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WASHINGTON UNIVERSITY IN ST. LOUIS
Interdisciplinary Program in Movement Science

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Exploring the Complexities of Real World Upper Limb Performance after Stroke
by
Kimberly J. Waddell

A dissertation presented to
The Graduate School
of Washington University in
partial fulfillment of the
requirements for the degree
of Doctor of Philosophy

May 2019
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Kimberly Waddell

Washington University in St. Louis

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Dedicated to my parents and Kyle.

Abstract of the Dissertation

Exploring the Complexities of Real World Upper Limb Performance after Stroke

by

Kimberly J. Waddell

Doctor of Philosophy in Movement Science

Washington University in St. Louis, 2019

Professor Catherine E. Lang, Chair

Stroke is the leading cause of long-term disability in the United States. Hemiparesis, or weakness on one side of the body, is a common impairment following a stroke. Approximately 80% of individuals with stroke will experience upper limb paresis, with only a small percentage regaining full functional use of their paretic upper limb. Individuals report ongoing difficulties with incorporating their paretic upper limb into routine activities after a stroke. Rehabilitation interventions often try to increase real world upper limb use by improving what an individual is capable of doing (i.e. capacity) in the rehabilitation clinic. Both clinicians and researchers assume that improving in-clinic capacity translates to increased use (i.e. performance) in daily life. For this dissertation, we explicitly tested the assumption that improved upper limb capacity translates to increased upper limb performance, or use, in daily life. Additionally, we explored known factors that influence human behavior (e.g. confidence, motivation) as they relate to upper limb performance, or use, in adults with stroke.

Using sensors (i.e. wrist-worn accelerometers), we tested the assumption that improved in-clinic upper limb capacity translates to increased upper limb performance, or use, in daily life in adults with chronic (≥ 6 months) upper limb paresis post-stroke. Testing this common assumption provided important insights into the efficacy of an in-clinic intervention for improving upper limb use in the free-living environment.

Many personal, environmental, biological, and psychosocial factors influence human behavior and the activities individuals choose to engage in throughout their day. There is a growing emphasis on the potentially powerful role self-efficacy and other psychosocial factors may play in the stroke recovery process. Currently, there are limited data on how psychosocial factors, specifically related to the upper limb, evolve over the critical period of motor recovery (< 6 months post-stroke). Here, we quantified the natural time course of belief further improvement of the paretic upper limb is possible, confidence, and motivation to use the paretic upper limb in daily life, as well as self-reported barriers to upper limb recovery. These data provide a more robust understanding of how psychosocial factors evolve as overall recovery improves.

Additionally, these data provide important information about potential mechanisms for action for future upper limb interventions.

The final project of this dissertation maps the natural trajectory of upper limb performance over the first 12 weeks post-stroke. Presently, no studies have examined the natural trajectory of sensor-measured upper limb performance over the same period of time when majority of upper limb motor recovery occurs. We sought to characterize the relationship between upper limb

performance and psychosocial factors by testing belief, confidence, and motivation as potential moderators of upper limb performance in daily life.

The reported findings show that in-clinic improvements in upper limb capacity do not directly translate to increased upper limb performance, or use, in daily life in the chronic phase of stroke recovery. Indeed, improving what someone is capable of doing does not indicate their behavior will change in daily life. These results help distinguish between upper limb capacity and upper limb performance. While conceptually similar, they are distinct constructs. Belief, confidence, and motivation to use the paretic upper limb in daily life are remarkably high early, and remain high over the first 24 weeks (6 months) post-stroke. Upper limb performance in daily life does improve early (<12 weeks) after stroke. This change, however, is not moderated by belief, confidence, and motivation. Together, this dissertation provides multi-dimensional information related to upper limb performance after stroke. These results will lead to a more integrated approach for optimizing upper limb performance outcomes, a top priority for people post-stroke.

Chapter 1: Introduction

This introductory chapter begins with an overview of stroke and its increasing burden on the United States healthcare system and survivors. It then transitions to a thorough discussion of capacity and performance, two terms defined by the International Classification of Functioning Framework,¹ that are used throughout this thesis. Specific emphasis is placed on how upper limb capacity and performance are measured after stroke, and the corresponding limitations of these measures. Next, there is a discussion related to the importance of examining the natural trajectory of both UL use in daily life and related psychosocial factors early after stroke. Three psychosocial factors (belief, confidence, and motivation) are introduced. Finally, belief, confidence, and motivation, as well as self-perceived barriers to UL recovery are proposed as potential mechanisms that may moderate UL use in daily life early after a stroke.

1.1 Stroke is expensive and a significant health problem

Stroke is the leading cause of complex, long-term disability.²⁻⁴ Every 40 seconds, someone in the United States will experience a stroke.³ With the increasing aging population in the United States, the incidence of stroke is projected to rise in the coming years.² The United States spends approximately \$40.1 billion healthcare dollars annually on direct and indirect stroke care.^{2,3} By 2035, projected stroke costs in the United States will more than double from \$40.1 billion to \$94.3 billion.² Advances in acute medical care have reduced the overall stroke mortality rate.^{2,3,5} As a result, more individuals are surviving a stroke but living with chronic, long-term disability. The increasing number of survivors with motor, cognitive, and psychological/emotional deficits creates an urgent need for streamlined medical and rehabilitation services to help improve medical care and reduce stroke-related disability.

Nearly 80% of stroke survivors will experience some degree of upper limb (UL) paresis.⁶ Recovery of UL function is relatively poor, with only 5 to 20% of individuals regaining full function of the paretic UL.⁷ At just 6 months post-stroke, nearly 65% of survivors report difficulty incorporating their paretic UL into everyday tasks.⁸ The ongoing deficits in UL function can limit performance in daily life. For example, at 6 months after stroke, 57% of survivors report discontinuing meaningful activities in their everyday life.⁹ Over a 24-hour period, healthy, neurologically intact adults use their two hands together 95% of the time.¹⁰ The reported difficulty with incorporating the paretic UL into everyday tasks may be attributed, at least in part, to UL paresis.

Individuals with stroke identified improving UL function as a top research priority for stroke rehabilitation.¹¹ As a result, the research community has invested significant time and research dollars to develop efficacious, in-clinic UL interventions to improve UL function both early^{12,13} and later^{14,15} after stroke. These interventions often include a secondary measure of self-reported UL performance, or use, in daily life (e.g. Motor Activity Log¹⁶ or Stroke Impact Scale¹⁷). Until recently, it was often assumed the in-clinic improvements in UL capacity directly translated to increased UL performance in daily life. Indeed, this ostensible assumption is partially supported when UL performance in daily life is quantified using self-report measures.^{14,18} This assumption, however, is not supported by emerging evidence using a direct measure of UL performance (e.g. wearable sensors).¹⁹⁻²¹ The assumption that improved UL capacity directly translates to increased UL performance has yet to be explicitly tested in adults with UL paresis post-stroke.

1.2 Capacity and performance: Understanding the ICF

The World Health Organization's International Classification of Functioning, Disability, and Health Framework (ICF) is a comprehensive framework for measuring both individual and population health.^{22,23} The ICF is a valuable tool for evaluating and understanding the complex nature of health and disability. Figure 1 outlines the three ICF domains: body structures/functions, activity, and participation. The ICF model emphasizes an individual's health along these domains, and serves as a useful tool for understanding functional limitations following a health event, such as a stroke.^{22,24,25} Capacity and performance, two terms used throughout this thesis, are qualifiers of the activity domain.

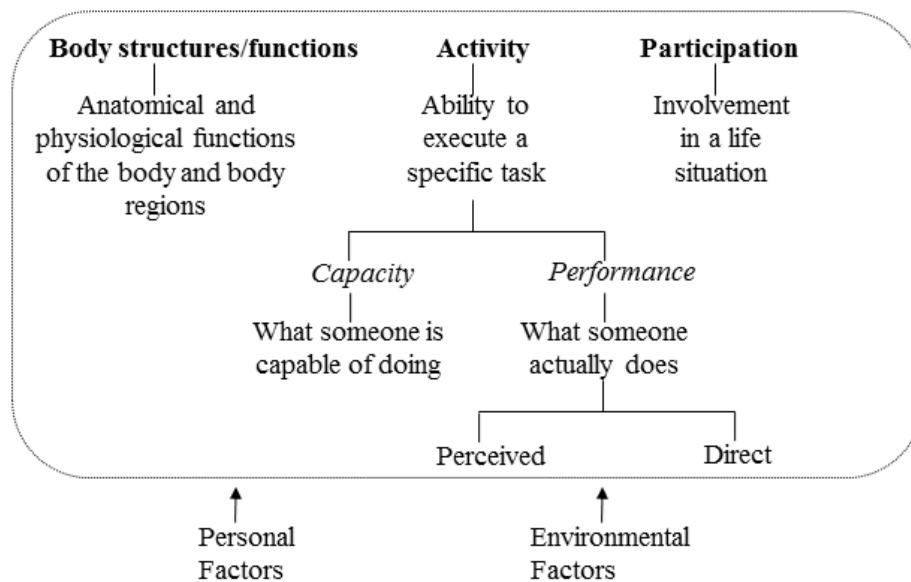


Figure 1.1 Adapted International Classification of Functioning, Disability, and Health Framework (ICF)

1.2.1 Motor capacity

Capacity is defined as what someone is capable of doing in a standardized, or controlled, environment.^{1,22} A standardized environment has removed the environmental barriers that may interfere with an individual's ability to complete a task and provides identical testing conditions

for every person.¹ Standardized clinical assessments quantify capacity in a clinic or laboratory setting.

One of the most common standardized assessment of UL capacity after a stroke is the Action Research Arm Test (ARAT).²⁶ Additional assessments of UL capacity include the Wolf Motor Function Test,²⁷ Box and Blocks,²⁸ Nine Hole Peg Test,²⁹ and the Jebsen Taylor Hand Function Test.³⁰ These UL capacity assessments are highly correlated with each other and also with measures of UL impairment,³¹ and provide important information related to what an individual is capable of doing within a controlled environment. The term impairment is associated with the body structure/function domain of the ICF (Figure 1). Impairment of the UL results from stroke-related damage to cortical and subcortical brain structures. Examples of UL impairment after stroke include decreased range of motion and strength, poor coordination, spasticity, and sensory loss. Impairments are quantified using standardized assessments, such as the Fugl-Meyer, dynamometry, and the Modified Ashworth Scale. Upper limb capacity is also a predictor of participation in life roles post-stroke.³² Participation (Figure 1) is defined as involvement in a life situation (e.g. going to a place of worship, hiking). Individuals report limitations with participating in life roles over the months and years following a stroke. Common validated assessments of participation after stroke include the Assessment of Life Habits, Frenchay Activities Index, the Activity Card Sort, and the Stroke Impact Scale.

One limitation of these standardized measures of UL capacity is their failure to include bilateral tasks as part of their design. Given the bilateral requirement (to varying degrees) of most UL tasks,¹⁰ it has become increasingly important to include bilateral assessments when measuring

UL capacity. The Chedoke Arm and Hand Activity Inventory (CAHAI)^{33,34} is likely the most common measure of bilateral UL capacity after stroke. The CAHAI is underutilized compared to the unilateral assessments listed above. The greatest limitation, however, is the inability of UL capacity measures to provide information about UL performance, or use, in the free-living environment.

1.2.2 Motor performance

Performance is defined as what a person actually does outside of the clinic or laboratory.¹

Performance, compared to capacity, is more complex for several reasons. First, a non-standardized environment includes a combination of physical, social, and personal factors that either facilitate or hinder performance. These factors exist in various combinations and are not consistent across individuals. Second, quantifying UL performance in daily life is difficult. In person observation is both costly and infeasible. As a result, self-report and sensor measures are used to quantify perceived and actual performance, respectively.

Self-report measures quantify perceived UL performance. The Motor Activity Log (MAL) is a common self-report measure of UL performance in daily life.¹⁶ The MAL queries individuals on how often (amount of use) and how well (quality of use) they used their paretic UL across 28 everyday tasks (e.g. turn on a light, make a sandwich) over the previous week.¹⁶ The Stroke Impact Scale (SIS) is another common self-report measure.¹⁷ The SIS includes several subscales, each probing a different area of stroke recovery (e.g. mobility, communication, memory, and arm/hand function). The SIS-Hand scale includes five questions and asks the individual to rate how difficult it is to use their paretic UL for each task (e.g. turn a doorknob).¹⁷ Several studies of

UL rehabilitation post-stroke have reported a significant change in UL performance in daily life when using self-report measures.^{14,18,35}

Limitations of self-report

Self-assessment of performance requires several cognitive processes and the ability to accurately recall information from the past.³⁶ As a result, self-report measures are vulnerable to recall bias and/or social desirability bias, which can compromise results. Recall bias occurs when there is either an intentional or unintentional deviation in the recalled details of an event from what actually occurred.³⁷ The magnitude of recall bias in any given study can either inflate or attenuate the effect size, leading to inaccurate results.³⁷ The recall bias associated with self-report measures is well-documented in the physical activity literature^{36,38-40} and health related quality of life research.⁴¹ Interestingly, recall bias is greater when recall (i.e. memory) is poor.⁴² This is of particular concern in stroke rehabilitation, given the prevalence of memory impairment following a stroke.⁴³⁻⁴⁵

Self-report is often limited by social desirability bias as well.⁴⁶ Social desirability bias occurs when an individual modifies their answer due to fear of feeling embarrassed or desire to project a favorable image.⁴⁷ Similar to recall bias, social desirability bias can lead to an inaccurate effect size and measurement error.^{47,48} Social desirability bias is common in physical activity and nutrition research.^{49,50} The ongoing threat these biases, and others, pose to self-report research have contributed to the development of other non-invasive, direct measures of UL performance post-stroke.

