustained a unilateral lesion at least 1 year prior to participation in this project; (2) paresis confined to one side; (3) absence of a brainstem and/or cerebellar lesion; (4) absence of severe concurrent medical problems (eg, cardiorespiratory impairment, changes in management of hypertension); (5) absence of any acute or chronic painful condition in the upper extremities or spine; (6) capacity to provide informed consent; (7) ability to elevate their limb against gravity up to the horizontal plane and to generate some active elbow extension; and (8) Fugl-Meyer Assessment (FMA) (Fugl-Meyer et al., 1975) within the range of 10 to 40 out of a possible 66 and 2 to 5 out of a possible 7 in Chedoke-McMaster Stroke Hand Assessment (CMSAh) (Gowland et al., 1993). Stroke individuals were assigned to 1 of 2 groups: individuals with severe impairment (n = 13, FMA = 10-25/CMSAh = 2-3) and individuals with moderate impairment (n = 13, FMA = 26-40/CMSAh = 4-5). All
participants gave informed consent for participation in this study, which was approved by the Institutional Review Board of Northwestern University in accordance with the ethical standards stipulated by the 1964 Declaration of Helsinki for research involving human subjects.

3.3.2 Experimental setup

The experiment was carried out using an arm coordination training 3-D system (ACT³D, Figure 3.1A), which consists of a modified HapticMaster robot (Moog-FCR BV, the Netherlands) and a Biodex chair and T-base support system (Biodex Medical Systems, Shirley, NY). The ACT³D allows for free movement in 3 dimensions and was used to modulate forces applied to the arm while lifting the arm thus changing shoulder abduction (SABD) loading levels (Sukal et al., 2007; Ellis et al., 2008; Ellis et al., 2016). Prior to the experiment, each participant’s maximal SABD torque was measured using a manual dynamometer (Lafayette Instrument Company, Lafayette, IN) placed just proximal to the axis of rotation of the elbow, close to the lateral epicondyle of the humerus, in a limb configuration of 85° shoulder abduction, 45° shoulder flexion, 90° elbow flexion. This limb configuration depicted the arm posture at the start of the reach where the participant lifted the upper arm to the side of the body to the level almost parallel to the horizontal plane through the shoulder and then positioned with the tip of the fingers aligned with the mid-sagittal plane in front of the body. Once the maximal SABD torque was obtained, each participant was seated in a Biodex chair (Biodex Medical Systems, Shirley, NY) with the trunk strapped to the back of the chair to prevent unwanted movement of the upper body. The to-be-tested forearm was placed in a forearm orthosis and the fingers/palm placed over a cylinder. The cylinder was rigidly attached to the orthosis and instrumented with a pressure sensor mat (Pressure Profile System Inc, Los Angeles, CA; Figure 3.1C). The orthosis/cylinder setup was also rigidly coupled
to the end effector of the ACT$^{3D}$. The sensor mat allowed real-time measurement of the pressure generated under each finger and thumb during the hand grasping task (Figure 3.1D). The grasping pressure measurements were converted to provide a distribution of forces generated by the thumb and fingers. Hand kinematic data was collected using 2 Optotrak camera systems (Optotrak 3020 and Optotrak Certus, Northern Digital Inc, Waterloo, Ontario, Canada). Five infrared, light-emitting diode markers were placed on the tip of the thumb and each finger. Nine additional markers were embedded in a Styrofoam ball to form a rigid body which was placed on the back of the hand (Figure 3.1C). The rigid body provided a dynamic reference for the markers on the thumb and fingers, so that upper limb movement did not affect the kinematic measurements of the thumb and fingers.

**Figure 3.1 Experimental Setup**
A) ACT\textsuperscript{3D} system; B) visual feedback during the task; C) a close-up of the hand attachment which shows the rigid body, the TactArray sensory mat, and all the markers attached to the fingertips; D) an example of force (unit: N) distribution measured by the TactArray sensory mat; E) demonstration of the hand pentagon area.

3.3.3 Experimental Protocol

At the beginning of the task, participants were first required to find the home position and then to reach out to a distant target (Figure 3.1B). The reaching target was located one arm length away in front of the participant on the horizontal plane at the level of 90° shoulder abduction. Once the participant successfully acquired the target, he or she was instructed to either lift up (a SABD task) or not (table task). Each participant was given 2 seconds to lift the arm off the table (SABD task), or stay relaxed (table task). After 2 seconds, while maintaining the arm in a lifted (SABD task) or supported position (table task), the participant was instructed to perform 1 of the 2 hand tasks, either hand opening or grasping with a maximal effort. Participants were required to continue to maximally open the hand or grasp for a period of 5 seconds, followed by relaxation of the hand. SABD tasks included 2 levels of loading: 25\% or 50\% of maximal SABD torque, and the table condition in which the participant’s arm was fully supported. ACD\textsuperscript{3D} was programmed to generate forces in the vertical direction resulting in a percentage of the participant’s maximal shoulder abduction once the arm is lifted off the haptic table (i.e., approximately an increase of 5° to 10° shoulder abduction). Ten to 12 repetitions of each hand task (n = 2) at each level of SABD (n = 3) were performed in a randomized order.

3.3.4 Data collection and analysis

A hand pentagon area (HPA), shown to be an effective measure in evaluating hand opening ability (Supuk et al., 2005), was used as the primary measure to quantify hand opening. HPA was
defined as the area of the pentagon formed by the tip of the thumb and fingers (Figure 3.1E). All participants were asked to rest their hand on the cylinder prior to the trial and the resting HPA formed by the initial hand posture on the cylinder served as baseline. The pentagon area was baseline corrected to zero while the hand was relaxed on the cylinder and then normalized to the maximal HPA to facilitate between-subject comparisons during hand opening. To calculate the area, HPA was broken down into 3 triangular areas, each of which was formed by the thumb and 2 fingertips, as shown in the equation,

$$HPA = S_{TIM} + S_{TMR} + S_{TRL}$$

where $S_\Delta$ denotes the triangular area, T, I, M, R, L are abbreviations for thumb, index, middle, ring and little fingers. Normalized HPA was calculated by dividing HPA by the maximal HPA measured when the hand was placed on a flat surface with maximal finger abduction. Peak HPA value was first identified during the hand opening period, and then an averaged HPA over a 100ms time window, centered at the peak value, was calculated as the HPA for one trial during a certain abduction condition. Marker location was collected at a sampling rate of 30 Hz. One participant in the severe group and three participants in the moderate group were excluded from data analysis due to difficulty in tracking the thumb position.

The synergy-induced grasping forces and the total grasping forces were calculated as the sum of the forces generated by the thumb and fingers averaged over the lifting phase without a grasp and with a grasp in a hand grasp task, respectively (Figure 3.4). The lifting phase without a grasp referred to the duration in which each participant only needed to lift the arm while generating a certain shoulder abduction load without any voluntary grasping (5.5-8 seconds in Figure 3.4).
The lifting phase with a grasp referred to the duration in which the participant was asked to maximally grasp the cylinder (8-13 seconds in Figure 3.4) while lifting the arm with a specific shoulder abduction load. To quantify the grasping forces, the peak value during the hand grasping period was first identified, and then an averaged grasping force over a 100-ms time window, centered over the peak value, was calculated as the grasping force per trial for a certain shoulder abduction load level. Volitional component of the grasping forces was defined as the difference between the total grasping forces and the synergy-induced grasping forces. On average, a total of 10 to 12 trials at each condition were included to quantify the total and synergy-induced grasping forces. Palm pressure areas were not considered due to the inconsistent measurements across participants. Maximal grasping forces were calculated as the average of the largest 3 total grasping forces across all trials and was used for normalization. Finger/thumb pressure was sampled at 100 Hz. One participant in the severe group and 2 participants in the moderate group were excluded due to difficulty in measuring the thumb forces on the sensory mat.

3.3.5 Statistics

A mixed 2-way analysis of variance (ANOVA) with repeated measures was conducted to determine whether loading (Table, SABD25, SABD50), group (severe, moderate, control) and/or their interaction explain the measured changes in HPA and total and synergy-induced grasping forces. Tests for homogeneity of variances and sphericity were run to avoid violating these assumptions. All the data used in this study are normally distributed (Shapiro-Wilk test) and thus satisfied the assumptions of an ANOVA. Post hoc comparisons with the Bonferroni adjustment were adopted to compare within-subject differences. Unless specified otherwise, results are
presented as mean ± standard error. Statistical significance was set at \( P < .05 \). The statistical analysis was performed using the IBM SPSS version 22 software.

A.

![Graph showing Hand Pentagon Area (%) over time for different conditions](image)

B.
Figure 3.2 Pentagon area changes

Pentagon area changes in (A) one individual with stroke and (B) one control individual. For the table condition, participants were instructed to open the hand at time 0 second. For SABD loading, at time 0 second, subjects were instructed to lift the arm and at time 2s, subjects were instructed to open the hand maximally and hold it for five seconds. Normalized maximum HPA for the individual with stroke: 119.93 cm$^2$, and for the control individual: 118.63 cm$^2$.

3.4 Results

3.4.1 Hand pentagon area during opening

Figure 3.2 depicts the changes of HPA in one individual with moderate stroke and one control individual between the Table/SABD25/SABD50 conditions when each participant tried to open the hand with a maximal effort. The HPA curves highlight a different trend between these two participants. While the control individual was able to open the hand with a consistent HPA at all levels of SABD condition, the stroke individual’s hand opening was affected by an increasing SABD loading.
The 2-way ANOVA with repeated measures for the maximal HPA found a significant effect of group (P < .000) and an interaction effect of loading * group (P < .000). Post hoc analysis with Bonferroni adjustment showed that the control group had the largest HPA, and the moderate group showed significantly greater HPA than the severe group. It was also found that maximal HPA decreased significantly with increased SABD loading in individuals with moderate stroke but neither in the severe group nor in the control group (Figure 3.3A). HPA was not observed in the severe group, but instead these participants generated grasping forces when they were trying to open the hand (Figure 3.3B). Implementation of the 2-way ANOVA for grasping forces during hand opening resulted in a significant effect of loading (P < .000), group (P < .000), and an interaction effect of loading * group (P < .000). Post hoc analysis with Bonferroni adjustment demonstrated that the severe group generated significantly greater amount of grasping forces during hand opening than the moderate and able-bodied group (P < .000). The severe group also generated significantly greater grasping forces at 50% of SABD loading than at 25% of SABD loading (P < .000) and during the table condition (P < .000). There was no significant difference in grasping forces between SABD loading conditions during hand opening for the moderate group. Grasping forces during hand opening were not observed in the control group.

Note that the moderate group showed both a hand pentagon area (Figure 3.3A) and grasping forces generated during hand opening (Figure 3.3B). This occurred because moderately impaired individuals could not extend all 5 digits as controls during hand opening. In these participants, there were some digits that could be more extended than others. The number of extended digits varied among participants. As a result, the moderate group generated a HPA, due to partial hand opening, and grasping forces simultaneously. It is also worth noting that there were error bars for the severely impaired group (Figure 3.3A). This is because some severely impaired
individuals, when asked to maximally open the hand, generated greater finger flexion, which resulted in a smaller HPA than the resting HPA. After baseline correction, this smaller HPA was converted into a negative value and therefore created the error bars in Figure 3.3A.

A.

B.
Figure 3.3 Hand Pentagon Area and Grasping Forces during Hand Opening

A). Pentagon area for severe (N=12), moderate (N=10), and control (N=10) groups. B). Grasping forces during hand opening for severe (N=12), moderate (N=11), control groups (N=10). *: p<0.05, **: p<0.01; ***: p<0.001.