Accelerometry

Accelerometry is a valid, reliable, non-invasive measure of direct UL performance in both healthy adults^{10,51} and adults with stroke.^{19,52-56} These small sensors are similar to a FitBit© and provide answers to long-standing questions related to real time behaviors in daily life after stroke.⁵⁷ Accelerometry records movement in terms of acceleration and quantifies various aspects of UL movement such as total duration of movement,¹⁰ movement of one UL compared to the other (bilateral information),^{52,54} and information about the intensity of movement.^{52,54} Wrist-worn accelerometry effectively removes the burden of information recall and does not require individuals to estimate how often or well an activity was performed over previous days.

Limitations of accelerometry

While not vulnerable to recall or social desirability bias, wrist-worn accelerometry does not have the capacity to register the type of activity and distinguish between activities with similar kinematic profiles (e.g. typing vs. chopping vegetables). Studies are underway to identify the specific activities performed in daily life using accelerometer data. These studies require machine learning and predictive algorithms, but have limited success thus far.⁵⁸⁻⁶⁰ Additionally, accelerometry does not provide information about the quality of UL movement, an issue important to some clinicians and researchers.

A substantial amount of work has exposed the discrepancy between self-report and direct measures with physical activity data (correlations between the two measures range from -0.7 to 0.7).^{36,38-40} Emerging research suggests this discrepancy is also true in adults with spinal cord injury⁶¹ and stroke.^{62,63} While self-reported UL performance (MAL) and accelerometry are

moderately correlated,^{56,64} there is a high degree of variability and inconsistency between self-reported UL performance and sensor measured UL performance in adults with stroke (see Appendix C).⁶³ Thus, perceived and direct performance are two distinct constructs and the measures used to quantify both constructs cannot be used interchangeably.

Personal & Environmental Factors

Personal and environmental factors are often independent of the health condition but play a role in the disease process.^{1,22} Both personal and environmental factors can influence all domains of the ICF (Figure 1) and likely play a substantial role in UL performance in daily life. Personal factors include demographic characteristics such as age and education level in addition to personality factors (e.g. coping strategies), social determinants of health (e.g. socioeconomic status), and psychosocial factors (e.g. motivation, self-efficacy).¹ Environmental factors include the physical, social, and attitudinal environment that serve as both barriers and facilitators to functioning.^{1,22} While personal factors are difficult to modify, some environmental factors can be modified in the home to help facilitate participation in life roles following a stroke.⁶⁵

Summary

In summary, the ICF Framework provides a robust lens to view the interconnectedness and complexities of stroke related disability. All too often, rehabilitation interventions focus on specific domains (e.g. decreased strength, impaired memory) of the larger, complex disability. While not inherently wrong, this approach can leave little overlap between domains in terms of goals and interventions. A consequence of this may be limited understanding of how other factors, such as confidence and motivation, may influence outcomes. Moving forward, an

integrated approach to not just UL rehabilitation but all stroke rehabilitation may lead to improved overall outcomes.

1.3 Trajectories of recovery

1.3.1 Upper limb performance

The recovery trajectories of UL impairment and capacity over the first 6 months post-stroke are well documented.⁶⁶⁻⁷⁰ The majority of UL impairment and capacity recovery occurs during the first 3 months post-stroke. The magnitude of change slows between 3-6 months and by 6 months, UL recovery has plateaued. Understanding the recovery trajectory of UL impairment and capacity helps clinicians and researchers know when the critical period of motor recovery occurs. This critical period is proposed as the ideal time for rehabilitation services and informs interventions designed to improve UL impairment or UL capacity. The recovery trajectories of somatosensory impairment,⁷¹ cognitive impairment,^{43,72} lower extremity motor capacity and walking,^{66,73} language,⁷⁴ neuropsychiatric,⁶⁷ quality of life,^{75,76} and general illness^{77,78} after stroke have also been explored to varying degrees. To date, no research has explored the natural trajectory of UL performance in daily life early after stroke.

The purpose of rehabilitation is to improve overall performance in daily life. The paucity of studies characterizing UL performance over the first weeks and months post-stroke may be a direct consequence of assuming improved UL capacity directly translates to increased UL performance. Presently, researchers do not know if UL performance can improve early after stroke, absent of a controlled intervention. It is important to determine if UL performance can improve during the first 3 months post-stroke, the critical recovery period for UL impairment and capacity. Mapping the natural trajectory of UL performance in daily life is important for

future clinical trials designed to increase UL performance in everyday tasks. Characterizing UL performance in daily life, however, requires thoughtful consideration of factors beyond the motor system, such as belief, confidence, and motivation to use the paretic UL in everyday tasks and self-perceived barriers to UL recovery.^{79,80}

1.3.2 Psychosocial factors

To date, no research has explored how psychosocial factors, such as belief improvement of the paretic UL is possible, confidence, and motivation to use the paretic UL in everyday tasks, and self-perceived barriers to UL recovery evolve over the first 6-months post-stroke. Belief, confidence, and motivation are empirically derived factors from Social Cognitive Theory^{79,80} and Social Determination Theory⁸¹⁻⁸³ and have received considerable attention from the rehabilitation community in recent years.⁸⁴ The limited knowledge of these psychosocial factors comes from cross-sectional data in survivors who are 4-7 years post-stroke.⁸⁵⁻⁸⁷ While valuable, these data may differ from the early months post-stroke, especially in the presence of acute psychological distress that is common after sudden health events.⁸⁸ Additionally, cross-sectional data cannot capture the inherent dynamic nature of these psychosocial factors⁸⁰ and how they may change across the recovery process. Quantifying these factors over the first 6 months after stroke will provide valuable information into how these factors evolve as UL impairment and capacity, as well as general recovery, improves. This information will provide critical insight into when belief, confidence, and motivation are highest and when might be an ideal time to leverage these factors as part of rehabilitation interventions. In contrast, if there exists a time when these psychosocial factors are low, real world benefit from motor interventions may be limited.

Characterizing the natural time course of these psychosocial factors and self-perceived barriers to recovery is essential for future interventions designed to increase UL use in everyday activities. Belief further improvement of the paretic UL is possible, confidence, and motivation to use the paretic UL in everyday tasks may be potential mechanisms for action to improve UL performance in daily life. Additionally, addressing self-perceived barriers to UL recovery may be a key target for future rehabilitation interventions.

Belief

Individual belief that further improvement of the paretic UL is possible may influence the type of activity or amount of UL use in daily life. Belief that recovery is possible is a coping mechanism after stroke.⁸⁹ Preliminary research suggests it may be important for treatment adherence and the overall stroke recovery process.^{85,90} Individuals with stroke identified belief in further recovery as a marker of a positive, or good recovery process, and the loss of belief as a marker of poor recovery.⁸⁵ An individual may possess a strong desire to use their paretic UL in everyday tasks if they believe that further improvement is possible. In contrast, if an individual believes their UL will not improve, they may have less incentive to use their UL in everyday activities because the perceived benefit may be minimal. At 5 years post-stroke (when motor recovery has plateaued), 84% of survivors believed further improvement of their paretic UL was possible.⁸⁶ This remarkably high level of belief suggests other factors beyond the motor system (e.g. personal, social, environmental) may influence an individual's belief further recovery is possible post-stroke.

An individual's perceived self-efficacy is marked by their beliefs about their capabilities to complete different activities and maintain control over different situations.^{91,92} These efficacy beliefs, in many ways, determine the types of activities people choose to perform.⁷⁹ A person with high efficacy beliefs will approach activities and situations with greater confidence compared to someone with low efficacy beliefs.^{91,93} Additionally, a person who believes they possess the abilities to acquire the necessary skills through practice or previous skill mastery will also be more motivated to engage in specific activities compared to those with low efficacy beliefs.

Confidence

Stroke survivors identified improving confidence to perform activities as a top research priority.¹¹ Confidence in one's ability to successfully complete an activity is considered a marker of recovery⁹⁴ and a key predictor of performance.^{94,95} Individuals with greater confidence in their abilities are more likely to engage in activities compared to those with low confidence.⁹⁴

Confidence is a key component of self-efficacy.^{91,93} Prior success or failures substantially influence confidence to perform future activities. To date, very little is known about how confidence changes over the first 6 months following a stroke and how it may influence UL performance in daily life.

Motivation

Motivation is a critical component of behavior change⁸⁴ and motor learning.⁹⁵ Self-efficacy acts upon motivational processes that ultimately influence behavior.⁹¹ Motivational processes are

influenced by cognition, specifically forethought.⁹¹ Motivation to perform an activity is simultaneously influenced by one's beliefs about their skills and abilities, the activity goal, the anticipated outcome, and the planned course of action.^{79,91} An individual will experience higher task-specific motivation if they are confident in their skills, have realistic goals, and believe they can accomplish the intended outcome with little to no difficulty.^{91,95}

Understanding how motivation to use the paretic UL in everyday life evolves over the early months post-stroke is important for designing future UL interventions. There is an emerging interest in how motivation may influence motor and behavioral outcomes post-stroke.^{84,96} While important, the first critical step is to characterize individual motivation across time. Quantifying the time course of motivation to use the paretic UL in everyday activities will capture its inherent dynamic nature.⁷⁹ There may be periods in the recovery process when motivation is low and novel techniques to improve motivation would be required. Alternatively, when motivation is high, clinicians and researchers can capitalize on this to help increase overall UL performance in daily life.

Barriers to performance

Barriers to performance or recovery can hinder a person's ability to engage in a meaningful activity. An individual with high levels of motivation or confidence to engage in an activity may be limited due to barriers. For example, psychosocial barriers (e.g. depression, stress level), personal barriers (e.g. age, educational level), social barriers (e.g. social support, family support), and cognitive barriers (e.g. impaired memory) are all strongly correlated with medication adherence.^{97,98} Barriers such as lack of time, access to facilities, social support, health status,

outcome expectancy, and individual motivation can restrict physical activity levels.^{99,100} After a stroke, individuals report environmental barriers (e.g. transportation), health status, severity of stroke deficits, and motivation as barriers to engaging in regular physical activity.¹⁰¹ Quantifying barriers to UL recovery after a stroke will help identify potential therapy targets for clinicians and researchers to address with their interventions.

The paucity of studies exploring self-perceived barriers to UL performance in daily life are from individuals who are, on average, 4-7 years post-stroke.⁸⁵⁻⁸⁷ While important, the recovery process several years post-stroke is markedly different from the first few months following a stroke. For example, 80% of survivors will receive a referral for rehabilitation services immediately after their stroke.¹⁰² In the United States, rehabilitation services fade over time with few survivors receiving therapy at 6 months, not to mention several years post-stroke. As a result, barriers such as access to healthcare services that are common several years post stroke may not be as common early after stroke.^{86,87} The perceived barriers to recovery will likely be different early after stroke (< 6 months) during the time of rapid, notable recovery when compared to several years post-stroke when little recovery occurs.

1.4 Psychosocial Factors and UL performance

Human behavior is a dynamic process, influenced by many individual, social, and environmental factors.⁸⁰ The choice to perform and accomplish an activity requires ongoing reflection and predictions about one's ability to succeed.⁷⁹ Social Cognitive Theory reflects this dynamic, reciprocal relationship between a person and the broad network of social and environmental influences that contribute to behavior.^{79,80,103} Self-efficacy is a key component of Social Cognitive Theory. Self-efficacy, characterized by belief about one's abilities and confidence in

one's skills to perform, influences many domains of stroke recovery such as physical activity,¹⁰⁴ balance and walking,¹⁰⁵ independence with activities of daily living,¹⁰⁶ onset of post-stroke depression,¹⁰⁷ and overall well-being.¹⁰⁸ Motivation, a key element of Social Determination Theory,⁸¹⁻⁸³ has previously shown to influence motor learning⁹⁵ and behavior⁸⁴ and has been identified as a potential target for improving rehabilitation outcomes post-stroke.^{96,109} Presently, there are no available data to describe the potential relationship between these psychosocial factors (belief, confidence, and motivation) and UL performance in daily life.