3.4.2 Grasping force generation

Figure 3.4 depicts the changes of grasping forces in one individual with moderate stroke and one control individual between the Table/SABD25/SABD50 conditions when each participant tried to grasp with a maximal effort. The most evident difference between the stroke and control figures is that during the lifting phase (5.5s-8s), the stroke individual generated an increased level of synergy-induced grasping forces with SABD loading, in contrast to the control individual. However, the total grasping forces generated during the grasping phase (8-15s) were largely indistinguishable between SABD loading conditions and between groups.
Figure 3.4 Grasping Forces in One Stroke Individual and One Control Individual

Grasping force changes in (A) one individual with moderate stroke and (B) one control individual. Participants were instructed to start to reach at time 0 second. For SABD loading, at time 5.5 second, subjects were instructed to lift the arm and at time 8 second, subjects were instructed to grasp the cylinder maximally and hold it for five seconds. For the table condition, subjects did not lift the arm. Normalized maximum grasp forces for the individual with stroke: 258.6 N, and for the control individual: 465.3 N.

Figure 3.5 illustrates the group results for grasping forces generated during SABD loading without grasp (in blue, i.e., synergy-induced grasping forces) and with grasp (in blue + yellow, i.e., total grasping forces). The 2-way ANOVA with repeated measures found a significant effect of
loading (P < .000), group (P < .000), and an interaction effect of loading * groups (P = .000) for synergy-induced grasping forces, but showed no effects of loading (P = .15), groups (P = .36), or loading * groups (P = .85) for total grasping forces. Post hoc tests with Bonferroni adjustment indicated that both severe and moderate groups showed significantly greater synergy-induced grasping forces than the control group. Synergy-induced grasping forces were also significantly greater in the severe group than the moderate group. Additionally, synergy-induced grasping forces significantly increased with SABD loading in the 2 stroke groups but not in control group (Figure 3.5). In contrast, the total grasping forces were not significantly different between groups and remained consistent between SABD loading conditions.

3.5 Discussion

The main finding of this study is that following a stroke, increased SABD loading results in greater synergy-induced wrist/finger flexion, which progressively limits the ability to volitionally open the paretic hand or control volitional grasping forces. Individuals with more severe impairment are no longer able to open their hands and generated net grasping forces when asked to open the hand.
Figure 3.5 Grasping Forces in Severe Stroke Group, Moderate Stroke Group and Control Group

Grasping forces in individuals with severe (N=12) and moderate (N=11) chronic hemiparetic stroke, and control individuals (N=10). Grasping forces generated due to SABD loading (blue) and SABD loading + Grasp (blue + yellow) are shown in each group. The blue bridges and asterisks indicated the within-group and between-group significance in synergy-induced grasping force under the SABD loading conditions. TB: fully supported by the haptic table; 25: 25% of maximal SABD torque; 50: 50% of maximal SABD torque. *: p<0.05, **: p<0.01; ***: p<0.001.

3.5.1 Possible neural mechanisms

Volitional hand function, particularly requiring fine and fractionated finger control, relies on the integrity and volume of the corticospinal tract (Lawrence and Kuypers, 1968). Following a stroke, the individual’s ability to volitionally control the hand is often seriously affected due to a loss of corticospinal projections from the ipsilesional hemisphere. The neural mechanisms underlying the expression of flexion synergy are not yet fully known, but it has been suggested that residual undamaged bulboospinal pathways, particularly the reticulospinal tract, may play a role in post-stroke hand function (Miller and Dewald, 2012; Lan et al., 2014; Baker, 2011; Baker
et al., 2015). For example, in the monkey primate, recovery of upper limb function after damage to the motor system utilizes the reticulospinal tract in order to relay motor commands targeting motoneurons projecting to extrinsic and intrinsic hand muscles, especially of finger flexors (Baker, 2011; Baker et al., 2015). More specifically, it was found that mono- and disynaptic inputs from reticulospinal fibers to the forearm flexor and intrinsic hand muscles were significantly increased after a lesion of the pyramidal tract, while inputs to the extensors showed no change (Baker et al., 2015). In humans there is indirect evidence, using transcranial magnetic stimulation, that stroke-induced losses in corticospinal and corticoreticular pathways (collectively called corticofugal pathways) from the ipsilesional hemisphere may result in strengthening of the connections in the contralesional corticoreticulospinal pathways (Schwerin et al., 2008; Schwerin et al., 2011; Alagona et al., 2001; Strens et al., 2003). The upregulated use of the contralesional corticoreticulospinal tract may explain relatively greater preservation of wrist and finger flexion than the extension given the connectivity of the contralesional reticulospinal system (Davidson et al., 2006; Davidson et al., 2007). For instance, monkey primate studies using spike-triggered averaging to explore the effect of reticulospinal stimulation on arm and hand muscles, demonstrated that the reticulospinal tract tends to facilitate flexors and suppress extensors ipsilaterally, and facilitate extensors and suppress flexors contralaterally (Davidson et al., 2006; Davidson et al., 2007). Consequently, an increased reliance on the contralesional corticoreticulospinal pathway, as a function of shoulder abduction, may cause abnormal muscle coactivation patterns between shoulder abduction and elbow and wrist/finger flexion due to the extensive branching of this pathway at the level of the spinal cord (Baker et al., 2015; Peterson, 1984; Peterson et al., 1979; Illert et al., 1978). Additionally, an upregulated corticoreticulospinal pathway (Schwerin et al., 2008) is expected to increase its neuromodulatory drive which may
further enhance the reticulospinal’s ionotopic effect on wrist and finger flexor motoneurons poststroke (McPherson et al., 2008). Previous studies examined the effect of such upregulated neural drive by increasing shoulder abduction loading on the paretic side and found that hand flexion was involuntarily coupled to the shoulder and elbow after stroke (Miller and Dewald, 2012).

In this study, the reduced HPA in the moderate group and the increased level of grasping forces in the severe group as a function of SABD loading during hand opening can be explained by an increased reliance on the reticulospinal tract. There is also indirect evidence that after a stroke the contralesional corticoreticulospinal tract has been upregulated (Schwerin et al., 2008; Jang et al., 2013), which results in a deviation of kinematics and kinetics of the impaired hand with a flexion bias. Interestingly, the SABD loading did not show an impact on the total grasping forces, while the synergy-induced grasping forces increased. This suggests that more severely impaired individuals have lower capability to control volitional grasp, especially when lifting with a greater SABD loading due to the increased contribution of synergy-induced grasping forces. Compared with the table condition, a greater portion of neural resources may be allocated to driving the shoulder when the participants lift with SABD loading, leaving more limited neural resources to volitionally drive the hand. In contrast, control participants were not affected by the SABD loading and maintained a consistent level of maximal volitional grasping forces.

3.5.2 Impact of changes in muscle properties at the paretic hand

Alterations in muscle properties such as muscle atrophy, muscle stiffness, and contracture have been reported along with neurologic changes following stroke (Kamper et al., 2003; Kamper et al., 2006; Triandafilou et al., 2012). While the relative contribution of these muscular changes to hand dysfunction within the context of flexion synergy is still not fully understood, past studies
have suggested that the impact of muscle properties on the hand impairment is quite small in comparison with the contribution from neural sources. For instance, from the work of Kamper (Kamper et al., 2006) in measuring mechanical contribution to hand impairment, it was shown that muscle contracture in the paretic hand represented at most 20% of the peak isometric extension in the non-paretic hand, suggestive of small effect of the muscle property changes on hand impairment compared to neural-induced motor impairments. Another study investigating muscle atrophy after stroke reported that muscle size in the paretic hand was reduced with respect to the muscle size in the nonparetic hand, but it further addressed that the relatively small percent atrophy observed in this study could not account for the marked motor impairments in hemiparetic stroke (Triandafilou et al., 2012).

In our study, we strived to reduce the impact of biomechanical factors on the paretic hand by purposefully placing the fingers over the cylinder allowing unconstrained finger extension (Figure 3.1) rather than using an isometric setup or being inside a cast. The initial flexed hand posture permitted us to greatly reduce the possible contribution of passive stiffness generated at the wrist and fingers. Additionally, passive stiffness induced pressures were measured by the sensory mat and were baseline corrected to eliminate its impact on the grasping measures. By making these efforts to minimize the potential impact of these muscle property changes, we were able to concentrate on synergy-induced grasping forces, total grasping forces, as well as changes of the hand pentagon area.

3.5.3 Clinical implications for recovery of hand function after stroke

Use of the corticoreticulospinal tract has been suggested as a potential candidate for the recovery of hand function post stroke (Baker, 2011; Baker et al., 2015). Although outputs from
the reticulospinal tract are considered to be too weak to significantly activate motoneurons of hand muscles (Baker et al., 2015), it is believed that the neuromodulatory component of the reticulospinal system has been upregulated as well following stroke-induced loss of corticoreticular projections (McPherson et al., 2008). After such a change in neuromodulation mediated via reticulospinal tract, the synaptic drive could be enhanced to strengthen the activation of especially finger flexor motoneurons (Schwerin et al., 2008; Drew et al., 1986). However, an upregulated reticulospinal tract may also come at a cost of deleterious effects especially when activating shoulder abductors, resulting in more involuntary flexion generated at the wrist and fingers and thus preventing any effective recovery of hand function (Miller and Dewald, 2012). Given the results from the present study, an upregulated reticulospinal tract reduces the ability to volitionally open the hand and results in the generation of grasping forces, especially among individuals with more severe impairment. Thus, the use of the corticoreticulospinal tract for hand recovery may not be functionally effective. While the increased SABD loading did not affect the total grasping forces during hand grasping, the reduction in volitional control is related to the increased synergistic drive presumably by progressively relying more on the corticoreticulospinal tract, which is believed to act as the backup system to the corticospinal pathway (Baker, 2011; Baker et al., 2015; Honeycutt et al., 2013).

Using inhibitory transcranial cathodal direct current stimulation (tDCS) over the contralesional motor cortex has shown to be effective in enhancing motor skills acquisition of the paretic hand following a mild stroke (Zimerman et al., 2012). Other efforts aiming at reducing the reliance on the contralesional corticoreticulospinal tract may also have a positive effect on the recovery of arm function. For instance, improvement in the reaching area was reported following an intervention implementing progressive SABD loading (Ellis et al., 2005; Ellis et al., 2009).
possibly by using the remaining corticofugal resources from the lesioned hemisphere. Similarly, facilitatory anodal tDCS over the lesioned motor cortex increases reaching distance during 25% of maximal SABD loading following stroke (Yao et al., 2015). However, it is not yet clear whether such interventions can be extended to the recovery of hand function. To establish an effective treatment for the hand, it is recommended that clinical efforts should target on reducing the impact of neural drive descending via the corticoreticulospinal tract, either through induced inhibition of the reticular formation or through the increased use of remaining corticofugal projections from the lesioned hemisphere to reduce the expression of the flexion synergy and increase dexterity of the paretic hand.

Extensor weakness undoubtedly plays an important role in the inability to open the hand in the presence of the flexion synergy, particularly in more severely impaired individuals (Kamper et al., 2006). As the results shown in Figure 3.3, the severe group showed no sign of opening not only because of the increased wrist and finger flexion but possibly also due to the very weak activation of the extensors. Efforts aimed at reducing the impact of the flexion synergy will help decrease the grasping forces generated during hand opening, but may not be as effective in severely impaired individuals compared to moderately impaired individuals due to weakness in the extensors (Kamper et al., 2006).

3.6 Future studies

Future studies should focus on understanding the structure and function of the corticoreticulospinal tract and its impact on hand disability following stroke. Quantification of the volume and integrity of contralesional corticoreticular projections and ipsilesional corticofugal projections using magnetic resonance imaging may help elucidate the changes in neural drive and
advance our understanding of neural mechanisms underlying the expression of the flexion synergy. Additionally, the progressive increase in SABD loading while reaching and opening the hand to grasp an object should be included in any future intervention, especially in individuals with moderate upper extremity impairment who retain some ability to open the hand. This is likely to reduce the negative effects of the flexion synergy on hand function over time.
4 INCREASED SYNERGISTIC NEURAL DRIVE, AS REVEALED BY EMG/EMG WAVELET COHERENCE, IS RELATED TO HAND IMPAIRMENT IN INDIVIDUALS WITH POST-STROKE FLEXION SYNERGY

4.1 Abstract

Background: Prior evidence has shown that increasing shoulder abduction loading progressively reduces the ability to voluntarily open the paretic hand and control grasping forces in individuals with moderate to severe hemiparetic stroke. Abnormal coupling of shoulder abduction with wrist and finger flexion (i.e. flexion synergy) is common in 40% to 60% of the stroke population, however, the precise underlying neural mechanisms are still under debate. In this study, we propose to investigate whether the expression of flexion synergy on the paretic hand is related to the increased shared neural drive to the shoulder abductor and wrist/finger flexor muscles.