If these psychosocial factors moderate UL performance in daily life in the early months post-stroke, then future interventions specifically targeting these factors are warranted. With the growing emphasis on belief, confidence, and motivation as a means to improve performance in daily life, this will be the first experiment to explicitly test if UL performance is moderated by psychosocial factors early after stroke.

Summary

Together, characterizing how belief further improvement of the paretic UL is possible, confidence and motivation to use the paretic UL in everyday tasks, and self-perceived barriers to recovery evolve over the first 6 months post-stroke will provide a more holistic understanding of UL performance in daily life. Additionally, this will be the first study to quantify these factors during the period of time when majority of recovery occurs. This, combined with the uncertainties of how UL capacity and performance are related, led to the proposed aims for this dissertation.

1.5 Specific Aims

Aim 1: Examine the translation of in-clinic UL capacity gains to increased UL performance in daily life. This is a secondary analysis from a Phase II clinical dose-response trial in a chronic (≥ 6 months) stroke cohort.

Hypothesis 1a: Individuals with significant UL capacity gains will demonstrate increased UL performance in daily life compared to individuals with insignificant capacity gains.

Hypothesis 1b: There will be no dose-response relationship to UL performance in daily life.

Hypothesis 1c: Concordance (i.e. paretic hand = dominant hand) will not modify UL performance in daily life.

Aim 2: Determine the natural trajectory of self-perceived barriers and psychosocial factors related to UL performance over the first 6 months following a stroke. Using a longitudinal inception cohort, a health behaviors survey will quantify psychosocial factors and self-perceived barriers to UL performance at 2, 4, 6, 8, 12, 16, 20, and 24 weeks post-stroke.

Hypothesis 2a: Belief, confidence, and motivation will be high immediately after stroke and persist over 24 weeks.

Hypothesis 2b: The total number of perceived barriers to UL use will be the highest immediately after stroke and decline over 24 weeks.

Hypothesis 2c: Depressive symptomatology and cognitive impairment will have a negative association with belief, confidence, and motivation to improve UL performance.

Aim 3: Characterize the relationship between psychosocial factors, self-perceived barriers, and UL performance over the first 12 weeks post-stroke. Using the same longitudinal cohort, wrist-worn accelerometers will quantify UL performance at 2,4,6,8, and 12 weeks post-stroke.

Hypothesis 3a: UL performance will significantly increase over the first 12 weeks post-stroke.

Hypothesis 3b: Individual belief, confidence, and motivation to improve UL performance will significantly moderate UL performance.

Hypothesis 3c: A greater number of self-perceived barriers will result in less UL use in daily life (negative association).

Implications for rehabilitation

Together, these aims will be the first to examine the translation of UL capacity gains to daily life post-stroke, characterize how belief, confidence, and motivation evolve over the first 6-months post-stroke, map the natural trajectory of UL performance early after stroke, and explore the potentially mediating role of these psychosocial factors on UL performance. The knowledge gained here will increase our overall understanding of how other factors beyond the motor system may influence UL performance outcomes. This will provide critical information for future UL interventions designed to improve individual outcomes after stroke.

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Chapter 2: Does task-specific training improve upper limb performance in daily life post-stroke?

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2.1 Abstract

Background: A common assumption is that changes in upper limb (UL) capacity, or what an individual is capable of doing, translate to improved UL performance in daily life, or what an individual actually does. This assumption should be explicitly tested for individuals with UL paresis post-stroke. Objective: To examine changes in UL performance after an intensive, individualized, progressive, task-specific UL intervention for individuals at least 6 months post-stroke. Methods: Secondary analysis on 78 individuals with UL paresis who participated in a Phase II, single-blind, randomized parallel dose-response trial. Participants were enrolled in a task-specific intervention for 8 weeks. Participants were randomized into 1 of 4 treatment groups with each group completing different amounts of UL movement practice. UL performance was assessed with bilateral, wrist-worn accelerometers once a week for 24 hours throughout the duration of the study. The six accelerometer variables were tested for change and the influence of potential modifiers using hierarchical linear modeling. Results: No changes in UL performance were found on any of the 6 accelerometer variables used to quantify UL performance. Neither changes in UL capacity nor the overall amount of movement practice influenced changes in UL performance. Stroke chronicity, baseline UL capacity, concordance, and ADL status significantly increased the baseline starting points but did not influence the rate of change (slopes) for participants. Conclusions: Improved motor capacity resulting from an intensive outpatient UL intervention does not appear to translate to increased UL performance outside the clinic.

2.2 Introduction

A large proportion of individuals post-stroke experience significant difficulty incorporating their paretic hand into daily activities and they often identify improved upper limb (UL) function as a

top rehabilitation priority.¹⁻⁴ Despite the resources spent on stroke rehabilitation, individuals continue to experience ongoing barriers with performing activities at home and will ultimately discontinue 57% of their daily activities.⁵ Given the importance of both upper limbs in daily activity,⁶ decreased daily performance following stroke is likely influenced by UL paresis. Clinical interventions to address UL paresis are often aimed at improving UL capacity, which describes an individual's ability to execute a task, or what a person is capable of doing, within the structured environment of a clinic or laboratory.⁷ A common assumption is that improvement in UL capacity directly translates to improved UL performance. Performance describes what individuals actually do in their current environment, outside of the clinic or laboratory.⁷ Recent research has emphasized the importance of measuring capacity and performance separately.^{8,9}

Protocol-based UL motor interventions can improve capacity after stroke.¹⁰⁻¹⁴ Less clear is whether gains made in UL capacity, measured with standardized assessments (e.g. Action Research Arm Test¹⁵ [ARAT] and Wolf Motor Function Test¹⁶), translate to improved UL performance, or use, in daily life. Several studies have reported increased UL performance when measured via self-report,^{10,17-19} and individuals with larger improvements in UL capacity demonstrate a positive trend towards clinically significant changes in self-reported performance.^{10,17,19} Self-report measures, however, are subject to many report biases including cognitive deficits^{20,21} and social desirability.²² Self-report measures often rely on an individual's ability to recall activities completed over a previous week, which may be of particular difficulty for individuals with stroke, given the high prevalence of cognitive impairment.^{23,24} Pilot studies that have used a more quantitative measure of UL performance, i.e. accelerometry, report little to no improvement in UL performance in daily life, despite gains in UL capacity.²⁵⁻²⁷ The growing

emphasis on efficient, evidence-based rehabilitation services demands an evaluation of the relationship between change in UL capacity and change in UL performance in post-stroke chronic UL paresis.

In this analysis, we examine changes in performance in the community that resulted from an individualized, intensive, progressive, task-specific UL intervention. We explicitly test the assumption that increased UL capacity translates to increased UL performance using data from a recent clinical trial.¹⁴ Finally, we examine the effect of dose (i.e. amount) of task-specific movement practice on UL performance in daily life.

2.3 Methods

This paper is a secondary analysis from a Phase II, single-blind, randomized, parallel dose-response trial (NCT 01146379).¹⁴ Individuals were recruited for this study via the Brain Recovery Core database and the Cognitive Rehabilitative Research Group at Washington University in St. Louis, MO. Inclusion criteria were: 1) ischemic or hemorrhagic stroke as determined by a stroke neurologist and consistent with neuroimaging; 2) time since stroke ≥ 6 months; 3) cognitive skills to actively participate, as indicated by scores of 0-1 on items 1b and 1c of the National Institutes of Health Stroke Scale (NIHSS);²⁸ 4) unilateral UL weakness, as indicated by a score of 1-3 on item 5 (arm item) on the NIHSS; and 5) mild-to-moderate functional motor capacity of the paretic UL, as indicated by a score of 10-48 on the ARAT.^{15,29,30} The lower limit of 10 on the ARAT meant that participants had at least some ability to open the hand, grasp and lift off the table at least 2-3 test items. Exclusion criteria were: 1) participant unavailable for 2-month follow-up; 2) inability to follow-2-step commands; 3) psychiatric diagnoses; 4) current participation in other UL stroke treatments (e.g. Botox); 5) other

neurological diagnoses; 6) participants living further than one hour away and were unwilling to travel for assessment and treatment sessions; and 7) pregnancy. The trial was approved by the Washington University Human Research Protection Office and all participants provided informed consent.

Clinical trial details and primary outcomes have been reported.¹⁴ Briefly, the primary aim of the trial was to determine the range of doses of UL task-specific practice that produce the largest change in UL functional capacity in individuals with chronic UL paresis. Participants were randomized into one of four groups. Dose was quantified by the total number of repetitions achieved over the course of the intervention. The four dose groups were: 3200 (100 repetitions/session; median = 13.6 hours of active practice), 6400 (200 repetitions/session; 20 hours of active practice), 9600 (300 repetitions/session; 26.3 hours of active practice), and individualized maximum, respectively. Participants completed four treatment sessions per week for 1-hour over eight weeks. The individualized maximum group completed 300 repetitions per session and continued their enrollment past the 8 weeks until specific stopping criteria were met (32.8 hours of active practice).¹⁴ The >32 hours of active practice in the individualized maximum group is likely equivalent to the total scheduled therapy time in the constraint induced movement therapy trials (≥ 65 hours),³¹ given that active practice is often 50% or less of scheduled time.^{32,33} At least once every two weeks throughout the length of enrollment, participants were asked questions related to UL performance at home (e.g. what new activities have you tried with your arm?) and new activities were identified and discussed to help facilitate increased UL performance at home. The primary outcome for the trial was the ARAT, a valid and reliable measure of UL capacity.³⁴⁻³⁶

2.3.1 Performance Measures

UL performance was measured with bilateral, wrist-worn accelerometers (w GT3X+, Actigraph, Pensacola, FL). Accelerometers are a well-established, valid, and reliable instrument for quantifying UL performance in both non-disabled adults^{6,9} and individuals with stroke.^{9,25,37-40} Accelerometers record accelerations along three axes in activity counts where 1 count = 0.001664 g. Data were sampled at 30 Hz and activity counts were binned into 1-second epochs for each axis using ActiLife 6 (Actigraph Corp., Pensacola, FL) software. Activity counts across each axis were combined to create a single vector magnitude value ($\sqrt{x^2+y^2+z^2}$) for each second.

Each participant wore bilateral, wrist accelerometers once a week for 26 hours throughout the intervention, at the conclusion of the intervention, and at 2-months follow-up. Using custom-written software in MATLAB (Mathworks Inc., Natick, USA) the first two hours of each recording were removed because this included the time in therapy session plus transportation home afterwards. Data from the remaining 24 hours at home were used for this analysis. The single day wearing period was chosen because previous research has shown this is an adequate representation of performance in non-employed adults^{6,40,41} and to ensure increased adherence to wearing the accelerometers multiple times over the course of the study. Accelerometers are waterproof so participants could wear them for all activities, including bathing. Accelerometers were worn during the night (sleeping) and those data are part of the 24 hours. Accelerometers were returned the next treatment session and the data were downloaded using ActiLife 6 software.

Six variables were calculated from the data collected over the 24 hours at home, with each variable quantifying different, but related, aspects of UL movement. Upper limb movements

associated with walking were included in our calculations. Previous work has established that walking does not influence the accelerometer ratio variables in individuals post-stroke.³⁷ Although inclusion of walking does not change the non-ratio variables for neurologically-intact adults,⁴² it is possible that the inclusion of walking could result in an overestimation of the non-ratio variables for participants with stroke. We first examined summary variables of UL performance with the use ratio (also called activity ratio) and hours of use. The use ratio is the hours of paretic limb use divided by the hours of non-paretic limb use and quantifies the contribution of the paretic limb relative to the non-paretic limb to an activity.⁶ Healthy, neurologically intact adults (54.3 ± 11.3 years of age, 53% female, and 84% right hand dominant, recruited to match the demographic characteristics of the trial participants)⁹ have a use ratio of 0.95 ± 0.06, indicating nearly equal amounts of UL movement during activities.⁶ A use ratio value close or equal to 1 indicates nearly equal durations of activity from both limbs while values less than 1 indicate greater non-paretic activity and values greater than 1 would indicate more paretic UL activity.⁶ The total hours of use is the total amount of time, in hours, the paretic limb was active, as measured by summing the seconds when the activity count was > 2, and is a broad measure of paretic limb activity over the recording period.^{6,9} Neurologically intact adults use their dominant UL 9.1 ± 1.9 hours and their non-dominant UL 8.6 ± 2.0 hours.⁶

We then more closely examined, on a second-by-second basis, the contribution of both limbs to activity and the intensity of movement with the magnitude ratio and bilateral magnitude, respectively. The magnitude ratio is the natural log of the vector magnitude of the paretic UL divided by the vector magnitude of the non-paretic UL, and describes the contribution of both limbs to an activity for each second of data.⁴³ A magnitude ratio value of 0 indicates both ULs

contributed equally to an activity.^{9,43} A negative magnitude ratio value indicates greater non-paretic UL activity and positive values indicate greater paretic UL activity.⁹ Across 74 healthy, non-disabled adults, the median magnitude ratio value (median of all the seconds recorded during 24 hours) averages -0.1 (0.3), indicating that both ULs are used nearly the same amount during activity.⁹ The bilateral magnitude measures the intensity of UL activity by summing the vector magnitude of the paretic UL and the non-paretic UL.⁴³ The bilateral magnitude distinguishes between high intensity and low intensity movements, for every second of data. Bilateral magnitude values of 0 indicate no movement and increasing values are indicative of more intense UL movement. A referent median value of 136.2 (36.6) has been established in non-disabled adults.⁹ Higher values are associated with activities requiring larger, faster movements, (e.g. placing boxes on an overhead shelf).⁴³ A low bilateral magnitude value would indicate smaller, less intense movements such as chopping vegetables.⁴⁴

The final quantification of UL performance examined only the paretic limb performance using the median paretic acceleration magnitude and the acceleration variability. The median paretic acceleration magnitude captures the individual's median acceleration value over the entire recording period.⁴⁵ The acceleration variability is the variance of the mean acceleration value over the recording period and explains the average distance of the paretic accelerations from the mean acceleration.⁴⁵ A higher value for both the median acceleration magnitude and acceleration variability indicates more overall UL movement and greater variability of movement, respectively.