Methods: A total of 28 individuals (stroke: 18, control: 10) participated in this study. Synergistic neural drive was quantified by calculating the wavelet coherence between EMG signals from the intermediate deltoid (mDEL) and the forearm muscles. Synergy-induced hand impairment was quantified by measuring the grasping forces generated in a grasping task and a pentagon area generated by connecting finger and thumb tips to quantify hand opening during shoulder abduction loading. Correlation analysis was conducted to determine whether the magnitude of wavelet coherence is related to grasping forces or pentagon area. Results: Overall, the stroke group showed significantly greater α-band coherence in the wrist/finger flexors and mDEL than the able-bodied group. The α-band coherence of wrist/finger flexors and mDEL has a positive relation with the synergy-induced grasping force and a negative relation with the hand pentagon area. Additionally,
the able-bodied group showed stronger $\beta$-band coherence in the wrist/finger flexors in a grasping task and stronger $\beta$-band coherence in the wrist/finger extensors in an opening task than the stroke group. **Conclusion:** Results from this study support the hypothesis of a stroke-induced strengthened shared neural drive to both shoulder abductor and wrist/finger flexors. The correlation of the $\alpha$-band coherence of the wrist/finger flexors and mDEL with the hand pentagon area and the grasping forces suggests that synergy-induced hand impairment is related to an increased shared neural drive to flexor synergy muscles.
4.2 Introduction

Previous evidences of synchronized activities of motor unit firing or EMGs (Farmer et al., 1993a; Farmer et al., 1993b) revealed that motoneuron pools of synergistic muscles share a common presynaptic drive. After a stroke, an abnormal movement pattern, commonly known as flexion synergy, is often expressed in the paretic upper extremity and described as the stereotypical muscle coactivation pattern of the shoulder abductor with the elbow flexor and wrist/finger flexors (Dewald et al., 1995; Miller and Dewald, 2012; Lan et al., 2017). Functionally, the flexion synergy limits the ability to voluntarily open the hand and/or grasp an object, especially when the paretic arm is lifted at the same time (Lan et al., 2017). In this study, we propose to determine whether the flexion synergy-induced hand impairment is related to increased reliance on neural resources that provide a shared neural drive to the shoulder abductor and wrist/finger flexors. It is postulated that an increased shared neural drive should produce EMGs that are more synchronized between flexion synergy muscles (i.e. shoulder abductor and wrist/finger flexors) in individuals with moderate to severe stroke compared to age-matched able-bodied individuals.

Earlier studies suggest that a loss of the corticospinal tract (CST) and the increased use of contralesional cortico-reticulospinal tract (CRT) could contribute to the expression of flexion synergy (Dewald et al., 1995; Miller and Dewald, 2012; Lan et al., 2017). Such a greater use of alternative brainstem mediated neural tracts produces motor activities such as action potentials or EMGs synchronizing in different frequency ranges from an intact neural system (Farmer et al., 1993a). Specifically, in able-bodied individuals, common presynaptic inputs that propagate via the CST generate motor unit synchronization in the $\beta$-band (16~30Hz) (Farmer et al., 1993a; Farmer et al., 1993b; Gross et al., 2000). But brain injury that has caused a loss of the CST, such as following a stroke for example, often results in little $\beta$-band synchronization between intrinsic
hand muscles (Farmer et al., 1993a). Conversely, synchronization in the $\alpha$-band (8–13Hz) has been found in both individuals with stroke and able-bodied individuals. For instance, Farmer and colleagues found the $\alpha$-band motor unit synchronization between pairs of motor units in the intrinsic hand muscles was preserved after stroke (Farmer et al., 1993a). In able-bodied individuals, Kilner showed there was corticomuscular coherence in the frequency range of 6–12Hz and 16–30Hz during a precision grip (Kilner et al., 1999). Several studies also reported gross wrist/hand movements, such as slow wrist extension, associated with the $\alpha$-band synchronization (Kakuda et al., 1999; Wessberg and Kakuda, 1999). CRT is comprised of fibers that relay motor commands via multiple interneurons to the spinal motor neurons. Compared to the CST, which is dominated by monosynaptic connections, the CRT delivers longer-latency excitation the slow-conducting, polysynaptic motor tracts to the spinal motoneurons thus generating motor synchronization in a lower frequency range than the $\beta$-band. CRT does not only produce neural synchronization in muscles that function on a common joint, but it should also synchronize proximal and distal muscles through its simultaneous projections to the shoulder and the hand. There is evidence that stimulation of the ponto-medullary reticular formation in the monkey primate can elicit motor responses in the hand (Soteropoulos et al., 2012). This property permits CRT to innervate the impaired shoulder and hand muscles despite the loss of CST. More importantly, the motor responses of the hand elicited by stimulation of the reticular formation is flexor-biased in the paretic arm (Davidson and Buford, 2006; Davidson et al., 2007), which is consistent with the expression of flexion synergy observed in human hemiparetic stroke. These findings support the overall hypothesis that the CRT provides a shared neural drive resulting in coactivation of shoulder abductor and wrist/finger flexors and most likely underlies the expression of flexion synergy after stroke.
To further elucidate the possibility of a shared neural drive and its relation to the impaired hand function after stroke, this study proposes to test the following hypotheses: 1) there is greater EMG coherence in the $\alpha$-band between flexion synergy muscles in individuals with moderate to severe stroke than in able-bodied individuals; 2) there is greater EMG coherence in the $\alpha$-band between flexion synergy muscles than non-flexion synergy muscles (e.g. shoulder abductor and wrist/finger extensors) in individuals with moderate to severe stroke; 3) the able-bodied individuals show greater EMG coherence in the $\beta$-band than the stroke individuals between muscles that function around a common joint (e.g. wrist flexor and finger flexor); 4) $\alpha$-band EMG coherence between flexion synergy muscles is related to synergy-induced hand impairment. Preliminary findings reporting changes in between muscle coherences post-stroke have been published in previous conference proceedings (Lan et al., 2015; Lan et al., 2016).

4.3 Methods

4.3.1 Participants

A total of 28 individuals (stroke: 18, control: 10) participated in this study. Participant demographics are listed in Table 1. Able-bodied participants were age-matched to stroke participants and reported no history of cerebral vascular accidents. Qualified stroke participants met the following inclusion criteria: 1) Sustained a unilateral lesion at least one year prior to participation in this project; 2) Paresis confined to one side; 3) Absence of a brainstem and/or cerebellar lesion; 4) Absence of severe concurrent medical problems (e.g. cardiorespiratory impairment, changes in management of hypertension); 5) Absence of any acute or chronic painful condition in the upper extremities or spine; 6) Ability to elevate their limb against gravity up to horizontal level; and 7) Scored 10~40 out of a possible 66 in Fugl-Meyer Assessment (FMA).
(Fugl-Meyer et al., 1975); 8) Scored 2–5 out of a possible 7 in Chedoke-McMaster Stroke Hand Assessment (CMSAh) (Gowland et al., 1993); 9) Capacity to provide informed consent. All participants gave informed consent for participation in this study, which was approved by the Institutional Review Board of Northwestern University in accordance with the ethical standards stipulated by the 1964 Declaration of Helsinki for research involving human participants.

### Table 4.1 Participant demographics

<table>
<thead>
<tr>
<th></th>
<th>Stroke</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yrs)</td>
<td>59±9 (40-71)</td>
<td>55±12 (42-83)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>14/4</td>
<td>4/4</td>
</tr>
<tr>
<td>Time since stroke (Yrs)</td>
<td>11±7 (1-28)</td>
<td></td>
</tr>
<tr>
<td>Side of tested UE (L/R)*</td>
<td>9/9</td>
<td>0/8</td>
</tr>
<tr>
<td>UE FMA</td>
<td>26±10 (12-39)</td>
<td></td>
</tr>
<tr>
<td>CMSAh</td>
<td>3±1 (2-5)</td>
<td></td>
</tr>
</tbody>
</table>

Yrs-years; M-male; F-female; L-left; R-right; UE-upper extremity; FMA-Fugl-Meyer Assessment; CMSAh-Chedoke-McMaster Stroke Assessment (hand). Values are listed as Mean±SD (range).

*In this study, stroke participants were tested on the paretic side, and able-bodied participants were tested on the dominant side.

4.3.2 Experimental setup

The experiment was carried out with an arm coordination training 3D system (ACT3D, Figure 3.1A) (Sukal et al., 2007; Ellis et al., 2008), which consists of a modified HapticMaster robot (Moog-FCR B.V., the Netherlands), a Biodex chair and T-base support system (Biodex Medical Systems, Shirley, NY). Prior to the experiment, each participant’s maximum shoulder abduction (SABD) torque was measured using a manual dynamometer (Lafayette Instrument Company, Lafayette, IN, USA) placed just proximal to the axis of rotation of the elbow, close to
the lateral epicondyle of the humerus, in a limb configuration of 85° shoulder abduction, 45° shoulder flexion, 90° elbow flexion. Then each participant was seated in a Biodex chair with the trunk strapped to the back of the chair to prevent unwanted movement of the upper body. The to-be-tested forearm was placed in a forearm orthosis and the fingers/palm placed over a cylinder. The cylinder was rigidly attached to the orthosis and instrumented with a pressure sensor mat (Pressure Profile System Inc., Los Angeles, CA, USA, Figure 3.1C). The orthosis/cylinder setup was also rigidly coupled to the end effector of the ACT\textsuperscript{3D} robot. The sensor mat allows real-time measurement of the pressure generated under each finger and thumb during the hand grasping task (Figure 3.1D). Finger/thumb pressure was collected at a sampling rate of 100 Hz. Hand kinematic data was collected using two Optotrak camera systems (Optotrak 3020 and Optotrak Certus, Northern Digital Inc., Waterloo, ON, Canada). Five infrared, light-emitting diode markers were placed on the tip of the thumb and each finger. Nine additional markers were embedded in a Styrofoam ball to form a rigid body, which was placed on the back of the hand (Figure 3.1C). The rigid body provided a dynamic reference for the markers on the thumb and fingers, so that upper limb movement would not affect the measurements of the thumb and fingers. Marker location was collected at a sampling rate of 30 Hz.

Surface EMGs were collected with an Avatar physiological recorder (Electrical Geodesics, Inc., Eugene, OR) from intermediate deltoid (mDEL), flexor carpi radialis (FCR), flexor digitorum superficialis (FDS), extensor carpi radialis (ECR) and extensor digitorum communis (EDC). Signals were sampled at a rate of 1000 Hz. A low-pass filter with a cut-off frequency of 450Hz was applied during collection.
4.3.3 Experimental Protocol

At the beginning of the task, participants were instructed to match the home position and then to reach out to a distant target (Figure 3.1B). Once the participant successfully acquired the target, the participant was instructed to lift the arm against a SABD load equaling 50% of the subject’s maximum SABD torque. Each participant was given 2 seconds to lift the arm. After 2 seconds, while maintaining the arm in a lifted position, the participant was instructed to perform either hand opening or grasping with a maximal effort for 5 seconds. Ten to twelve repetitions of each hand task were performed in a randomized order.