These variables can detect differences between participants with stroke⁹ and, with the exception of the bilateral magnitude, are responsive to change in UL function following a task-specific intervention in individuals with UL paresis post-stroke.⁴⁵ While not responsive to change in UL function, the bilateral magnitude may be a valuable variable for quantifying the intensity of bilateral movement, which is of interest to rehabilitation professionals.

2.3.2 Statistical Analysis

All data were analyzed in R, an open source statistical computing program. The primary analysis used hierarchical linear modeling (HLM), also referred to as linear mixed effects regression analysis,^{14,46} for all six accelerometer variables. HLM is applied to longitudinal data and is an extension of a traditional regression analysis.⁴⁶ In contrast to repeated measures ANOVA, HLM allows for modeling of individual intercepts and slopes over time in addition to modeling potential moderators of the intercepts and slopes. HLM does not require the same number of assessments across participants and can account for missing data, therefore participants with varying assessment sessions can still be included in the analysis.⁴⁶ Slopes for each variable were of primary interest for this analysis, as they quantify the amount of change in UL performance over the duration of the study. Preliminary analyses indicated that nonlinear model components were not necessary. The group level intercepts and slopes are derived from the individual intercepts and slopes for each variable.⁴⁶

We initially analyzed change in UL performance across the entire sample by testing growth curves for all six variables, with individual time trajectories nested within participants (Model 1). This model allowed us to estimate the intercept and slope for the entire sample. Next, we tested the relationship between change in UL capacity (i.e. ARAT score) and change in UL

performance with nested models. Participants were stratified into two groups, those who improved ≥ 6 points on the ARAT and those who did not improve at least 6 points, as the 6 point value has been previously described as an estimate of the minimal clinically important difference for individuals with chronic stroke.³⁵ These two groups (dummy coded) were added to Model 1 and time was nested within each participant, with individual intercepts and slopes allowed to vary randomly. We evaluated the potential influence of change in UL capacity on both the intercepts and slopes (via group x time interaction). Nested models were compared using χ^2 tests and the final, best fit model for change in UL capacity was identified (Model 2). Additionally, a new series of nested models were created to test for a potential dose effect on UL performance by adding treatment group (dummy coded), and a group by time interaction to Model 1, yielding a final model identified as Model 3. Outliers were identified using Cook's distance and when necessary, models were re-evaluated with outliers excluded. Across all levels of analysis, no outliers significantly influenced the results. We verified the inferences reported from the models using bootstrapping procedures and no differences were found as a result of this procedure. Finally, we evaluated the potential modifiers of time post-stroke (months), baseline UL capacity (i.e. ARAT score), concordance (dominant side = affected side), and activities of daily living (ADL) status (i.e. requires assistance vs. independent) and their influence on change in UL performance over time for all six variables. Each modifier was added to Model 1 separately, and the effects of the modifier on the intercept (baseline) and the slope (interaction between modifier and time) were evaluated (Models 4-7). Time post-stroke is widely assumed to be a predictor of UL performance, therefore we tested its influence on both initial baseline intercept and change over time (i.e. slope). Baseline ARAT scores were grand mean centered across all participants.

Concordance and ADL status were tested because they have previously been shown to modify UL performance in daily life.⁴⁴

Visual representations of accelerometer data were examined using density plots which display second-by-second data for the magnitude ratio (x-axis) and bilateral magnitude (y-axis) over the entire recording period, at every assessment time point. Example density plots have been previously published for healthy, neurologically intact adults (Figure 1, Bailey et. al; Supplemental Figure 1, Doman et. al²⁷; Figure 3, Hayward et. al⁴⁷). There are a few salient characteristics in healthy adults that should be considered when interpreting these density plots. First, in healthy adults, plots are symmetrical, indicating that both ULs are used similarly. The bottom portion is wide, and rounded, indicating that the majority of UL movements in a 24 hour period are low intensity. Additionally, the rounded edges or rims of the bowl-like structure represent movements when one limb is moving while the other is relatively still (e.g. holding a piece of paper with one hand while the other hand writes, holding a container with one hand and opening it with the other). The color bar represents the overall frequency of movement. Warmer colors (i.e. red and/or orange) represent more UL movement overall, and the small color bars on both sides of the density plot are specific to the frequency of unilateral non-paretic UL movement and unilateral paretic UL movement, respectively. While specific UL movements are highly variable across individuals,⁴³ the salient characteristics of these graphs are highly consistent across community-dwelling, neurologically-intact nondisabled adults.⁹ Six examples of individual patients from the baseline data of this same cohort can be seen in Figure 2 of Bailey et al. NNR 2015. Examples of how individual density plots change over time in persons with stroke can be seen in Figure 4B of Hayward et al.⁴⁷ and in Figure 1 in Doman et al.²⁷

2.4 Results

Seventy-eight of the 85 participants in the trial had available data for this analysis. Of the seven excluded participants, four had accelerometer recording errors, two withdrew from the study prior to the intervention, and one did not consistently wear the accelerometers for > 6 hours at each assessment time point. Table 1 presents the demographic characteristics of the 78 participants and baseline values for the six accelerometer variables. The 6400 repetition group had low concordance (i.e. fewer people reporting their dominant side was the affected side).¹⁴ Individuals had mild to moderate levels of UL paresis at baseline and most of the participants were independent with basic activities of daily living.

Table 2.1 Participant demographics and baseline accelerometer intercepts by treatment group

	Total sample (n=78)	3200 Group (n= 19)	6400 Group (n=21)	9600 Group (n=21)	IM ^b (n=17)
Age (years)	61.9 ± 10.5	59.4 ± 12.5	62.6 ± 8.5	60 ± 8.3	62.4 ± 13.1
Gender	27 F, 51 M	6 F, 13 M	5 F, 16 M	10 F, 11 M	6 F, 11 M
Race	40 Caucasian 36 Af American 1 Asian 1 Multi-race	10 Caucasian 9 Af American	11 Caucasian 10 Af American	10 Caucasian 9 Af American 1 Asian 1 Multi-race	9 Caucasian 8 Af American
Type of stroke	56 ischemic 10 hemorrhagic 12 unknown	14 ischemic	16 ischemic	15 ischemic	11 ischemic
Months post-stroke	12 (5, 221)	11 (6, 180)	13 (6, 221)	13 (5, 54)	12 (6, 144)
Affected side	36 L, 42 R	8 L, 11 R	11 L, 10 R	11 L, 10 R	6 L, 11 R
% Concordance ^a	51%	58%	33%	48%	71%
% Independent with ADL	79%	89%	71%	86%	71%
% Completed ≥ 32 treatment sessions	81%	89%	76%	71%	88%
Baseline ARAT ^c score	32.4 ± 11.2	34.1 ± 7.9	31.9 ± 13.1	32.1 ± 12.3	31.7 ± 11.2
Post-intervention ARAT score ^d	36.9 ± 12.9	39.1 ± 8.7	36.4 ± 14.5	35.6 ± 15.4	36.5 ± 13.4
Post-intervention #2 ARAT score ^e	35.9 ± 13	38 ± 9.4	34.4 ± 14.1	34 ± 15.2	37.1 ± 13.8
Baseline Values					
Use Ratio	0.66 ± 0.23	0.67 ± 0.19	0.61 ± 0.19	0.67 ± 0.21	0.73 ± 0.33
Hours of Use	4.73 ± 2.12	4.72 ± 2.42	4.09 ± 2.23	4.82 ± 1.45	5.4 ± 2.32
Magnitude Ratio	-3.04 ± 2.86	-2.81 ± 2.68	-3.52 ± 2.96	-2.99 ± 2.81	-2.78 ± 3.21
Bilateral Magnitude	89.29 ± 27.45	86.91 ± 34.34	83.64 ± 25.45	94.76 ± 21.38	92.02 ± 28.78
Median acceleration	15.53 ± 17.61	14.21 ± 15.38	11.67 ± 13.06	17.67 ± 19.59	19.38 ± 22.28
Acceleration variability	45.56 ± 17.46	45.22 ± 15.86	41.04 ± 13.07	49.61 ± 20.49	46.27 ± 19.91

Values reported as means ± SD or median (range) as determined by distribution of data

^a = Concordance = dominant side is paretic side; values here indicate the percentage of the sample who identified their dominant upper limb as the paretic upper limb

^b = Individualized Maximum

^c = Action Research Arm Test; scores range from 0-57 points with higher scores indicating more normal movement

^d = Assessment completed immediately after the final treatment session

^e = Assessment completed 2 months after conclusion of intervention

Overall, there was no change in UL performance across all 78 participants on any of the six accelerometer variables. The final model for 5 of the 6 variables included the linear effect of time which produced better fitting models for the use ratio ($\chi^2= 15.08$, $df =3$, $p = 0.002$), hours of paretic limb use ($\chi^2= 15.45$, $df=3$, $p = 0.001$), the magnitude ratio ($\chi^2= 15.08$, $df =3$, $p = 0.03$), median acceleration ($\chi^2= 10.84$, $df = 3$, $p = 0.01$), and the acceleration variability ($\chi^2= 12.24$, $df=3$, $p = 0.007$). For the sixth variable, the bilateral magnitude, the addition of a linear effect of time was not significant ($\chi^2= 2.76$, $df =3$, $p = 0.43$), indicating that time did not increase the predictive ability of the model and was not a significant predictor of change. Time was still included in the final model to acquire a slope value for the bilateral magnitude and also test potential modifiers of the slope. Rates of change, quantified as model slopes are reported in the top row of Table 2, in units of change per week. The slopes for each accelerometer variable were not significantly different from zero.

Table 2.2 Slopes \pm SE for entire sample, by group, ARAT change score, and potential modifiers

	Use Ratio	Hours of Use	Magnitude Ratio	Bilateral Magnitude	Median Acceleration	Acceleration Variability
Entire sample^a	-0.0005 \pm 0.0009	-0.027 \pm 0.01	-0.023 \pm 0.013	-0.15 \pm 0.09	-0.03 \pm 0.06	-0.04 \pm 0.05
Change in ARAT^b						
ARAT change \geq 6 pts	0.0013 \pm 0.002	-0.006 \pm 0.02	-0.008 \pm 0.03	-0.01 \pm 0.18	0.032 \pm 0.12	0.061 \pm 0.1
Group^c						
3200	0.0004 \pm 0.002	-0.015 \pm 0.02	-0.005 \pm 0.024	-0.18 \pm 0.19	-0.13 \pm 0.12	0.07 \pm 0.1
6400	0.0006 \pm 0.002	-0.037 \pm 0.03	-0.005 \pm 0.03	-0.30 \pm 0.27	0.02 \pm 0.17	-0.04 \pm 0.14
9600	-0.0028 \pm 0.002	-0.022 \pm 0.03	-0.078 \pm 0.03	0.005 \pm 0.27	0.01 \pm 0.17	-0.28 \pm 0.15
IM	-0.0004 \pm 0.002	-0.034 \pm 0.03	-0.008 \pm 0.03	-0.12 \pm 0.26	0 \pm 0.17	0.08 \pm 0.14
Modifiers						
Chronicity (months) ^d	0.000008 \pm 0.00002	0.0001 \pm 0.0003	0.0004 \pm 0.0003	-0.002 \pm 0.002	0.0001 \pm 0.002	-0.0006 \pm 0.001
Baseline ARAT ^e	0.0001 \pm 0.0001	0.0003 \pm 0.001	0.00003 \pm 0.001	-0.006 \pm 0.01	-0.002 \pm 0.01	0.005 \pm 0.005
Concordance ^f	-0.0017 \pm 0.002	-0.025 \pm 0.02	-0.03 \pm 0.03	-0.118 \pm 0.19	-0.081 \pm 0.12	-0.08 \pm 0.12
ADL independence ^g	-0.0013 \pm 0.002	-0.014 \pm 0.026	-0.032 \pm 0.03	-0.173 \pm 0.22	-0.055 \pm 0.14	-0.048 \pm 0.13

Slope values reported as rate of change per week over the duration of the study.