4.3.4 Data collection and data analysis

*Pentagon area and grasping force*

Hand pentagon area (HPA), shown to be an effective measure in evaluating hand opening ability (Supuk et al., 2005), was used as the primary measure in the present study for hand opening. HPA was defined as the area of the pentagon formed by the tip of the thumb and fingers (Figure 3.1E), and was baseline corrected to zero while the hand was relaxed on the cylinder. HPA was broken down into three triangular areas, each of which was formed by the thumb and two fingertips, as shown in the equation,

\[
HPA = S_{TIM} + S_{TMR} + S_{TRL}
\]

where \( S_\Delta \) denotes the triangular area, T, I, M, R, L are abbreviations for thumb, index, middle, ring and little fingers. Normalized HPA was calculated by dividing HPA by the HPA
measured when the hand was placed on a flat surface and the fingers maximally spread apart. Marker location was collected at a sampling rate of 30 Hz.

The synergy-induced grasping forces were calculated as the sum of the forces generated by the thumb and fingers averaged during lifting. Palm pressure areas were not considered due to the inconsistent measurement across participants. Maximal grasping forces were calculated as the average of the largest three grasping forces across all trials and was used for normalization. Finger/thumb pressure was collected at a sampling rate of 100 Hz.

**Wavelet coherence**

Wavelet coherence was used to examine the linear dependency of two surface EMGs in the time-frequency domain (Torrence and Compo, 1998). Wavelet coherence uses wavelet transform to analyze time series that contain nonstationary power at many different frequencies. It overcomes the weakness of non-wavelet coherence that uses finite Fourier transform and is considered efficient and reliable in detecting the synchronizing activity between two time-series (Daubechies, 1990; Grinsted et al., 2004; Jevrejeva et al., 2003). In this study, the Morlet wavelet was applied for transformation. Proposed by Torrence and Webster (Torrence and Webster, 1999), wavelet coherence of two time-series $x$ and $y$ is defined as,

$$R_n^2(s) = \frac{|S(s^{-1}W_{n}^{XY}(s))|^2}{S(s^{-1}|W_{n}^{X}(s)|^2) \cdot S(s^{-1}|W_{n}^{Y}(s)|^2)}$$

where $W_{n}^{X}(s)$ and $W_{n}^{Y}(s)$ are the wavelet transform of time series $x$ and $y$, $W_{n}^{XY}(s)$ is the cross wavelet transform, $S$ is a smoothing operator, defined as,
\[ S(W) = S_{scale}(S_{time}(W_n(s))) \]

where \( S_{scale} \) denotes smoothing along the wavelet scale axis and \( S_{time} \) smoothing in time. Details regarding the definition of smooth factor can be found in Grinsted’s study (Grinsted et al., 2004).

Wavelet coherence of the following muscle pairs was calculated: FDS-mDEL, FCR-mDEL, EDC-mDEL, ECR-mDEL, FDS-FCR, and EDC-ECR. Monte Carlo stimulations were applied to determine the 5% statistical significance level of the coherence (Grinsted et al., 2004). For the proximal and distal pair, the average of FDS-mDEL and FCR-mDEL coherence was used to represent the flexors-mDEL coherence. Similarly, extensors-mDEL coherence represented the average of EDC-mDEL and ECR-mDEL coherence.

4.3.5 Statistics

A 3-way mixed ANOVA was conducted to determine whether an interaction effect existed between muscle pairs (flexors/extensors), hand tasks (opening/closing) and groups (the stroke/able-bodied groups) in explaining the EMG-EMG coherence. Data were first examined to be normally distributed and have no significant outliers. Tests for homogeneity of variances and sphericity were also used to check whether these assumptions were violated. Post hoc comparisons with the Bonferroni adjustment were adopted to compare within-subject and between-group differences. A Pearson’s product-moment correlation (2-tailed) was run to assess whether there was a correlation between the \( \alpha \)-band flexors-mDEL coherence and synergy-induced grasping force as well as the HPA in the stroke group. Strength of association was moderate if the absolute
value of correlation coefficient lied in between 0.5 and 0.7 and strong if it was greater than 0.7. Statistical significance was set at \( p<0.05 \). All statistical analysis was performed with IBM SPSS version 22.

### 4.4 Results

Figure 4.1 presents an example of one stroke case and one able-bodied case performing a hand grasping task while lifting with 50% of the maximal SABD torque (SABD50). Grasping forces generated by the stroke participant and the able-bodied participant are shown in Figure 4.1A and Figure 4.1D, respectively. EMG recordings from FDS, FCR and mDEL are shown in Figure 2B and 2E and are aligned with the grasping forces. Figure 4.1C and 4.1F show the coherence heat map in the time-frequency domain from three pairs of EMG recordings, namely, FCR-FDS, FCR-mDEL, FDS-mDEL. For all these 3 pairs, the stroke participant demonstrates strong EMG-EMG coherence in the 8~13Hz during the holding phase of maximal grasp while the able-bodied participant shows little in the same frequency range. In contrast, in the \( \beta \)-band (16~30 Hz), the stroke participant shows no activities, while able-bodied participant demonstrates some in the coherence between the wrist and finger flexors (i.e. FCR and FDS).

Figure 4.2 compares the group results of the EMG-EMG coherence between different muscle pairs in the \( \alpha \)-band for the hand grasping task (Fig. 4.2A-B) and hand opening task (Fig. 4.2C-D). The height of bar in Figure 4.2 represents the mean value of significant coherence in the range of 8-13Hz in each tested group. Error bars are presented to show the standard error in each group. For the task of hand grasping in Figure 4.2A, the stroke group shows significantly higher coherence in flexors-mDEL than the able-bodied group (\( p<0.01 \)). Such significance is also found by comparing the coherence between flexors-mDEL and extensors-mDEL in the stroke group.
(p<0.01), suggesting a flexor-biased facilitation in the synchronized activities between mDEL and wrist/finger muscles. However, no such difference is found in the able-bodied group. For the task of hand opening in Figure 4.2C, there is also greater coherence of flexors-mDEL in the stroke group than the able-bodied group (p<0.05), and greater coherence in the flexors-mDEL than the extensors-mDEL in the stroke group (p<0.05), showing that the flexor-biased facilitation is not specific to the task of hand grasping. Figure 4.2B and 4.2D compare the group difference in the coherence of FDS-FCR and EDC-ECR. In both grasping and opening tasks, the FDS-FCR pair shows greater coherence than the EDC-ECR pair in the stroke group (p<0.05 and p<0.01, respectively). FDS-FCR coherence is also greater in the stroke group than the able-bodied group in the grasping task (p<0.05) and in the opening task (p<0.05). Mixed ANOVA results on the interactions is available in Table 2.

Figure 4.3 compares the group results of the EMG-EMG coherence between different muscle pairs in the β-band for the hand grasping task (Fig.4.3A-B) and hand opening task (Fig.4.3C-D). No significant differences are found between the stroke and the able-bodied group in the flexors-mDEL and extensors-mDEL in Figure 4.3A and 4.3C. Interestingly, in the able-bodied group a task-dependent facilitation in the agonist over the antagonist in the FCR-FDS and ECR-EDC pairs is found. Specifically, for the hand grasping task in Figure 4.3B, the able-bodied group shows greater coherence in FCR-FDS than the stroke group (p<0.05). Within the able-bodied group, the FCR-FDS coherence is also greater than the ECR-EDC coherence (p<0.05). For the hand opening task in Figure 4.3D, the able-bodied group shows greater coherence in ECR-EDC than the stroke group (p<0.05). Within the able-bodied group, the ECR-EDC coherence was also greater than the FCR-FDC coherence (p<0.05). However, no such significance was found in the stroke group. Mixed ANOVA results on the interactions are shown in Table 3.
Pearson’s correlation analysis was conducted to find whether there is a linear relation between the synergy-induced hand impairment and the wavelet coherence in the flexors-mDEL. For the hand grasping task, a moderate correlation between synergy-induced grasping forces and the $\alpha$-band flexors-mDEL coherence is found ($p=0.034$, $r=0.50$), as shown in Figure 4.4A. Synergy-induced grasping forces increase with greater $\alpha$-band flexors-mDEL coherence. Two individuals shown in the upper section of the figure 4.4A did not follow the regression line as well as others. They show a relatively weaker flexion synergy and stronger coherence than others. These two samples do not affect the results as removing them produced a stronger correlation ($p=0.020$, $r=0.57$). For hand opening in Figure 4.4B, there a strong negative correlation between the HPA and the $\alpha$-band flexors-mDEL coherence ($p=0.019$, $r=-0.76$) is shown. HPA increased as the $\alpha$-band flexors-mDEL coherence decreases. Nine stroke individuals were included for this analysis as the other half were too severe to open the hand. The observed power with these nine individuals is about 75%.
4.5 Discussion

By comparing the wavelet coherence of multiple pairs of muscles, we found there was greater EMG-EMG coherence in the flexion synergy muscles of the paretic upper extremity among individuals with chronic hemiparetic stroke than in able-bodied individuals. Specifically, 1) there was greater coherence between paired wrist/finger flexors and between wrist/finger flexors and shoulder abductor (referred collectively as ‘flexor coherence’ below) than between paired wrist/finger extensors and between wrist/finger extensor and shoulder abductor (referred collectively as ‘extensor coherence’ below); 2) the flexor coherence is significantly greater in the $\alpha$-band but not in the $\beta$-band in individuals with a stroke; 3) the higher level of flexor coherence in the stroke group than the able-bodied group is found in both the grasping and hand opening tasks; 4) in particular, the $\alpha$-band flexors-mDEL coherence has a positive relation with the synergy-induced grasping force and a negative relation with the HPA in the stroke group. It is also important to point out that the able-bodied group showed a task-dependent facilitation in the agonist over the antagonist in the $\beta$-band, which is not evident in the stroke group. A detailed discussion is provided below.
Figure 4.2 Coherence difference between stroke and able-bodied group in the α-band.

(A-B) Group results of wavelet coherence during hand grasping in the α-band. (A) Mean coherence between mDEL and wrist/finger flexors and wrist/finger extensors. (B) Coherence between FDS-FCR and EDC-ECR. EDC: extensor digitorum communis; ECR: extensor carpi radialis. (C-D) Group results of wavelet coherence during hand opening in the frequency range of 8-13Hz. (C) Coherence between mDEL and wrist/finger flexors and wrist/finger extensors. (D) Coherence between FDS-FCR and EDC-ECR. Flexors-mDEL was the average value of FCR-mDEL and FDS-mDEL coherence; Extensors-mDEL was the average value of ECR-mDEL and EDC-mDEL coherence. *: p<0.05; **: p<0.01.
4.5.1 Coherence in the flexors

The findings of greater coherence between the flexion synergy muscles in the stroke group than the able-bodied group or than the extensor coherence suggest that there should be a greater stroke-induced dependence on pathways that facilitate flexor synergy muscles in the paretic arm. It is likely that stroke has induced a profound change in how the motor commands are delivered to spinal motoneuron pools. In able-bodied cases, motor commands responsible for fine and fractionated control of the distal joints are delivered via the CST, which allows able-bodied individuals to independently control the proximal and distal joints in a demanding functional task, such as reaching-to-grasp an object. However, this level of independent joint control is lost in individuals with moderate to severe stroke during lifting of the paretic arm which results in abnormal muscle coupling with the wrist and fingers flexors (Miller and Dewald, 2012). The greater flexor coherence found in the stroke group indicates that there is a larger synergistic neural drive shared by the shoulder abductor and wrist/finger flexors, a likely result from a greater reliance on motor pathways that coactivate both proximal and distal muscles of the paretic upper extremity.

It is not entirely clear which motor pathway is responsible for the synergistic neural drive. However, there is growing indirect evidence pointing to the contralesional corticoreticulospinal tract (Dewald et al., 1995; Miller and Dewald, 2012; Lan et al., 2017) as playing an important role. One of the reasons is that the corticoreticulospinal tract has neural projections to both shoulder muscles and hand muscles. For example, in one study examining hand control in humans, it was shown that activation of reticulospinal tract resulted in coordinated movement of the whole hand (Honeycutt et al., 2013). More recent animal work also reported that the reticulospinal tract could facilitate muscles acting at the fingers and therefore it is considered as the primary resource in
distal joint control following loss of the CST after stroke (Baker, 2011). Additional evidence in the monkey primate showed that reticulospinal stimulation results in facilitation of elbow/wrist and finger flexors on the non-impaired side (Davidson and Buford, 2006; Riddle et al., 2009) and extensors at the contralateral side. Another monkey primate study showed that following a unilateral lesion of the pyramidal tract, the amplitude and incidence of synaptic inputs to forearm flexors increased significantly, while inputs to extensors remained unaffected (Baker et al., 2015). This flexor-facilitation in the paretic upper extremity is consistent with our findings of the greater flexor coherence in the stroke group, suggesting the reticulospinal tract may be responsible for mediating the flexor coherence. Fibers originating from the cortex bifurcate at the brainstem level and form a bilateral connection with the reticular formation. As stroke interrupts the ipsilesional corticofugal projections, which include both corticospinal tract and corticobulbar tract, the contralesional corticoreticular input may be upregulated resulting in both greater metabotropic input to flexor motorneurons thus amplifying the ionotropic input to the elbow/wrist and finger flexors (McPherson et al., 2008). For the able-bodied individuals, in which corticofugal input remains intact, projections to the hand muscles and the impact on the distal joints via the corticoreticular tract is relatively small (Baker, 2011), as shown by the limited α-band coherence in this group (Figure 4.1).
Figure 4.3 Coherence difference between stroke and able-bodied group in the β-band.

(A-B) Group results of wavelet coherence during hand grasping in the β-band. (A) Mean coherence between mDEL and wrist/finger flexors and wrist/finger extensors. (B) Coherence between FDS-FCR and EDC-ECR. (C-D) Group results of wavelet coherence during hand opening in the β-band. (C) Coherence between mDEL and wrist/finger flexors and wrist/finger extensors. (D) Coherence between FDS-FCR and EDC-ECR. Flexors-mDEL was the average value of FCR-mDEL and FDS-mDEL coherence; Extensors-mDEL was the average value of ECR-mDEL and EDC-mDEL coherence. *: p<0.05; **: p<0.01.
A

Synergy-induced grasping force

Flexors-mDEL coherence

\[ y = 0.0344x + 0.0288 \]
\[ r = 0.5008 \]
\[ n = 18 \]
\[ p = 0.03427 \]

B

Pentagon Area

Flexors-mDEL coherence

\[ y = -0.0368x + 0.0587 \]
\[ r = 0.7556 \]
\[ n = 9 \]
\[ p = 0.01852 \]
4.5.2 Coherence in the α- and β-band

Human motor behavior is closely associated with changes in the oscillatory activities, in which the α-band and β-band oscillation were reported to play an important role. For example, Feurra and his colleagues (Feurra et al., 2011) demonstrated that a local application of transcranial alternating current stimulation (tACS) at β-band on the primary motor cortex had an effect of increasing the size of motor evoked potentials (MEPs). This means that the neural oscillation induced by tACS in the cortical areas was likely to have changed the excitability of the corticospinal pathway that resulted in greater MEPs, suggesting the functional significance of the β-band oscillation in motor behavior. β-band oscillation was also found to be related to several aspects of motor task such as low level constant force generation (Conway et al., 1995), movement preparation and execution (Tzagarakis et al., 2015; Zaepffel et al., 2013). In able-bodied individuals, neural projections to the hand muscles are characterized by oscillatory activity in the β-band (Farmer et al., 1993a). Such oscillatory activity has been previously observed from pairs of motor units using intramuscular EMG coherence (Farmer et al., 1993a), surface EMG (Baker et al., 1997), electroencephalography (EEG) (Conway et al., 1995) and magnetoencephalography (MEG) (Gross et al., 2000). β-band oscillation is understood to originate from an oscillatory neural drive at the cortical level (Farmer et al., 1993a; Gross et al., 2000) and is believed to propagate via the fast-conducting lateral CST (Farmer et al., 1993b; Kilner et al., 1999; Marsden et al., 2000; Mima et al., 2000). Consequently, little β-band oscillation between intrinsic hand muscles was
shown in individuals with stroke (Farmer et al., 1993a). However, the $\alpha$-band coherence remained following a stroke (Farmer et al., 1993a). In the past, the $\alpha$-band oscillation has been linked to cognition (Klimesch, 1999) and working memory (Klimesch, 2012; Jensen et al., 2002. Many studies also showed that $\alpha$-band synchronization was related to tremor (Budini et al., 2014; Katja et al., 2015), gross hand movement (Kakuda et al., 1999; Wessberg and Kakuda, 1999), and precision grip (Kilner et al., 2003; Muthukumaraswamy and Johnson, 2004). Studies have associated the $\alpha$-band coherence with gross hand movement such as slow wrist extension (Kakuda et al., 1999; Wessberg and Kakuda, 1999). Kilner and colleagues reported seeing both 6~12Hz and 15~30Hz corticomuscular coherence during precision grip (Kilner et al., 2003). More recent studies also suggest that the $\alpha$-band coherence between the hand motor cortex and the rest of the brain after stroke is closely associated with a patients’ motor performance such that neurofeedback training of $\alpha$-band coherence improved motor performance (Mottaz et al., 2015). The $\alpha$-band oscillation might originate from local reticular circuits (Grosse and Brown, 2011; Nishimura and Isa, 2011), or from loops via the reticular formation involving e.g. the cerebellum (Soteropoulos and Baker, 2006; Pellerin and Lamarre, 1997; Welsh et al., 1995), or cuneate nucleus, where there is evidence of intrinsic rhythmicity around 15Hz (Canedo et al., 1998; Marino et al., 1999).

In the current study, we are seeing two different coherence results in the $\alpha$-band and in the $\beta$-band. In the $\alpha$-band, flexor coherence is stronger in both proximal-distal and distal-distal muscle pairs than the extensor coherence, suggesting an increase reliance on the flexor-biased contralesional corticoreticulospinal pathway post-stroke. In another intramuscular EMG-EMG synchronization study, Farmer and colleagues (Farmer et al., 1993a) reported finding significant values of coherence in the lower frequency range (<12Hz). He explained that the occurrence of the coherence in this range reflected low-frequency modulation of the $\beta$-band ‘carrier frequency’
of branched presynaptic inputs or the frequency content of other common branched or non-branched presynaptic inputs. Evidence has shown that the significant values of coherence in the \( \alpha \)-band should be generated by activity in inputs different from those generating the \( \beta \)-band coherence, and they possibly represent two different underlying mechanisms. Compared to its fast-conducting counterpart CST, relaying neural pulses to spinal cord motoneuron pools via a polysynaptic, slow-conducting pathway is expected to produce a longer latency in delivering motor commands and results in EMG-EMG coherence in a frequency band lower than the \( \beta \)-band. On the other hand, in the \( \beta \)-band we did not see a difference in EMG-EMG coherence between the proximal muscle and the distal muscle pair. However, the able-bodied group demonstrated stronger FCR-FDC coherence than ECR-EDC coherence in a grasping task, and stronger ECR-EDC coherence than FCR-FDC coherence in a hand opening task. It therefore seems that in the \( \beta \)-band the able-bodied group had the ability of synchronizing the neural drive to facilitate the agonists that function at a given joint (i.e. FDS and FCR for grasping, EDC and ECR for opening). It is our understanding that the observed ability of modulating the FCR-FDC and ECR-EDC coherence in the \( \beta \)-band reflects the integrity of the CST and its functional importance in motor control. While the able-bodied group preserved this ability, the stroke group showed no changes in the coherence to favor the agonist between tasks. This suggests that while the contralesional cortico-reticulospinal tract might be able to serve as an alternative pathway for the hand control after stroke, motor activity resulting from this pathway is functionally inadequate since the post-stroke brain appears to lack the task-dependent facilitation of agonists that is evident in the intact brain.
4.5.3 Coherence and post-stroke hand impairment

Results from our previous study showed that the pentagon area during the hand opening task decreased with greater levels of SABD loading in the stroke group but not in the able-bodied group (Lan et al., 2017). Additionally, individuals with chronic hemiparetic stroke demonstrated a reduced ability of controlling the volitional grasping forces as the SABD loading increased. Both results suggest that SABD loading had a negative impact on the ability to volitionally control the hand during opening and grasping post hemiparetic stroke. In the current study, we found a positive relationship between the $\alpha$-band flexors-mDEL coherence and synergy-induced grasping force and a negative relation between the $\alpha$-band flexors-mDEL coherence and HPA. This finding, for the first time, links hand impairment with an increased synergistic neural drive to the shoulder and the hand.

The clinical implication of the current finding is that treatment targeted at regaining the hand function among individuals affected by flexion synergy, should emphasize reducing the synergistic neural drive as measured by the wavelet coherence. Some progress has been reported in enhancing motor skills acquisition of the paretic hand using inhibitory transcranial cathodal direct current stimulation (tDCS) over the contralesional motor cortex. Another example is improvement in the reaching distance using facilitatory anodal tDCS over the lesioned motor cortex. In these cases, tDCS delivers stimulation effectively inhibiting the shared neural drive originating from the contralesional side and thus reducing the impact of flexion synergy on activation of wrist and finger muscles. As this neurological motor impairment is hard to quantify, the $\alpha$-band flexors-mDEL coherence measure may potentially serve as a biomarker for evaluating the effects of intervention in treating synergy-induced hand impairment. However, this application will require future investigation.
4.5.4 Technique applied to remove cross-talk

To remove the impact of electrical crosstalk on EMG coherence between distal and distal muscles, a novel algorithm proposed by Kilner and colleagues was applied to the EMGs before wavelet transform (Chan et al., 1996). The algorithm used a ‘blind signal separation’ concept developed by Chan to design the unmixing filters, which were applied to the observed signals to recover the original signals. This method has been proven to be effective in eliminating electrical crosstalk between surface EMG recordings while keeping the synchronized component with the signal.
5 REDUCING THE IMPACT OF SHOULDER ABDUCTION LOADING ON THE CLASSIFICATION OF HAND OPENING AND GRASPING IN INDIVIDUALS WITH POST STROKE FLEXION SYNERGY

5.1 Abstract

Application of neural machine interface in individuals with chronic hemiparetic stroke is regarded as a great challenge, especially for classification of the hand opening and grasping during a functional upper extremity movement such as reach-to-grasp. The overall accuracy of classifying hand movements, while actively lifting the paretic arm, is subject to a significant reduction compared to the accuracy when the arm is fully supported. Such a reduction is believed to be due to the expression of flexion synergy, which couples shoulder abduction with elbow/wrist and finger flexion, and is common in up to 60% of the stroke population. Little research has been done to develop methods to reduce the impact of flexion synergy on the classification of hand opening and grasping.

In this study, we proposed a novel approach to classify hand opening and grasping in the context of the flexion synergy using a wavelet-coherence-based filter. We first identified the frequency ranges where the coherence between the shoulder abduction muscle and wrist/finger flexion muscles is significant in each participant, and then removed the synergy-induced EMG component with a subject-specific and muscle-specific coherence-based filter. The new approach was tested in 21 stroke individuals with moderate to severe motor impairments. Employing the filter, fourteen participants gained classification accuracy in a range of 0.1% to 14%, while four showed 0.3% to 1.2% reduction in accuracy. The remaining three participants were excluded from
comparison due to the lack of significant coherence, thus no filters were applied. The improvement in classification accuracy is significant ($p=0.017$) when the shoulder abduction loading equals 50% of the maximal torque.