^a= Results from Model 1, slope is change over time (week)

^b= Results from Model 2, slope is interaction of time x ARAT change

^c = Results from Model 3, slope is interaction of time x treatment group

^d= Results from Model 4; Values reported for a 1-unit change in chronicity (i.e. 1 month), slope is the interaction of time x chronicity

^e= Results from Model 5; Values reported for 1-point increase in baseline ARAT score (e.g. for every one point increase in baseline ARAT score, the participant's slope increased by 0.0001 on the use ratio), slope is interaction of time x baseline ARAT score

^f= Results from Model 6; Values reported for individuals who indicated their dominant UL was the paretic UL, slope is interaction of time x concordance

^g= Results from Model 7; Values reported for individuals who were independent with basic activities of daily living (ADL; e.g. bathing, dressing, toileting), slope is interaction of time x ADL independence

To test the possibility that some changes in performance were masked in the entire sample, we grouped participants based on changes in UL capacity. Seventy-five participants had available data for this portion of the analysis. The three excluded cases withdrew from the study prior to the first assessment after treatment was initiated, and therefore did not have an ARAT change score. Individuals who had larger changes in UL capacity (ARAT change score ≥ 6 points, $n=36$) started better (higher baseline intercepts) for the use ratio ($p < 0.001$), hours of paretic limb use ($p = .007$), magnitude ratio ($p < .001$), median acceleration ($p < .001$), and acceleration variability ($p < .001$), as would be expected (values not shown). Despite the better starting points, the interaction between ARAT change and time did not influence the rates of change between the two groups (p values $> .05$) and all slopes were still not significantly different from zero (Table 2, second row of data).

The addition of treatment group, and the interaction between treatment group and time also did not change the results. Figure 1 illustrates the lack of group effect on all six variables. No significant intercept and slope differences existed between groups and results from general linear hypothesis tests indicated none of the group slopes were significantly different from zero for any of the six variables (all p -values > 0.05). Results of the group effects are reported in the middle rows of Table 2. Finally, we tested potential modifiers that have previously been shown to influence UL performance.⁴⁴ Time post-stroke, baseline UL capacity, concordance, and ADL status influenced the starting points (i.e. better baseline intercepts) as expected, but did not influence change over time (model slopes calculated from time x modifier interaction, all p -values > 0.05 , slope values reported at the bottom of Table 2). Specifically, time post-stroke significantly influenced the use ratio ($p = 0.04$) and magnitude ratio ($p = 0.03$) intercepts,

respectively, but was not a significant modifier of the remaining four intercept values. Baseline UL capacity and ADL status significantly influenced the intercepts of all six variables, and concordance significantly influenced the use ratio ($p < .001$), magnitude ratio ($p = 0.01$), median acceleration ($p = 0.04$), and acceleration variability ($p = 0.04$) intercepts.

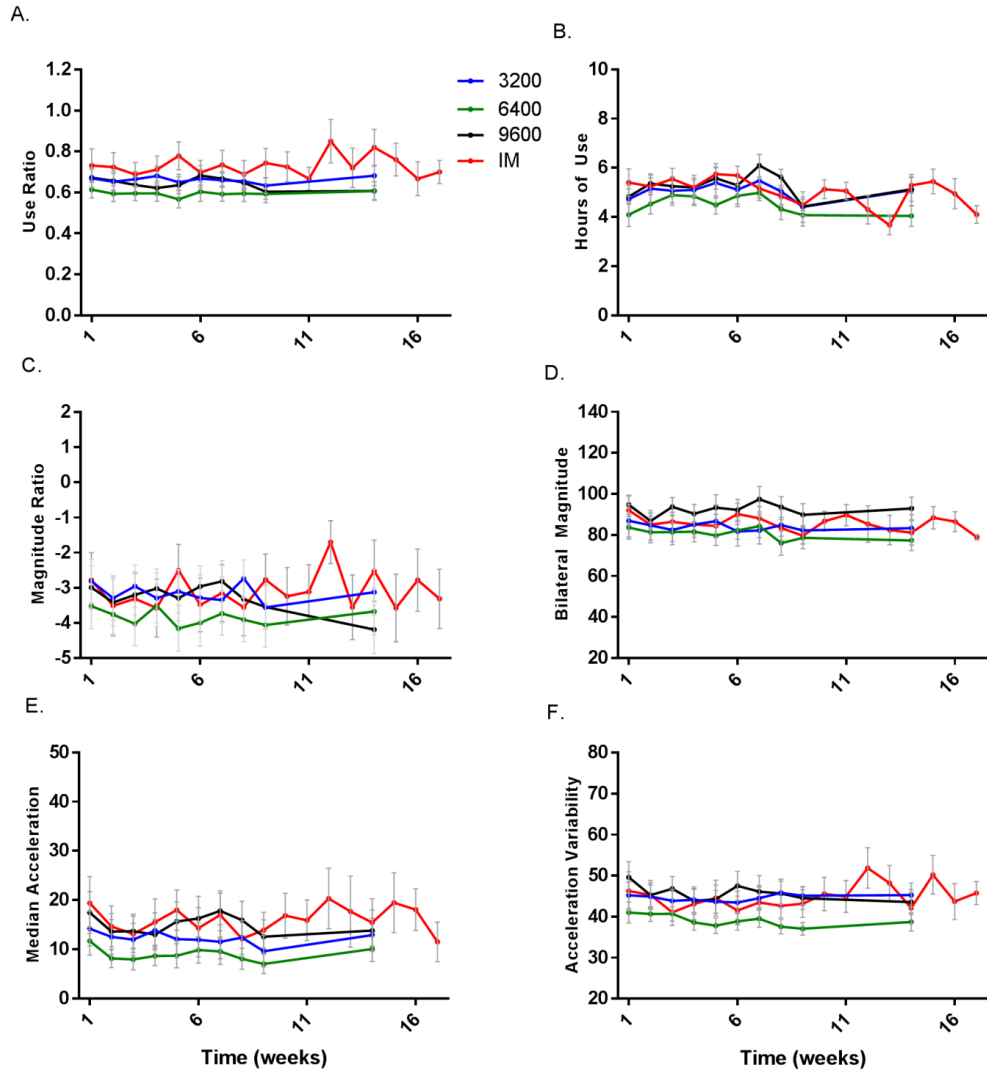


Figure 2.1 UL performance over time for all six accelerometer variables by dose group. Values are group means \pm SE for each assessment. Week 1 corresponds to the baseline assessment, and subsequent weeks correspond to the weekly assessment out to the immediate post-intervention assessment and follow-up assessment. Participants in the individualized maximum (IM) group were allowed to continue beyond the 8-week enrollment period until specific stopping criteria were met, observed here by the presence of additional data points.

Figure 2 provides representative individual examples of the lack of change in UL daily performance. Despite substantial changes in UL capacity, participants 1 (10 point ARAT change) and 2 (18 point ARAT change) show no change in performance from baseline to post-intervention. The pictures from these two participants are not distinctly different from participant 3 (3 point ARAT change). Compared to healthy, neurologically intact adults, the density plots in Figure 2 are all asymmetrical, with mostly negative magnitude ratio values that indicate increased non-paretic UL activity. An absence of warmer colors indicate less movement overall, with no change in the frequency of movement from baseline to post-intervention. There is a noticeable peak in the center of participant 1's density plot at week four (i.e. a higher bilateral magnitude value), indicating more intense movements, but this was not sustained by the post-intervention assessment. While some participants showed small fluctuations such as this one, no subjects showed sustained changes over time.

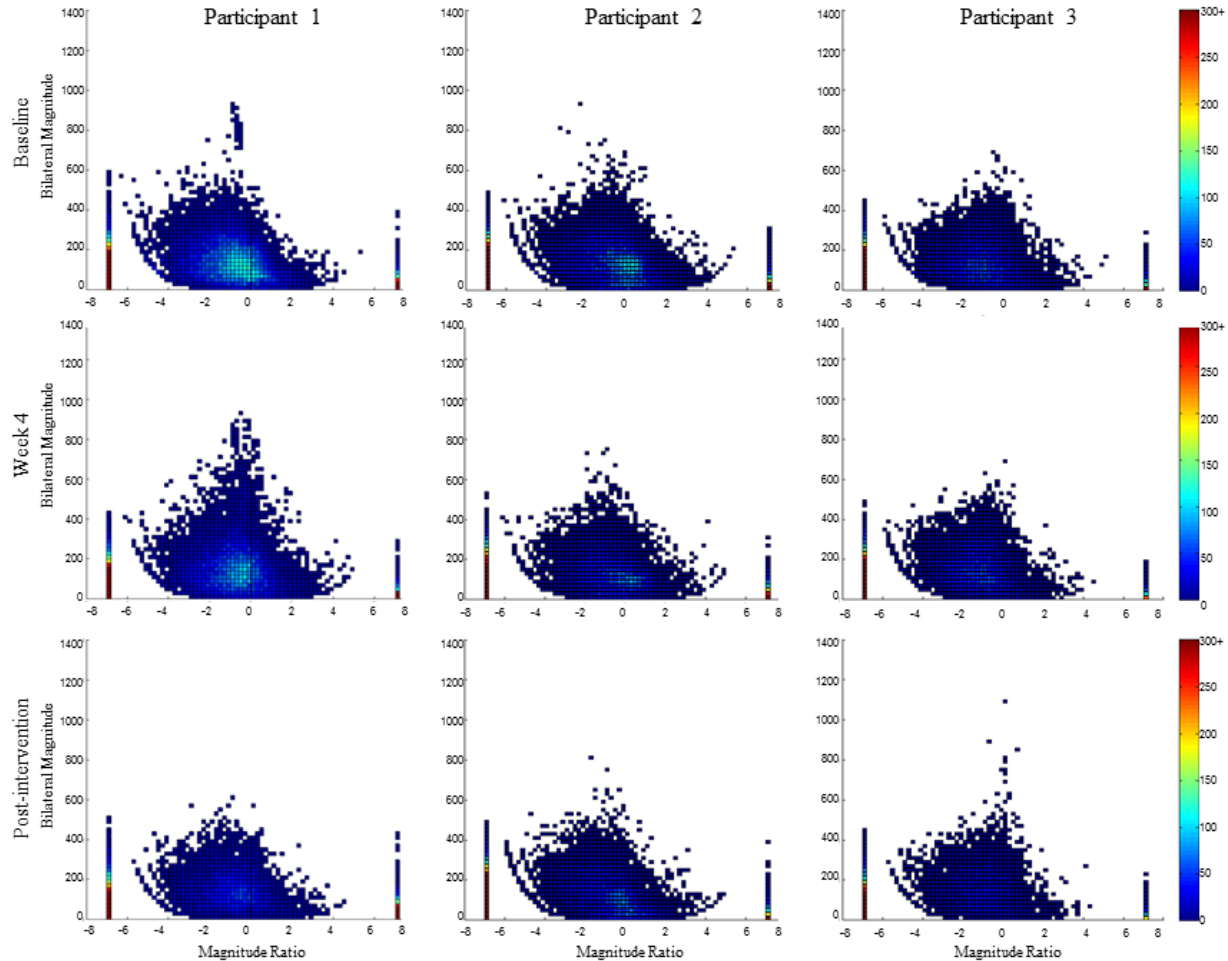


Figure 2.2 Density plots showing second-by-second data from three representative participants. Time points are from baseline (top), week four (middle), and post-intervention assessments (bottom). The y-axis (Bilateral magnitude) represents the intensity of movement, with higher values indicating larger, more intense movements. The x-axis (Magnitude ratio) represents the contribution of each limb to an activity, with 0 indicating equal UL contribution, negative values indicate more non-paretic UL movement and positive values indicate more paretic limb movement. The color scale shows overall frequency of UL movement, with warmer colors indicating more UL movement. The small bars on each side of the plot indicate non-paretic (negative) and paretic (positive) unilateral movement. Overall, participants had a moderate level of UL paresis at baseline (participant 1 = 38 points; participant 2 = 35 points, and participant 3 = 36 points). Participants 1 and 2 demonstrated 10-point and 18-point changes in ARAT score, respectively. Participant 3 increased 3 points on the ARAT. Regardless of UL capacity changes, there was no evidence of sustained changes in performance.

2.5 Discussion

We evaluated changes in UL performance in daily life resulting from a task-specific intervention using a quantitative measure of performance. None of the 78 participants increased their UL performance in daily life, as measured by the six accelerometer variables. Dividing the sample into groups based on changes in UL capacity or dividing the sample into groups based on amount of motor practice failed to produce changes in performance over time. Additionally, despite having various effects on the initial intercepts, none of the modifiers influenced change over time (slopes). Thus, UL task-specific training, designed to improve UL capacity in the clinic may be unable to improve UL performance in daily life. This is contrary to the long-standing clinical assumptions that improving UL capacity directly translates to improved UL performance in daily life.

A key reason people are referred to motor rehabilitation services is to improve UL performance in daily life. With the cost of stroke expected to exceed 2.2 trillion dollars by 2050,⁴⁸ it is striking that not one person changed UL performance after this carefully delivered intervention.¹⁴ These results are consistent with a few other studies that have begun to identify a discrepancy between changes observed in the rehabilitation clinic (i.e. capacity) and a failure to increase UL performance in daily life both for adults^{26,49} and children⁵⁰ (but see⁵¹). When changes seen in the clinic do not carry over to life at home, then it is time to reconsider what is being delivered in the clinic and how it might need to be changed.

One argument against these striking results is that perhaps the accelerometers failed to capture change that really occurred. There are numerous studies of UL interventions post-stroke that have reported a positive increase in UL performance in daily life when measured via self-

report^{10,17-19} and for individuals earlier after stroke, the MAL and use ratio are correlated.³⁸ Self-perception of changes in UL performance is a valuable component of the rehabilitation process, but perhaps not the whole story. We cannot completely rule out the possibility that other variables from the accelerometers would show changes. In deciding on these 6 variables however, we did test a number of others that were not useful (e.g. highly variable across neurologically intact population).^{39,43} Our accelerometers were on the wrists, so we also cannot completely rule out the possibility that small, dexterous movements of the fingers improved and we did not capture this. This second possibility is also unlikely, since pilot testing with accelerometers picked up most of the hand/finger movements,^{43,52} particularly the less efficient and uncoordinated movements of the paretic hand and fingers post-stroke.

There are several possible reasons for these striking results. First, this study included those with chronic (≥ 6 months) stroke when habits have likely already formed. Perhaps changes in UL performance would be observed if task-specific training was delivered earlier after stroke. Second, changes in capacity may be insufficient or not enough to improve UL performance in daily life. There may be a specific threshold for UL capacity that must be exceeded to drive changes in UL performance.^{53,54} Third, UL performance is not solely a function of UL capacity but dependent on other factors such as motivation, health behaviors, and environmental supports. It is likely that these results are a combination of all three proposed reasons. Future studies could examine the timing of intervention to improve UL performance post-stroke, as some pilot studies have reported changes in both UL capacity and UL performance earlier after stroke.^{27,55} Additional studies could explore other potential factors related to UL performance such as health behaviors and motivation, and explicitly test interventions that target these factors. Indeed, the

36 participants who demonstrated improvements in capacity (i.e. ARAT change ≥ 6 points) may be ideal candidates for interventions targeting UL performance in daily life, given their ability to change at this stage of recovery.

Several limitations influence the interpretation of these data. First, wearing sensors on the upper limbs could potentially cause people to do more with their ULs in daily life. Sensor data were collected weekly with more than 8 assessments. Thus the novelty of wearing the devices likely wore off early. If anything, we may have overestimated UL performance in daily life within the first few assessments. Second, the sensor-based methodology quantifies movement but does not quantify specific activities or movement parameters (e.g. speed, efficiency, accuracy). It is possible that some participants made small improvements in these parameters that went unmeasured. These changes, however, were not sufficient to change the involvement of the paretic limb either in total duration (use ratio) or on a second-by-second basis (magnitude ratio).

2.5.1 Conclusions

We found no evidence of improvement in UL performance in daily life in 78 people with long-standing paresis post-stroke who completed an 8-week individualized, intensive, progressive, task-specific intervention. Neither changes in UL capacity nor the overall dose (i.e. amount) of movement practice influenced changes in UL performance. These results expose an emerging problem in stroke rehabilitation. Rehabilitation services, and the providing clinicians, may be changing what people can do while they are in the rehabilitation clinic, but these benefits do not carry over to improved UL performance at home, when measured with wrist-worn accelerometers. If a primary goal of rehabilitation is to improve performance in daily life for individuals post-stroke, then it is imperative that future research investigate this emerging issue.

2.6 Acknowledgements

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2.7 References

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Chapter 3: Belief, confidence, and motivation to use the paretic upper limb in daily life over the first 24 weeks after stroke

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3.1 Abstract

Background and Purpose: The recovery patterns of upper limb (UL) impairment after stroke are well-documented. Factors such as belief that paretic UL improvement is possible, confidence, and motivation to use the paretic UL in everyday tasks are unexplored early after stroke. The purpose of this study was to characterize belief, confidence, and motivation to use the paretic UL in daily life, and self-perceived barriers to UL recovery over the first 24 weeks post-stroke.

Methods: This was a longitudinal cohort study (n=30) with eight assessment sessions over 24 weeks. Belief, confidence, and motivation to use the paretic UL and self-perceived barriers to UL recovery were quantified via survey and analyzed using descriptive statistics. Change in the number of self-perceived barriers between weeks 2 and 24 was tested using a paired samples t-test. The relationship between UL capacity, depressive symptomatology, cognition and each psychosocial factor were examined using Spearman's rank-order correlation analyses. **Results:** Belief, confidence, and motivation to use the paretic UL were high across the 24 weeks, with little variation. There was no difference between the average number of barriers from weeks 2 to 24. There was no relationship between the clinical measures and belief, confidence, and motivation at week 2, 12, or 24. **Discussion and Conclusions:** Low levels of belief, confidence, and motivation may not emerge until much later in the recovery process. The lack of consistent correlation between psychosocial factors and clinical outcomes suggests belief, confidence, and motivation may not be as vulnerable to functional status early after stroke as previously thought.

3.2 Introduction

By 2050, direct and indirect stroke costs are expected to exceed \$1 trillion dollars,¹ creating an urgent need for streamlined medical and rehabilitation services to reduce stroke-related disability. The purpose of rehabilitation is to help improve performance in daily life.

Performance, defined by the International Classification of Functioning (ICF) as what a person actually does outside of the clinic or laboratory,² is a complex construct and likely influenced by many factors. Following a stroke, the multitude of deficits commonly observed makes performance in daily life even more restricted. Upper limb (UL) performance, or use, in daily life is no exception. Until recently, it was assumed that improved UL performance was directly linked to improved UL capacity, or what someone is capable of doing inside the clinic or laboratory.² This assumption is not supported by evidence.³⁻⁶ As a result, there exists an urgent need to explore other factors that may influence UL performance in daily life.

Motor sequelae post-stroke, compared to psychological/emotional impairment, are well established and receive a considerable amount of attention from the research community.⁷⁻⁹ Quantifying psychosocial factors (belief, confidence, and motivation) and self-perceived barriers to performance in daily life is an important step in understanding how these factors may influence UL performance early after stroke. Belief, confidence, and motivation are empirically derived factors from Social Cognitive Theory^{10,11} and Social Determination Theory,¹²⁻¹⁴ two common behavioral theories. An individual's belief and confidence to perform specific tasks can influence activity selection and completion.¹⁵ Indeed, self-efficacy (belief, confidence, and motivation being key components of self-efficacy¹⁵) post-stroke mediates walking performance,^{16,17} and is positively associated with physical activity,¹⁸ balance and walking,^{17,19} independence with activities of daily living,^{20,21} onset of post-stroke depression,²² and overall well-being.²³ Confidence is often linked to recovery, where increased confidence is a marker of progress while low levels of confidence may restrict individuals from reaching full recovery

potential.²⁴ Motivation has been identified as a potential target for improving rehabilitation outcomes.²⁵⁻²⁷

Despite the influence of these factors on the above stroke outcomes, little is known about how individual belief, confidence and motivation to use the paretic UL in daily life, and self-perceived barriers to UL recovery evolve over the first 6 months following a stroke. Knowledge of psychosocial factors specific to UL recovery and use in daily life comes from cross-sectional studies of chronic (> 6 months) stroke survivors.²⁸⁻³⁰ While valuable, these data may differ from early stroke recovery, especially in the presence of acute psychological distress that is common after sudden health events such as stroke.³¹ Indeed, the rapid motor and functional changes frequently observed early after stroke may influence individual belief, confidence, and motivation to use the paretic UL in daily life differently than in the chronic phase, when the magnitude of change is often smaller. Understanding how these factors might change over the first 6 months post-stroke provides critical information for future performance-based UL interventions. Additionally, understanding how self-perceived barriers to UL recovery evolve over the first 6 months may also identify therapy targets to help improve overall UL use in the free-living environment.

The purpose of this study was to characterize individual belief, confidence, and motivation to use the paretic UL in daily life over the first 24 weeks, or 6 months, post-stroke. A secondary purpose was to quantify self-perceived barriers to UL recovery over the same period. As rehabilitation research continues to emphasize performance in daily life, understanding how factors beyond the motor system evolve will provide critical insights into the sequelae of

psychosocial factors post-stroke. These data are necessary for the design of future trials that aim to increase performance in daily life. While this report examines these issues in UL performance, the results are important for all domains of stroke rehabilitation.

3.3 Methods

This was a longitudinal, prospective, inception cohort study. Participants were recruited from a large, urban hospital via the Stroke Patient Access Core at Barnes Jewish Hospital. Participants were enrolled within 2 weeks of a first-ever stroke, with residual UL paresis. Specifically, participants were included if the following criteria were met: 1) within two weeks of a first-ever ischemic or hemorrhagic stroke, confirmed with neuroimaging; 2) presence of UL motor deficits within the first 24-48 hours post-stroke, as indicated by a National Institutes of Health Stroke Scale (NIHSS) Arm Item score of 1-4 or documented manual muscle test grade of <5 anywhere on the paretic UL; 3) able to follow a 2-step command, as measured by a NIHSS Command Item score of zero; and 4) anticipated return to independent living, as indicated by the acute stroke team. Participants were excluded from the study if any of the following criteria were met: 1) history of previous stroke, neurological condition, or psychiatric diagnoses; 2) presence of other comorbid conditions that may limit recovery (e.g. end-stage renal disease or stage IV cancer); 3) lives more than 90 minutes from study location; and 4) currently pregnant by self-report. All participants provided written, informed consent and the study was approved by The Human Research Protection Office at Washington University in St. Louis, MO.

Participants underwent eight assessment sessions over the first 24 weeks, or 6 months, post-stroke. A battery of assessments was administered by the research coordinator at 2, 4, 6, 8, 12, 16, 20, and 24 weeks with each session lasting approximately 30-60 minutes. Assessment

sessions were completed every 2-weeks in the beginning to capture the anticipated large, rapid improvements in UL capacity and then transitioned to every month as recovery slowed. Due to the observational design, the amount and type of rehabilitation services were not controlled for in this study. Instead, participants received rehabilitation services in accordance with the medical team's recommendations. The study assessments were administered in the research lab, inpatient rehabilitation hospitals, skilled nursing facilities, or the participants' homes, depending on location and travel abilities.

3.3.1 Study assessments

Individual belief, confidence, and motivation to use the paretic UL in everyday tasks and self-perceived barriers to UL recovery were quantified via survey. The survey was developed using focus group data from a large cohort of stroke survivors in Australia and modified for use in the United States.^{28,29} Using focus group data ensured the survey items quantified salient survivor concerns as opposed to researchers speculating what issues were most important to survivors. The modified survey consists of four sections: I. Participant estimation of total amount of time spent improving UL function, II. Self-perceived barriers to paretic UL recovery (e.g. not enough movement to work with, lack of support from health professionals), III. Statements about individual belief (I believe further improvement of my [paretic] arm and hand is possible), confidence (I feel confident to do what I need to do to use my [paretic] arm and hand in everyday tasks), and motivation (I want to be able to use my [paretic] arm and hand more in everyday tasks). Participants respond to the statements in section III using a 4-point Likert scale (4=strongly agree, 3=slightly agree, 2=slightly disagree, and 1=strongly disagree). The fourth section (IV), not included in this report, measured participant readiness to change/use the paretic UL in daily activities.

3.3.2 Additional assessments

Upper limb motor capacity was assessed using the Action Research Arm Test (ARAT).³² The ARAT is a valid and reliable measure of UL capacity for adults with stroke.³³⁻³⁵ The ARAT is a 19-item assessment with four subscales: grasp, grip, pinch, and gross motor. Scores for the individual items range from 0-3, where 0 = cannot complete, 1= performed partially, 2= task completed but with abnormal movement, and 3= performed normally. Individual items are summed and final scores range between 0-57, with higher values indicating better UL function.