Our findings suggest that the coherence-based filters can reduce the impact of flexion synergy by removing the synergy-induced EMG component and have the potential to improve the overall classification accuracy of hand movements in individuals with post stroke flexion synergy.
5.2 Introduction

Functional movements that demand independent joint control of the shoulder, elbow and wrist/fingers (e.g. reach-to-grasp) are essential to activities of daily living. Unfortunately, most individuals with chronic hemiparetic stroke have lost such ability due to the stereotypical muscle coactivation patterns between shoulder abductor, elbow flexor and wrist/finger flexors, commonly referred to as the flexion synergy (Dewald et al., 1995, Sukal et al., 2007, Miller and Dewald, 2013, Lan et al., 2014, Ellis et al., 2016). Due to the expression of the flexion synergy, many individuals find it harder or even impossible to open the hand and/or grasp an object when lifting the paretic arm at the same time (Miller and Dewald, 2013, Lan et al., 2014). To overcome this difficulty, past studies have implemented statistical models to learn and translate the electrical biosignals (e.g. Electroencephalogram (EEG) or Electromyogram (EMG)) into control signals of external devices such as robotic exoskeletons (Collinger et al., 2013; Hortal et al., 2015) or functional electrical stimulation systems (Moritz et al., 2008; Pohlmeyer et al., 2009; Ethier et al., 2012). While moderate to high accuracies in learning and translating the post-stroke EMGs were reported (Sang et al., 2010, Xu and Zhou, 2012), none of them have given consideration of the deleterious effect of the flexion synergy.

Due to the flexion synergy, post-stroke EMG signals recorded at wrist and fingers during functional movements include two components (Miller and Dewald, 2013, Lan et al., 2016). One component is the voluntary EMG signals generated due to the voluntary contraction of wrist and finger muscles; and the other one is the synergy-induced EMG signals generated due to the involuntary contraction of wrist and fingers muscles associated with the activation of shoulder abductor muscles (Miller and Dewald, 2013, Lan et al., 2014). It has been shown that after a stroke synergy-induced EMG signals from the impaired hand can reach to a significant level with
increased shoulder abduction loading, even when a study participant was instructed to relax the hand (Miller and Dewald, 2013). These synergy-induced EMGs do not represent the intention of hand movements and thus are detrimental to the accurate classification of volitional hand movements (Lan et al., 2011). For example, when the impaired arm was fully supported, i.e., no effect of flexion synergy, the classification of hand movements can reach an overall accuracy of 96% with high-density myoelectric recordings (Xu and Zhou, 2012) or 95% with bipolar surface EMG recordings (Lan et al., 2011), but when lifting the paretic arm, the overall accuracy drops by 10% to 16% using EMG signals (Lan et al., 2011) or using EEG signals (Yao et al., 2015).

The overall goal of this study is to find out whether it is possible to reduce the impact of the flexion synergy on the classification accuracy of hand movements by removing the synergy-reduced EMG signals from the wrist and fingers muscles. It was noted from earlier findings that voluntary EMGs and synergy-induced EMGs may be generated using different neural pathways. The synergy-induced EMG signals are likely to be delivered via slow-conducting, polysynaptic contralesional corticoreticulospinal pathway, resulting in EMG-EMG oscillation in the alpha band (8-13Hz) between muscles that share the same neural projections (Lan et al., 2016). In contrast, voluntary EMGs are conveyed via fast-conducting, monosynaptic corticospinal pathway that produces EMG-EMG oscillation in the beta band (15-30Hz) (Farmer et al., 1993; Gross et al., 2000; Lan et al., 2016). With coherence analysis of EMGs between the shoulder abductor and wrist/finger muscles, it is possible to differentiate the synergy-induced EMGs from the voluntary EMGs by studying the coherence power during hand movements. It is our hypothesis that the overall classification accuracy in individuals with stroke should be improved after removing the synergy-induced EMGs with a specific filter. Such a filter should be coherence-based and subject-specific due to the expected between-subject variation in the frequency ranges where the coherence
of synergy-induced EMGs is significant. Classification accuracies before and after the filtering will be compared and discussed.

5.3 Methods

5.3.1 Participants

A total of 29 individuals (Stroke: 21, Control: 8) participated in this study. Participant demographics are listed in Table 4.1. Control participants were age-matched to the stroke participants and reported no history of cerebral vascular accidents. Stroke participants were selected from the Clinical Neuroscience Research Registry that is housed in the Rehabilitation Institute of Chicago, as well as from individuals residing in the Chicago area who wished to participate in the study. Qualified stroke participants met the following inclusion criteria: 1) Sustained a unilateral lesion at least one year prior to participation in this project; 2) Paresis confined to one side; 3) Absence of a brainstem and/or cerebellar lesion; 4) Absence of severe concurrent medical problems (e.g. cardiorespiratory impairment, changes in management of hypertension); 5) Absence of any acute or chronic painful condition in the upper extremities or spine; 6) Capacity to provide informed consent; 7) Ability to elevate their limb against gravity up to horizontal and to generate some active elbow extension; and 8) Fugl-Meyer Assessment (Fugl-Meyer et al., 1975) within the range of 10~40 out of a possible 66 and 2~5 out of a possible 7 in Chedoke-McMaster Stroke Hand Assessment (Gowland et al., 1993). All subjects gave informed consent for participation in this study, which was approved by the Institutional Review Board of Northwestern University in accordance with the ethical standards stipulated by the 1964 Declaration of Helsinki for research involving human subjects.
Table 5.1 Participant demographics

<table>
<thead>
<tr>
<th></th>
<th>Stroke</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yrs.)</td>
<td>59±9 (40-71)</td>
<td>55±12 (42-83)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>15/6</td>
<td>5/3</td>
</tr>
<tr>
<td>Time since stroke (Yrs)</td>
<td>11±7 (1-28)</td>
<td></td>
</tr>
<tr>
<td>Sides of tested UE* (L/R)</td>
<td>17/4</td>
<td>0/8</td>
</tr>
<tr>
<td>UE FMA</td>
<td>26±10 (12-39)</td>
<td></td>
</tr>
<tr>
<td>CMSAh</td>
<td>3±1 (2-5)</td>
<td></td>
</tr>
</tbody>
</table>

Yrs = years; M = male; F = female; L = left; R = right; UE = upper extremity; FMA = Fugl-Meyer Assessment; CMSAh = Chedoke-McMaster Stroke Assessment (hand); Values are listed as Mean±SD (range).

*In this experiment, the stroke subjects were tested at the paretic UE while the control subjects were tested at the dominant UE.

5.3.2 Equipment and Setup

The experiment was carried out using an arm coordination training 3-D system (ACT3D, Figure 5.1A), which consists of a modified HapticMaster robot (Moog-FCR B.V., the Netherlands), a Biodex chair (Biodex Medical Systems, Shirley, NY), and T-base support system (Biodex Medical Systems, Shirley, NY). The ACT3D allows for free movements in three dimensions and was used to modulate shoulder abduction torques applied to the tested arm.

For the experimental setup, each participant was seated in the Biodex chair with the trunk strapped to the back of the chair to prevent unwanted movement of the upper body. The to-be-tested forearm was placed in a forearm orthosis and the fingers/palm rested on a cylinder. The cylinder was rigidly coupled to the end effector of the ACD3D. Surface EMGs were collected using an Avatar physiological recorder (Electrical Geodesics, Inc., Eugene, OR) from intermediate deltoid (mDEL), flexor carpi radialis (FCR), flexor digitorum superficialis (FDS), extensor carpi
radialis (ECR) and extensor digitorum communis (EDC). EMGs were sampled at 1000Hz and preprocessed with a band-pass filter at a cutoff band of 5Hz~450Hz.

5.3.3 Protocol

Prior to the experiment, each participant’s maximum shoulder abduction (SABD) torque was measured using a manual dynamometer (Lafayette Instrument Company, Lafayette, IN, USA) placed just proximal to the axis of rotation of the elbow in a limb configuration of 85° shoulder abduction, 45° shoulder flexion, and 90° elbow flexion. Participants were presented with a home object and a target object on a monitor in front of them (Figure 5.1B). At the beginning of the task, participants were instructed to find the home object, trigger the trial and then reach out to the target object. Once the hand arrived at the target, the participant was given two seconds to lift the tested arm and hold the position. After the two seconds, while keeping the arm lifted, the participant was asked to perform one of the following three hand tasks for 5 seconds in a random order: 1) open the hand with a maximal effort; 2) grasp the cylinder with a maximal effort; 3) no hand movement. All participants performed these three hand tasks with two different shoulder abduction loadings equaling to 25% or 50% of the subject’s maximum SABD torque. Ten to twelve repetitions of each hand task were performed.

5.3.4 Data Analysis

5.3.4.1 Coherence

Wavelet coherence was used to examine the linear dependency of two sequences of surface EMGs in the time-frequency domain (Torrence and Compo, 1998), and is considered efficient and reliable in detecting the synchronizing activity between two time-series (Daubechies, 1990;
Jevrejeva et al., 2003; Grinsted et al., 2004). In this study, the Morlet wavelet was applied for transformation. Monte Carlo simulation methods were used to determine the 5% statistical significance level of the coherence (Grinsted, 2004). Wavelet coherences were calculated for each of following muscle pairs, i.e., FDS-mDEL, FCR-mDEL, EDC-mDEL, and ECR-mDEL for each participant and for all three hand tasks.

5.3.4.2 Algorithm

Without coherence-based filter

All EMG signals were manually segmented and concatenated to exclude the idling EMGs collected between hand tasks. A 250-ms long window was implemented to slide from the beginning to the end of the concatenated EMGs with a 50% increment and a 50% overlap between adjacent moving windows. Within each moving window, features were extracted based on the method proposed by Hudgins (Hudgins et al., 1993). This method proposes four features in the time domain: mean absolute value, zero crossings, slope sign changes and waveform length (see Table 5.2 for the definition of each of these 4 features).

Linear Discriminant Analysis (LDA) was used to classify the EMG signals in this study. LDA has been proved to be effective in EMG classification as well as with low computational cost (Scheme et al., 2011). For each of the hand tasks, LDA maximizes the posterior probability of Bayesian equation and assigns the class labels (i.e. hand open, grasp, or relax) with the largest possibility,

\[
\arg\max_j p(y_j|x_{ij}) = \frac{p(x_{ij}|y_j) * p(y_j)}{\sum_{i=1,j=1}^{n,m} p(x_{ij}|y_j) * p(y_j)}
\]
where $x_{ij}$ and $n$ represent the features and the number of features in the training set, $i$ indicated the $i$th feature, $j$ indicated the $j$th category, $y$ is classification category.

**Table 5.2** EMG features extracted in the time domain

<table>
<thead>
<tr>
<th>Features</th>
<th>Description</th>
<th>Features</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero crossing</td>
<td>$x_kx_{k+1} &lt; 0$ and $</td>
<td>x_k - x_{k+1}</td>
<td>\geq \varepsilon$</td>
</tr>
<tr>
<td>Absolute amplitude</td>
<td>$x_i = \frac{1}{L} \sum_{k=1}^{L}</td>
<td>x_k</td>
<td>$ for $i = 1, 2, ..., L$</td>
</tr>
</tbody>
</table>

$k$: the $k$th sample, $x$: the feature, $\varepsilon$: pre-defined threshold, $L$: window length, $|\Delta x_k|$: waveform length between two adjacent samples.

With coherence-based filter

Frequency ranges where coherence was significant were first identified during the three hand tasks. For each participant, significant ranges found in the three hand tasks were merged to determine the cut-off frequency for the band-stop filters ($4^{th}$ order Butterworth). Separate filters were built specific to each of the two SABD loading levels in this study. Concatenated EMG signals were then preprocessed with these coherence-based filters followed by feature extraction and LDA classification described above.
Figure 5.1 Experiment setup
A) ACT³D system with a monitor display; B) visual feedback during the task, step 1: to find the home position; step 2: found the home position and triggered the trial; step 3: to find the target position.

5.3.4.3 Dataset and Model Evaluation

For each participant, the dataset was split into a training set (75%) and a testing set (25%). The training set was used to train the model to learn and differentiate the EMG patterns of different
hand tasks. Ten-fold cross-validation was implemented to determine the best model that reported the highest detection accuracy in training set. The testing set was then used to assess the strength of the model and the extent to which the fitted model could generalize to the future data. The testing set was put aside until the model was complete with training.

Model was evaluated by calculating the classification accuracy within each of hand movement categories, as shown below,

\[
\text{accuracy} = \frac{\text{number of corrected classification}}{\text{total number of classification}} \times 100\%.
\]

The overall classification accuracy is the mean classification accuracy of the three hand tasks.