Cognitive function was screened using the Montreal Cognitive Assessment (MoCA).³⁶ The MoCA is a valid and reliable cognitive screening tool and is more sensitive in detecting mild cognitive impairment compared to the Mini Mental Status Exam.³⁷⁻³⁹ The MoCA tests for cognitive impairment across eight domains (visuospatial/executive functioning, naming, memory, attention, language, abstraction, delayed recall, and orientation), and scores range from 0-30, with scores < 26 indicating cognitive impairment.³⁶ Depressive symptomatology was examined using the Centers for Epidemiological Studies Depression Scale (CES-D)⁴⁰ that has been validated for use in adults with stroke.^{41,42} Scores for the CES-D range from 0-60, with higher scores indicative of greater depressive symptomatology. A simple demographics questionnaire collected pertinent demographic information. Lastly, participants self-reported if they were receiving rehabilitation, the setting (e.g. inpatient rehabilitation, outpatient), disciplines (e.g. physical therapy, occupational therapy, speech language pathology), and frequency per week.

Both the psychosocial survey and the CES-D require standardized scales, wherein the participants choose the appropriate response to each item of the test. For both assessments, the

respective scales were printed in large font, laminated, and placed in front of the participant. In effort to reduce information burden, the assessor would read each statement aloud, repeating upon request, and the participant would indicate either verbally or by pointing, their answer to each item. This was repeated for section III of the psychosocial survey and for every item on the CES-D. Reading each item to the participant eliminated the need for reading glasses that were often missing early after stroke and reduced overall fatigue. Participants reported satisfaction with this approach.

3.3.3 Statistical Analysis

All analyses were completed in R (version 3.3.2),⁴³ an open source statistical computing program. Descriptive statistics were calculated for belief, confidence, and motivation at each assessment week. The total number of self-perceived barriers was the sum of the total number of barriers identified. The average number of self-perceived barriers per participant and the standard error were calculated for each assessment week. The difference in the total number of self-perceived barriers at weeks 2 and 24 was tested using a paired samples t-test.

The relationship between the psychosocial factors (i.e. belief, confidence, and motivation), UL capacity (ARAT), depressive symptomatology (CES-D), and cognitive function (MoCA) were analyzed using Spearman rank-order correlation analyses. Correlation analyses were completed at weeks 2, 12, and 24, respectively, and Holm's method was applied to adjust for multiple comparisons. The significance level was established at $\alpha < 0.05$ for all analyses.

3.4 Results

Thirty of the thirty-two enrolled participants had available data for this analysis. The two excluded participants were a result of a screen failure and withdrawal prior to the first

assessment session. Table 1 reports key participant demographic information. Eight participants dropped out of the study between weeks 2 and 24, due to self-selected withdrawal (n=3), second stroke (n=1), fatal cancer diagnosis (n=1), fall resulting in fractured UL (n=1), and decline in medical status (n=2). Nearly all participants received rehabilitation services immediately after their stroke (week 2) and services tapered over the study duration. All participants were independent with basic activities of daily living prior to their stroke and 37% of the sample reported their dominant limb was their paretic limb (i.e. concordance).

Table 3.1 Participant demographics

	Total sample (n=30)
Age (years)	68.4 ± 9.9
Gender	12 F, 18 M
Race	23 Caucasian 6 African American 1 Asian/ Pacific Islander
Stroke type	30 ischemic
Stroke location	17 cortical 11 subcortical 1 cortical & subcortical 1 posterior circulation/cerebellar
Affected side	20 L, 10 R
Concordance, n (%) ^a	11 (37%)
Prior working status	21 not working 9 working at least part-time
% Independent with ADL prior to stroke	100%
% Living alone prior to stroke	20%
Self-reported comorbidities, median (range) ^b	2 (0,4)
% Receiving rehabilitation services	
Week 2 (n=30)	90%
Week 4 (n=27)	78%
Week 6 (n=26)	69%
Week 8 (n=24)	71%
Week 12 (n=22)	55%
Week 16 (n= 23)	48%
Week 20 (n=20)	35%
Week 24 (n=22)	23%
% Admitted to rehabilitation hospital at week 2	83%
Days post-stroke assessments administered	
Week 2	13.4 ± 2.9
Week 4	27.3 ± 1.9
Week 6	41.6 ± 3.1
Week 8	56.3 ± 2.6
Week 12	84.7 ± 2.9
Week 16	113 ± 4.1
Week 20	140 ± 2.1
Week 24	169 ± 2.7
Week 2 Values	
ARAT ^c	22.9 ± 21.4
MoCA score, median (range) ^d	21 (11, 29)
CES-D score, median (range) ^e	7 (0, 44)

Values are mean ± SD unless otherwise indicated

^a Dominant limb=paretic limb

^b Median number of comorbidities per participant

^c ARAT=Action Research Arm Test, scores range from 0-57, higher values=better function

^d MoCA= Montreal Cognitive Assessment, scored 0-30, lower scores may also reflect aphasia or fatigue

^e CES-D=Centers for Epidemiological Studies-Depression Scale; scored 0-60 with higher scores indicating greater depressive symptomatology

Across the 24-week study duration, there were high levels of belief, confidence, and motivation across the sample (median value=4, strongly agree). Figure 1 presents the percentage of responses using the Likert scale for each assessment session. Across all eight assessment sessions, the large majority of participants strongly agreed that further improvement of their paretic UL was possible (belief), they were confident to use their paretic UL, and were motivated to use their paretic UL in daily life. As seen in Figure 1, in the event individuals did not strongly agree to each question, they often slightly agreed, and rarely disagreed to any of the questions, at any point in time.

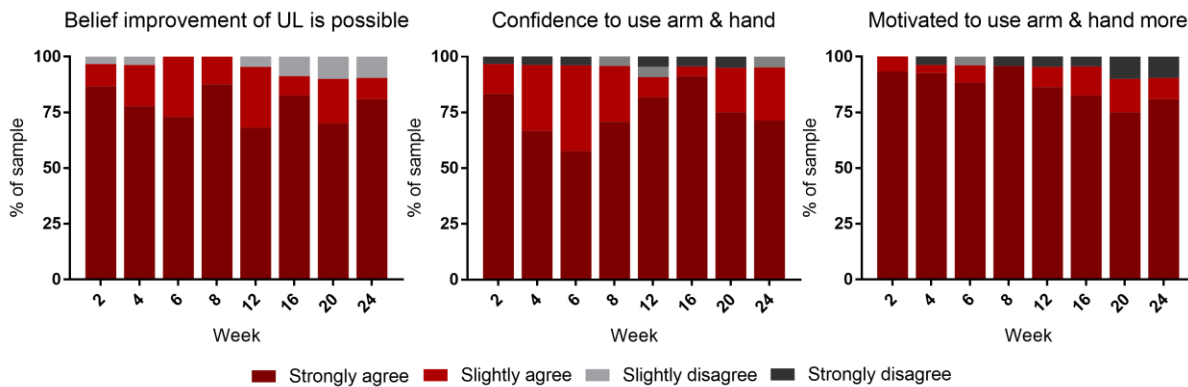


Figure 3.1 Percent of the sample who responded they strongly agreed, slightly agreed, slightly disagreed, or strongly disagreed to the individual statements of belief, confidence, and motivation. The large majority of participants indicated they strongly agreed further improvement of their paretic UL was possible (belief), and were confident and motivated to use the paretic UL in everyday tasks at every assessment session.

The average number of self-perceived barriers to UL recovery per participant slightly varied between week 2 (3.4 ± 2.7), week 12 (1.9 ± 2.2), and week 24 (2.2 ± 3.2). Figure 2 displays the average number of self-perceived barriers per participant across all eight assessment sessions. There was not a significant difference in the total number of self-perceived barriers between weeks 2 and 24 ($t=1.42$, 95% CI= $[-0.43, 2.23]$) for the 22 participants who had available data at

both time points. Table 2 lists the 13 possible barriers and the number of participants who answered “yes” to that barrier at weeks 2, 12, and 24. Overall, the top barrier varied across the three assessment periods, with nearly all participants indicating limited UL movement as a barrier at week 2, but this did not persist over time. The most common barrier at weeks 12 and 24 was feeling they could not do things correctly when attempting to use the paretic UL in daily life.

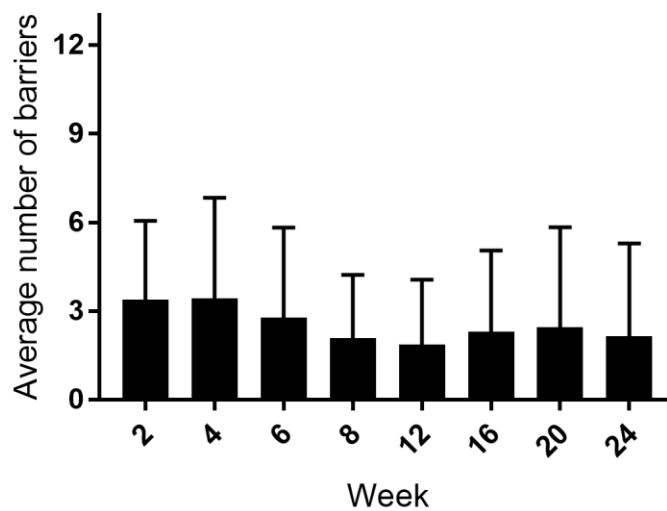


Figure 3.2 Average number of self-perceived barriers to UL recovery per participant across the eight assessment sessions. Values are mean \pm SE.

Table 3.2 Self-perceived barriers to recovery (value represents number of participants who indicated the listed barrier limited recovery)

	Week 2 (n=30)	Week 12 (n=22)	Week 24 (n=22)
Not enough movement to work with	22	5	3
Too many other things to deal with	14	1	6
Feeling I can't do things correctly	14	6	7
Lack of information	9	3	2
Other, more worrisome health problems	8	6	5
Too tired	8	5	5
Feeling what I do doesn't help	7	3	5
Too many other responsibilities	5	2	5
Lack of money	4	5	4
Difficulty getting out of the house	3	5	4
Lack of support from family/friends	3	0	1
Lack of support from health professionals	2	0	1
Not interested	2	0	1

There were no consistent relationships between belief, confidence, and motivation and UL capacity, depressive symptomatology, and cognitive function. Table 3 presents the correlation coefficients at weeks 2, 12, and 24. After correcting for multiple comparisons using Holm's method, no correlations were significant at any time point.

Table 3.3 Correlation coefficients at weeks 2 (n=30), 12 (n=22), and 24 (n=21)

	ARAT ^a			CES-D ^b			MoCA ^c		
	Week			Week			Week		
	2	12	24	2	12	24	2	12	24
Belief	0.07	-0.03	-0.01	-0.34	-0.29	0.13	-0.04	-0.07	-0.25
Confidence	-0.08	-0.17	0.58	-0.43	-0.04	0.18	0.12	-0.20	-0.05
Motivation	-0.34	-0.41	-0.09	0.03	0.19	0.54	-0.38	-0.18	-0.16

^a ARAT= Action Research Arm Test, scores range 0-57, with higher scores indicating better UL function

^b CES-D= Centers for Epidemiological Studies Depression Scale, scores range 0-60, with higher scores indicating greater depressive symptomatology

^c MoCA = Montreal Cognitive Assessment, scores range 0-30, with higher scores indicating better cognitive function

3.5 Discussion

This was the first study to quantify individual belief that further improvement of the paretic UL was possible, and confidence and motivation to use the paretic UL in daily life over the first 24 weeks post-stroke. Prior to this study, our limited knowledge of these factors came from cross-sectional data in chronic stroke cohorts.²⁸⁻³⁰ Quantifying these psychosocial factors early, over multiple assessment sessions, captures their dynamic nature which provides a more robust understanding of the recovery process. The key finding from this study was the high, unwavering levels of belief, confidence, and motivation over the first 24 weeks post-stroke. In the event participants did not strongly agree to each question, they often slightly agreed, and rarely disagreed.

Belief, confidence, and motivation to act in a given scenario influence actual behavior and activity selection.^{10,15,44} Thus, characterizing these factors over the first 24 weeks post-stroke, a critical time for recovery, provides novel insight into how these factors may evolve as

individuals progress, plateau, or decline early after stroke. There is a growing emphasis on motivation and other psychosocial/behavioral factors as possible targets for improving UL and stroke outcomes.^{25,26} Our data suggest that early after stroke, improving these psychosocial factors may not be as critical as previously thought. Instead, developing novel interventions with behavioral components (e.g. feedback, incentives) that exploit these high levels and promote UL use may help increase overall UL performance in daily life.

These data may be applicable to other stroke rehabilitation areas such as walking and balance. Limited longitudinal data exist to explain how belief, confidence, and motivation for balance or walking may change early after stroke. It is reasonable to assume that confidence, for example, may strongly influence walking behavior after stroke given the fear of falling or other safety concerns that can have significant repercussions. There are few, if any, substantial risks to using the paretic UL in daily life. The high levels of individual belief, confidence, and motivation reported here may be partially influenced by the relatively low risks of using the paretic UL in everyday tasks. Because stroke often results in multiple, complex impairments (e.g. cognitive, communication, and motor), future work will want to explore belief, confidence, and motivation for other stroke impairments both individually and as a group over time. Belief, confidence, and motivation to use the paretic UL may lessen when contextualized with other impairments (i.e. motivation to use the paretic UL may be reduced by heightened motivation to improve communication or resume walking).