5.3.5 Statistics

A mixed three-way ANOVA with repeated measures was conducted to determine whether loading (SABD25, SABD50), filter (before filtering, after filtering), hand task (relax, open, grasp) and/or their interaction explain the changes in classification accuracies. Post hoc comparisons with the Bonferroni adjustment were used to compare within-group differences. Unless specified otherwise, results are presented as mean ± standard error. Statistical significance was set at p<0.05. The statistical analysis was performed using the IBM SPSS version 22 software.
5.4 Results

SABD loading showed a negative impact on the overall accuracy in the stroke group (Figure 5.2, see p values in Table 5.3). Both groups showed high overall accuracy when the tested arm was fully supported, but the accuracy in the stroke group started to drop significantly during conditions where the participants lifted the paretic arm thus generating SABD loads. The control group was not significantly affected by SABD loading.

Figure 5.2 Increased SABD loading resulted in a significantly decreased accuracy rate in the stroke group. Mean and standard error of classification error rate in the stroke group (N=21) and in the able-bodied group (N=8). TABLE: participant’s tested arm was fully supported on a rigid flat surface. SABD25 and SABD50: participant lifted the tested arm with a weight that equaled to 25% and 50% of his/her maximal SABD torque, respectively.
The result of coherence analysis of EMGs is shown for one stroke participant and one able-bodied individual during grasping while generating a 50% of max SABD load (Figure 5.3).
Figure 5.3 Greater alpha-band coherence between mDEL and wrist/finger flexors in the stroke individual.

**Top:** post-stroke EMG signals from FDS and mDEL were presented during the hand grasp task while the stroke participant was lifting the paretic arm at the same time (SABD50); **Middle:** Wavelet coherence was calculated with the aligned EMG signals for the stroke participant, and the global coherence was plotted on the left side to show the coherence power aggregating over time; **Bottom:** Wavelet coherence and global coherence for a control individual (EMG signals for this control individual are not shown).

Significant coherence between wrist/finger flexors and mDEL in the alpha band (8~13Hz) was found in the stroke participant during the hand grasp task while such activities were mostly absent in the able-bodied individual (Figure 5.3). The increased alpha-band coherence during hand grasping while lifting the arm in the stroke individual suggested a greater level of shared neural drive to both muscles. The global coherence depicted the coherence power aggregated over time as a function of frequency, highlighting the frequency range where coherence power was the most prominent. It is evident from the global coherence figures that this stroke individual had a greater level of EMG-EMG synchronization that centered at around 8Hz.

Figure 5.4 shows a significant global coherence between wrist/finger muscles and mDEL for the hand grasping task with SABD loading at 50% of the max torque based on the Monte Carlo simulation approach in each of the participants. For each participant, the significant frequency range is represented by solid lines whose length denote the range and a solid filled circle whose location denotes the peak value. The figure shows that the stroke group has more significant coherence bands in the alpha band than the control group, especially for the more severely impaired individuals. Coherence in the beta band is not evident for the stroke group. Additionally, there is also great variation between subjects and between muscles in the alpha band coherence in the stroke group. For example, the significant coherence in the extensors are either very short (ECR for the severe cases in Figure 5.4C) or very rare (EDC for the severe cases in Figure 5.4D), while
coherence in the flexors is generally longer. Across all individuals, no one stroke individual shared the same significant frequency band as the other.

Based on the significant coherence bands found in all three hand tasks, the cut-off frequency for the band-stop filter was determined by the frequency ranges where coherence was significant for each muscle in each participant. This subject-specific, muscle-specific coherence-based filter (referred as ‘coherence filter’ below) was applied to the EMGs in each participant to remove the synergy-induced components from the original EMGs. For individuals (n=3) who showed the peak value as the only significant coherence or no significant bands, no coherence filter was applied. Results from these 3 individuals were not included in the statistical analysis either. Figure 5.5 showed the improvement in classification accuracy after applying the coherence filters to the stroke group at SABD50. Overall, fourteen subjects showed improvement in the classification accuracy, four subjects showed reduced accuracy after removing the synergy-induced EMGs. A mixed three-way ANOVA found significance in an interaction effect of loading*filters (p<0.05). Post-hoc analysis found no significant difference in the classification accuracy with the coherence filters applied at SABD25, but significantly greater improvement with the coherence filters at SABD50 (Table 4). One subject showed 14% improvement with the filter. It is expected that some individuals may respond very favorably to the filter. Nevertheless, even when eliminating this individual from the analysis, the conclusion still holds as the sample mean at SABD50 without this subject remains significant compared to the one without the filter (p=0.038).
Table 5.3 Mixed two-way ANOVA for overall accuracy rate

<table>
<thead>
<tr>
<th>Factor</th>
<th>Overall Accuracy Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>$p = 0.009$</td>
</tr>
<tr>
<td>Loading</td>
<td>$p = 0.000$</td>
</tr>
<tr>
<td>Loading*Group</td>
<td>$p = 0.048$</td>
</tr>
</tbody>
</table>

Post-hoc analysis

<table>
<thead>
<tr>
<th>Loading</th>
<th>Group (Control vs Stroke)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TABLE</td>
<td>$p = 0.093$</td>
</tr>
<tr>
<td>SABD25</td>
<td>$p = 0.015$</td>
</tr>
<tr>
<td>SABD50</td>
<td>$p = 0.011$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Loading (TABLE, SABD25, SABD50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>$P_{tb-25} = 0.000$</td>
</tr>
<tr>
<td></td>
<td>$P_{25-50} = 1.000$</td>
</tr>
<tr>
<td></td>
<td>$P_{tb-50} = 0.000$</td>
</tr>
<tr>
<td>Control</td>
<td>$P_{tb-25} = 1.000$</td>
</tr>
<tr>
<td></td>
<td>$P_{25-50} = 0.245$</td>
</tr>
<tr>
<td></td>
<td>$P_{tb-50} = 1.000$</td>
</tr>
</tbody>
</table>

5.5 Discussion

5.5.1 Novelty and Main Finding

Decoding EMG signals for neural-machine interface is a great challenge in the individuals with chronic hemiparetic stroke due to prevalent motor deficits such as flexion synergy (Lan et al., 2011, Yao et al., 2015). Many studies made great efforts acquiring better quality of EMGs or features to improve the overall classification accuracy. For example, Xu and Zhou have reported that using high-density EMG signals can achieve high classification accuracies in the stroke
individuals (Xu and Zhou, 2012). Englehart and Hudgins suggested optimal parameters for feature extraction such as window length, overlap, increment length to produce models with low bias and variances that can generalize well to the test data (Englehart and Hudgins, 2003, Scheme et al., 2011). Features in the time domain (Hudgins et al., 1993, Zhou et al., 2007), the frequency domain (Merletti et al., 1999, Li et al., 2014), and the time-frequency domain (Englehart et al., 1999, Zhou et al., 2007, Nurhazimah et al., 2016) have also been broadly investigated. While improvement of the overall accuracy has been reported, the limitation is that very few studies have given full consideration of the effect of the flexion synergy common in up to 60% of the stroke population nor proposed approaches that can reduce EMG contamination associated with activation of proximal arm muscles (Fougner et al., 2011, Lan et al., 2011).

This study proposed a novel approach to reduce the impact of the flexion synergy on classification of the hand movements in individuals with chronic hemiparetic stroke for future use in neural machine interfaces. A subject-specific and muscle-specific coherence-based filter was developed to remove the synergy-induced component in EMG signals collected from the forearm.

Table 5.4 Mixed three-way ANOVA for improvement in the overall accuracy rate

<table>
<thead>
<tr>
<th>Factor</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filter</td>
<td>$p = 0.05$</td>
</tr>
<tr>
<td>Task*Filter</td>
<td>$p = 0.106$</td>
</tr>
<tr>
<td>Loading*Filter</td>
<td>$p = 0.048$</td>
</tr>
<tr>
<td>Task<em>Loading</em>Filter</td>
<td>$p = 0.160$</td>
</tr>
</tbody>
</table>

Post-hoc analysis

<table>
<thead>
<tr>
<th>Loading</th>
<th>Group (Control vs Stroke)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABD25</td>
<td>$P_{\text{with filter} - \text{no filter}} = 0.443$</td>
</tr>
<tr>
<td>SABD50</td>
<td>$P_{\text{with filter} - \text{no filter}} = 0.017$</td>
</tr>
</tbody>
</table>
It was found that such filters can significantly improve the classification accuracy during a greater level shoulder abduction loading. To our knowledge, this is the first study in the field that took the effect of the upper limb flexion synergy during functional reaching, hand opening and grasping tasks into consideration.

**Figure 5.5** The overall classification accuracy improvement after applying the filters at SABD50 in the stroke group.

Positive and negative values indicate improvement and reduction in the accuracy after filtering, respectively.
5.5.2 Impact of Flexion Synergy on Classification Accuracy

It was previously reported that shoulder abduction loading had a negative impact on the overall classification accuracy of hand opening using either EMGs (Lan et al., 2011) or EEGs (Yao et al., 2015). Even in the able-bodied individuals, variations in the limb position can have a substantial impact on the robustness of EMG recognition (Fougner et al., 2011). The results in this study confirm these previous findings. It is now understood that the activation of shoulder abductors can result in the involuntary coactivation of the wrist and fingers (Miller and Dewald, 2013), and such involuntary expression of flexion synergy at the hand can be further enhanced by increased shoulder abduction loading on the paretic limb. The EMG signals in the flexors increased with shoulder abduction loading even when no voluntary hand movement was initiated (Miller and Dewald, 2013). Prior studies suggested that the synergy-induced EMG component might be delivered via the contralesional corticoreticulospi
culospinal pathway during increasing levels of shoulder abduction (Dewald et al., 1995, Miller and Dewald, 2013, Lan et al., 2016) and should not represent the volitional aspect of hand movement, thus resulting in a decrease in classification accuracy. It is worth noting that while the paretic limb was fully supported, the overall classification of the stroke group has an average of 98.5% accuracy, suggesting that the current feature extraction and classifier choice is sufficient to decode myoelectric patterns in the absence of flexion synergy. However, the same feature extraction and classifier choice is less effective in the presence of synergy-induced EMG, such as when lifting the weight of the arm. It also seems that the reduction in classification accuracy, due to increased shoulder abduction loading, is not strictly linear since the accuracy at SABD50 only decreased by 1.1% compared with SABD25. However, more and greater SABD loading conditions are needed to confirm the relationship between shoulder abduction loading and reduction in classification accuracy.
5.5.3 Variation in significant coherence frequency range

For both hand grasp and hand open tasks, there was great between-subject and between-muscle variation in the frequency ranges where the coherence between wrist/finger muscles and mDEL is significant, as shown in Figure 5.4. One explanation is the broad range of stroke severity included in this study. The severity of stroke participants in this study ranges from moderate to severe impairment, as demonstrated by Fugl-Meyer Assessment and Chedoke-McMaster Stroke Hand Assessment (see methods). It is possible that more severe individuals show greater coherence in the alpha band due to the increased reliance on the contralesional corticoreticulospinal pathway, resulting in a greater portion of synergy-induced EMGs at the wrist/fingers during shoulder abduction. The between-muscle variation is also evident across individuals. For example, in Figure 5.4 the significant coherence frequency range in the flexors is generally more common than the extensors. It was noted from previous studies that hand muscles receiving projections from the contralesional reticulospinal tract are flexor-facilitated on the impaired side (Davidson et al., 2006, Riddle et al., 2009), meaning activation of the flexors using this pathway is much stronger than the extensors. From evidence provided in monkeys which had recovered from a unilateral lesion of the pyramidal tract, it was shown that reticulospinal-induced amplitude and incidence of synaptic inputs to forearm flexors were significantly increased, while inputs to extensors remained unchanged (Baker et al., 2015). For the control group, the significant coherence frequency range is no more than sporadic across all muscles and subjects, indicating the reduced extent of shared neural drive to the shoulder and the hand compared to stroke participants.
5.5.4 Variation in Classification Improvement

EMG classification from some individuals (e.g. stroke participant 9) responded more favorably to the filtering process than others (e.g. stroke participant 1). Such difference may be related to the remained volume of ipsilesional corticospinal tract that is responsible for voluntary hand movements. Evidence from our preliminary work has shown that there is a near-linear relation between the remaining volume of ipsilesional corticospinal tract and the opening area of the hand in individuals with stroke, suggesting that the ability to control the hand movements depends on the integrity of remaining corticospinal tract after stroke. It is possible that individuals with a more intact ipsilesional corticospinal tract may have smaller room of improvement in classification accuracy. Conversely, individuals with great reliance on the contralesional corticoreticulospinal tract may benefit more from the coherence filter after the synergy-induced EMGs was removed. It is also important to point out that three stroke individuals showed zero improvement. This is because none of them showed significant coherence frequency ranges and therefore no filters were applied. Interestingly, four individuals showed reduced classification accuracy after applying the filters. This could be due to the artifact introduced by the filters that may have caused EMG signal attenuation, and EMGs from these four individuals may be particularly sensitive to such an artifact. It could also be because these four individuals already had limited voluntary EMGs in the first place thus removing the synergy-induced component brought little change in the overall classification accuracy.

5.5.5 Scientific Implication and Future Work

A common approach to preparing surface EMGs is to apply a band-pass filter with a cut-off frequency range of 20~450Hz. This is very much rooted in the previous work by De Luca and
colleagues demonstrating that most of the energy related to motion artifacts is in the frequency range from 0 to 20Hz (De Luca, 2002; De Luca et al., 2010). However, more recent evidence has shown that after stroke the central nervous system might have adopted an alternative motor control strategy that generates neural oscillation in the alpha range (Baker et al. 2015; Lan et al., 2014). This control strategy may emphasize using neural pathways that produce frequency contents under 20Hz and hence it was suggested as the potential target for post-stroke rehabilitation (Baker et al., 2015). That could imply that the EMG below 20Hz might contain useful motor information. Thus selectively removing the frequency content below 20Hz might be a more effective approach for pattern recognition of post-stroke EMGs and should be studied in more detail.

Future work should also extend the current experimental protocol to multiple abduction levels to better understand the benefits of applying filters to functional hand movements. Furthermore, integrating neuroimaging approaches into the current line of research can further help us to gain insight into the possible use of ipsilesional corticospinal and contralesional corticoreticulospinal tracts after stroke. This is likely to bring new perspectives to a more effective subject-specific future application of neural machine interface within the context of flexion synergy.
6 CONCLUSION AND FUTURE WORK

6.1 Conclusion

The current work compared changes in voluntary motor control of the hand when progressively increasing shoulder abduction loading in individuals with chronic hemiparetic stroke compared to able-bodied participants, adding to the existing knowledge about the involuntary flexion responses of the hand during shoulder abduction loading post-stroke. Individuals with moderate stroke showed a reduced ability in opening the hand, quantified using the hand pentagon area, with increased shoulder abduction loading, while the able-bodied individuals showed no significant differences. Individuals with severe impairment were not able to open the hand but instead generated grasping forces, which increased with greater shoulder abduction loading levels. It is worth noting that when participants were asked to grasp maximally, the total grasping forces did not change as a function of shoulder abduction loading. However, for the stroke group, the ability of controlling the grasping forces was reduced due to the greater contribution of involuntary grasping forces generated during increased levels of shoulder abduction loading. This was particularly the case for the severely impaired group compared to the moderately impaired group. For the able-bodied individuals in our sample, no such changes were observed. These findings align with the previous results that involuntary muscle torque and EMG activity at the wrist and fingers increased with shoulder abduction loading (Miller and Dewald, 2012).

It was expected that increased involuntary muscle torque at the wrist/finger flexors would result in smaller hand pentagon area during hand opening in the moderately impaired group. For the severely impaired group, which showed limited voluntary ability in hand opening, grasping
forces were generated due to the shoulder abduction loading. Similarly, the involuntary portion of grasping forces measured in the current study is consistent with the involuntary muscle torque found in Miller’s study. We found that the capacity of generating maximal forces at the hand remained the same, but the shoulder abduction loading changed ratio of involuntary grasping forces to the voluntary grasping forces only in the stroke samples.

This study also quantified the wavelet coherence between flexion synergy muscles and found that the EMG-EMG coherence in the alpha band (8-13 Hz) between shoulder abductor and wrist/finger flexors was greater in individuals with chronic hemiparetic stroke than in able-bodied individuals, suggesting that a shared neural drive might underlie the muscle coupling of shoulder abductor with the wrist/finger flexors post-stroke. Study of neural oscillation is a common approach to understand coactivation patterns and underlying neural mechanisms. It is understood that neural synchronization in the beta band reflects the use of fast-conducting, direct corticospinal projections to synergistic muscles (Farmer et al., 1993a; Farmer et al., 1993b). It is expected that the beta-band coherence is largely missing in the stroke group, which is consistent with previous findings (Farmer et al., 1993). We suggest that the emergence of the alpha band coherence is a result from using the slow-conducting, indirect cortico-bulbo-spinal tract in the contralesional hemisphere. This allows motor commands to descend from the cortical level to the motor neurons of the spinal cord, but at the cost of losing the control of individual motoneuron pools and replacing it with the coactivation of multi-segmental spinal motoneuron pools that project to shoulder, elbow and wrist/finger muscles simultaneously, resulting in the flexion synergy. Noted that the coherence in the flexors with shoulder abductor is significantly greater than the extensors in the stroke group but not in the able-bodied group. Interestingly, the able-bodied individuals showed the ability to modulate the coherence of agonist versus antagonist depending on the hand
task. For example, in the hand opening task, the able-bodied group has a higher coherence in the extensors than the flexor, which is the opposite in the hand grasping task. This was not found in the stroke group.

In addition to finding an increased alpha band coherence in the stroke group, there is a positive relation between the alpha-coherence magnitude and grasping forces. Individuals who show greater alpha-band coherence are very likely to have greater involuntary grasping forces during shoulder abduction loading. We also observed a negative relationship between the alpha-coherence magnitude and the hand pentagon area as individuals with greater alpha-band coherence also showed a smaller pentagon area during a hand opening task. This is the first evidence that associates changes in spinal neural drive in the frequency domain with the expression of flexion synergy.

We further explored the possibility of using a coherence-based filter to improve the accuracy for detecting the hand opening versus grasping and relaxing. It is evident that the overall accuracy in classifying hand movements is subject to a significant reduction with increasing levels of shoulder abduction loading in the stroke group but not the control group. We proposed a novel approach, based on results from wavelet coherence analysis, to remove synergy-induced from the overall EMG signals from wrist and finger muscles. A subject and muscle-specific filter was built to reduce the impact of flexion synergy. It was found that 14 out of 18 individuals with stroke showed improvement in classification accuracies with the filter, while 4 showed a decrease. It is interesting to note that some individuals responded favorably to the filters and others did not. One previous study has shown that different limb positions have a significant impact on the classification errors of movements in able-bodied individuals (Scheme et al., 2011).
6.2 Future Work

The over-a-decade quantitative research on the expression of flexion synergy has presented evidence of an impact of shoulder abduction loading on torque generated at the elbow (Dewald et al., 1995; Dewald et al., 2001; Sukal et al., 2006), involuntary torques and EMG activities of the hand (Miller and Dewald, 2012), and now voluntary control of the hand as part of the current project. Previously, we demonstrated the progression from an isometric experimental setup, in which subjects’ tested upper extremity was secured to a static loading cell (Dewald et al., 1995; Dewald et al., 2001; Miller and Dewald, 2012), to a dynamic setup, where subjects were allowed to move the test limb freely (Sukal et al., 2006; Miller and Dewald, 2012; Lan et al., 2014). It is now understood that flexion synergy involves movement coupling of shoulder abduction with elbow/wrist and fingers flexion. This stereotypical movement pattern affects the ability to perform functional movements that demands independent joint control of the shoulder, elbow, wrist and fingers in the paretic arm. Merits from the current body of work has both scientific and clinical implications, which opens opportunities for future research.

**Need to understand the shared neural drive of shoulder and the hand driven by the expression of flexion synergy.** The current study focuses on the shoulder-driven flexion synergy and emphasizes on the impact of shoulder abduction on the wrist and fingers. The primary reason is that it has been shown that the expression of flexion synergy initiated from the shoulder is a lot more prominent than the one from the hand (Sukal et al., 2014). In addition, in real-life situations, functional movements that involve a lifted arm are very common. In our current experiment, one of the tasks required subjects to grasp maximally while a lifting arm (i.e. a “dual task”). The result showed that this dual task produced more evident coherence between the shoulder abductor and wrist/finger flexors than a single task, which refers to the flexion synergy generated by the
activation of shoulder or the hand muscles. It is possible that the expression of hand-driven flexion synergy could be enhanced while lifting the arm, which in the current study resulted in a strong coherence between shoulder and wrist/finger EMG signals.

The limitation of the current study is its lack of direct evidence in determining whether the post-stroke brain indeed relies more on the contralesional cortico-reticulo-spinal pathway. To provide more direct evidence for this hypothesis, the following future research is recommended.

**Quantification of the relationship between the expression of the flexion synergy and the integrity of the ipsilesional corticospinal tract as well as the activation of contralesional cortico-reticulo-spinal tract.** The current results point out that the expression of the flexion synergy might be related to the remaining volume of ipsilesional corticospinal tract, and existing evidence has shown that the post-stroke motor function is correlated with the integrity of corticospinal tract (Maraka et al., 2014; Stinear et al., 2007). But the extent to which the remained corticospinal tract is correlated with the expression of the flexion synergy such as wrist/finger flexion torques and EMG activities is still remains to be determined. It is also believed the contralesional cortico-reticulo-spinal tract might be upregulated after stroke, which could also be related to the loss of the corticospinal as well as a loss of corticobulbar (collectively referred to corticofugal) tracts from the lesioned hemisphere. The theory can be simplified as: the loss of ipsilesional corticofugal tracts is compensated for by an increased reliance on intact neural pathways from the contralesional hemisphere such as cortico-reticulo-spinal tract and cortico-propriospinal tracts. It might be possible to describe the altered neural connectivity using an Artificial Neural Network model, which contains hidden layers representing the cortex, brainstem and different segments of the spinal cord. Imaging techniques such as MRI/DTI can then be used to quantify the volume and integrity of each tract and provide experimental values to support the
model. The experimental protocol for this work is currently under development. Preliminary data have shown promising results as we have found a linear relationship between the synergy induced reduction in hand pentagon area and an increased white-matter integrity, as determined with DTI, (compared to age-matched controls) of the contralesional reticulospinal tract in more impaired individuals with stroke.

Finally, there is a significant clinical need to develop real-time control of neuroprosthetics to regain basic hand function in individuals with chronic hemiparetic stroke. One of the biggest clinical implications of the current study is the ability to apply more effective neural machine interfaces to development of the mind-controlled neuroprosthetics. Such neuroprosthetics will allow stroke individuals to perform functional upper extremity movements intuitively by decoding their intention. To achieve this goal, it is necessary to 1) convert the current offline classification to real-time classification and maintain similar accuracies. The main challenge for this task is computational cost that comes along with processing the data; 2) develop EMG driven functional electrical muscle stimulators and/or robotic exoskeletons that can assist in performance basic functional hand tasks. Many post-stroke motor impairments such increased muscle tone and possibly spasticity, require special consideration for the design of such a device. Finally, functional electrical stimulation of wrist/finger extensors might overcome these impairments but stimulation signals can also introduce unnecessary noise to the EMG signals. This would require the ability to stimulate and records EMG simultaneously which has not been realized yet.

In conclusion, my thesis work opens up a number of interesting, albeit challenging new research avenues, that may lead to the improve functional use of the paretic upper limb in individuals post hemiparetic stroke.
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