Results from the correlation analyses show belief, confidence, and motivation are not associated with UL capacity, depressive symptomatology, and cognition in this sample. This is important

for future UL performance research. The common clinical domains tested here (capacity, depressive symptomatology, and cognition) appear less influential with psychosocial factors compared to other aspects of stroke recovery (e.g. walking, self-management). Belief, confidence, and motivation may be influenced by other, less common factors such as self-regulation,^{10,14} perceived competence and control,^{14,44} and environmental/social factors.¹⁰ Future research may want to explore these factors as they relate to belief, confidence, and motivation.

Several limitations influence the interpretation of these data. The small sample size limits the generalizability of these results, and a larger study is currently underway to validate these findings. Nearly all participants in this sample improved their UL capacity over the study duration, which may have contributed to the high levels of belief, confidence, and motivation. As expected in the 24 weeks following a stroke, some participants withdrew from the study prior to completing all eight assessment sessions. It is possible, although unlikely, these participants could have reported low levels of belief, confidence, and motivation. Additionally, and most importantly, belief, confidence, and motivation are complex constructs. In this study, we did not query every possible dimension of these constructs (e.g. intrinsic vs. extrinsic motivation). Future work may want to explore each construct in greater detail to provide a more robust understanding of what components may be most affected in the recovery process or utilize qualitative methods to develop a deeper understanding of these constructs in this population. Currently, there is a lack of UL-specific assessments to quantify these factors (e.g. no UL specific self-efficacy scale). It may be worthwhile to develop an UL-specific self-efficacy scale for future work given that self-efficacy is task-specific and varies across circumstances.^{45,46}

3.5.1 Conclusion

Just as there are recovery and disability trajectories,^{47,48} there is also a natural trajectory of psychosocial factors that can change as a result of biological, personal, and environmental factors. The initial 24 weeks after stroke often includes rapid, notable improvement in physical function, transitions between medical facilities and home, and attempts to return to pre-stroke routines and life roles. An individual's belief, confidence, and motivation to use the paretic UL in everyday tasks may be less vulnerable early after stroke to their changing functional status and environment than previously thought. As a result, future UL interventions may consider focusing more on reducing self-perceived barriers to UL recovery and other novel techniques that leverage high levels of confidence and motivation to increase UL use in everyday tasks. Devoting time and resources to characterizing these psychosocial factors for other stroke related deficits is a worthwhile endeavor given the dynamic nature of belief, confidence, and motivation. This will ultimately lead to more robust, multi-dimensional interventions that may help improve outcomes post-stroke.

3.6 Acknowledgements

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Chapter 4: Upper limb performance in daily life improves over the first 12 weeks post-stroke

This chapter has been submitted:

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4.1 Abstract

Background: Upper limb (UL) performance, or use, in daily life is complex and likely influenced by many factors. While the recovery trajectory of UL impairment post-stroke is well documented, little is known about the natural trajectory of sensor measured UL performance in daily life early after stroke and the potential moderating role of psychosocial factors.

Objective: To examine the natural trajectory of UL performance within the first 12 weeks post-stroke and characterize the potential moderating role of belief, confidence, and motivation on UL performance. Methods: This was a longitudinal, prospective cohort study quantifying UL performance and related psychosocial factors early after stroke. UL performance was quantified via bilateral, wrist-worn accelerometers over five assessment sessions for 24-hours. Individual belief, confidence, and motivation to use the paretic UL, and self-perceived barriers to UL recovery were quantified via survey. Change in four accelerometer variables and the moderating role of psychosocial factors was tested using hierarchical linear modeling. The relationship between self-perceived barriers and UL performance was tested via Spearman rank-order correlation analysis. Results: UL performance improved over the first 12 weeks after stroke. Belief, confidence, and motivation did not moderate UL performance over time. There was a negative relationship between UL performance and self-perceived barriers to UL recovery at week 2, which declined over time. Conclusions: Sensor measured UL performance can improve early after stroke. Early after stroke, rehabilitation interventions may not need to directly target belief, confidence, and motivation but may instead focus on reducing self-perceived barriers to UL recovery.

4.2 Introduction

Rehabilitation services aim to reduce the long-term effects of post-stroke disability. Motor system impairments are one of the top reasons individuals are referred for rehabilitation services.¹⁻³ Indeed, nearly 80% of individuals will experience some degree of upper limb (UL) paresis after a stroke.⁴ At 6 months, 65% of individuals will have difficulty incorporating their paretic UL into daily activities.^{5,6} Improving UL function is a top priority for many stroke survivors.⁷⁻⁹ As a result, researchers have invested significant time and money establishing several efficacious, protocol-based UL interventions both early¹⁰⁻¹³ and later^{14,15} after-stroke. These interventions are primarily designed to improve UL capacity. Capacity, quantified via standardized assessments in the rehabilitation clinic or laboratory, refers to what a person is capable of doing.¹⁶ It is often assumed in-clinic improvements in UL capacity directly translate to increased UL performance, or use, in daily life. Performance is defined by the International Classification of Functioning (ICF) Framework as what a person actually does outside of the clinic or laboratory.¹⁶ Recent research, however, does not support this assumption when performance is directly quantified via sensors (e.g. accelerometry).¹⁷⁻²⁰ Instead, this emerging body of research posits that while UL capacity and UL performance appear similar, they are distinctly different constructs.

The paucity of studies examining change in UL performance over the first 12 weeks after stroke,^{17,21} when majority of UL motor recovery occurs,^{22,23} is problematic. Understanding how UL performance changes during this critical period of motor recovery will provide important insights into the unique trajectory of real-world UL use after stroke. Preliminary data suggests some (n=2) individuals can improve UL performance early after stroke.²¹ Compared to the chronic phase (≥ 6 months), UL performance may increase over the first 12 weeks due to a

combination of factors unique to the early weeks post stroke: improvement in UL capacity, rehabilitation services, and less likelihood of learned non-use.²⁴ These early facilitating factors likely serve as barriers in the chronic phase of UL recovery.²⁰ Additionally, psychosocial factors and self-perceived barriers to UL recovery may influence UL performance in daily life early after stroke but have yet to be explored.

Recent work suggests a more robust philosophy, including the substantial role of individual agency (i.e. an active role through biology, belief, and self-regulatory systems),²⁵ in explaining the disparity between UL capacity and performance post-stroke.^{17,18} Psychosocial factors, such as belief, confidence, and motivation may underscore improved UL performance in daily life. Belief in one's ability to succeed in a task, despite setbacks or challenges, can profoundly influence the types of activities people choose to perform.²⁶ Both belief and confidence in one's prospective ability to complete a task are key components of self-efficacy.²⁷ Additionally, motivation is a key psychosocial factor for motor learning²⁸ and behavior change²⁹ and may potentially moderate real world UL performance as well. Recent work reports high levels of individual belief, confidence, and motivation early after stroke (Chapter 3). An important next step is to explore the potential moderating role of these psychosocial factors on UL performance early after stroke.

Thus, the purpose of this study was to examine the natural trajectory of UL performance within the first 12 weeks post-stroke, when the majority of motor recovery and rehabilitation services occur. A secondary purpose was to characterize the relationship between UL performance and psychosocial factors related to UL performance. We specifically focused on individual belief that

further UL improvement is possible, and individual confidence and motivation to use the paretic UL in daily life. A third, exploratory purpose was to examine the relationship between total self-perceived barriers to UL recovery and UL performance.

4.3 Methods

This was a longitudinal, prospective cohort study tracking UL performance and related measures over time. Potential participants admitted to a large, urban hospital were recruited via the Stroke Patient Access Center at Washington University. First-ever stroke survivors with residual UL paresis were enrolled within two weeks of their stroke. Participants were included in the study if the following criteria were met: 1) within two weeks of a first-ever ischemic or hemorrhagic stroke, confirmed with neuroimaging; 2) presence of UL motor deficits within the first 24-48 hours post-stroke, as indicated by a National Institutes of Health Stroke Scale (NIHSS) Arm Item score of 1-4 or documented manual muscle test grade of <5 anywhere on the paretic UL; 3) able to follow a 2-step command, as measured by a NIHSS Command Item score of zero; and 4) anticipated return to independent living, as indicated by the acute stroke team. Participants were excluded from the study if any of the following criteria were met: 1) history of previous stroke, neurological condition, or psychiatric diagnoses; 2) presence of other comorbid conditions that may limit recovery (e.g. end-stage renal disease or stage IV cancer); 3) lives more than 90 minutes from study location; and 4) currently pregnant by self-report. The Human Research Protection Office at Washington University in St. Louis, MO approved this study and all participants provided written informed consent.

Study participants completed five assessment sessions over the first 12 weeks post-stroke. The assessment battery was administered at 2, 4, 6, 8, and 12 weeks, with each assessment session

lasting 30-60 minutes. The study coordinator (first author) administered assessments. All study participants, to varying degrees, received rehabilitation services during this 12-week period. We did not control for the amount or type of rehabilitation services delivered to each participant in this observational study. Instead, each participant received therapy services in accordance with their overall plan of care established by the medical team. Assessments were administered in either the research lab, participants' homes, inpatient hospital wards, or other healthcare facilities depending on travel abilities.

4.3.1 Study assessments

Upper limb performance in daily life was quantified via bilateral, wrist-worn accelerometers (Actigraph Link, Pensacola, FL). Accelerometry is a valid and reliable measure of UL performance in both healthy adults^{30,31} and adults with stroke.³²⁻³⁵ Briefly, accelerometers record accelerations along three axes in activity counts where 1 count = 0.001664g. Data are sampled at 30 Hz, band-pass filtered between frequencies of 0.25 and 2.5 Hz, and down sampled into 1-second epochs (i.e. activity counts) for each axis using ActiLife 6 software (Actigraph Corp., Pensacola, FL). Activity counts are combined across the three axes to create a single value, a vector magnitude ($\sqrt{x^2+y^2+z^2}$), for each second of data.

Participants wore the accelerometers for 24-hours at each assessment time point. The 24-hour wearing period has previously shown to accurately reflect a typical day in adults with stroke (i.e. no difference between weekdays and weekends) and has high adherence rates.^{30,36,37} Participants were encouraged to wear the accelerometers at all times, including walking and bathing. Similar to previous work,^{30,31,34,35} accelerometry data were uploaded and processed using custom written software in MATLAB (Mathworks, Inc.). A threshold filter removed vector magnitude values <

2, which has been previously shown to significantly reduce variability and improve reliability of the accelerometer data.³³ Four accelerometry-derived variables were included in this analysis: hours of paretic UL use, use ratio, magnitude ratio, and bilateral magnitude. These accelerometer-derived variables quantify somewhat different aspects of UL performance in daily life. Two variables, hours of paretic UL use and the use ratio (or activity ratio), quantify total duration of movement while the magnitude ratio and bilateral magnitude are second-by-second variables.

Total hours of paretic UL use is the total time, in hours, the paretic UL was active over the 24-hour recording period, as measured by summing the seconds when the activity count was ≥ 2 .³⁰ On average, healthy, community-dwelling adults use their dominant UL 9.1 ± 1.9 hours/day and their nondominant UL 8.6 ± 2.0 hours/day.³⁰ The total hours of paretic UL use are then divided by the total hours of nonparetic UL use to derive a use ratio.^{30,38} A use ratio value of 1 would indicate both limbs are active the same amount of time while a value of 0.5 would indicate the paretic UL was active 50% of the time the nonparetic UL was active. A referent value of 0.95 ± 0.06 has been previously established in healthy, community-dwelling adults.³⁰ The magnitude ratio quantifies the contribution of each limb to an activity, for every second of data. The magnitude ratio value is the natural log of the paretic UL vector magnitude divided by the vector magnitude of the nonparetic UL.^{31,34} A magnitude ratio value of zero indicates equal contribution of both limbs to an activity. Negative magnitude ratio values represent greater use of the nonparetic UL while positive numbers represent greater paretic UL use. Previous work has established a median referent value of -0.1 (IQR 0.3) in healthy adults.^{31,34} Lastly, the bilateral magnitude value is the sum of the vector magnitudes of the paretic and nonparetic UL,

respectively.^{31,34} The bilateral magnitude is a measure of the intensity of movement, with higher numbers reflecting greater intensity. Healthy adults have a median referent bilateral magnitude value of 136.2 (IQR 36.6).^{31,34} The hours of paretic UL use, use ratio, and magnitude ratio are all responsive to change in UL function.³⁹ While not previously shown to be responsive to change, the bilateral magnitude represents intensity of movement, which may change during the early time period just after stroke.

Individual belief, confidence, and motivation to use the paretic UL was queried using a modified version of a survey developed from focus group data.^{7,8} The full details of the survey have been previously reported (Chapter 3).⁸ Here, two of the four sections were used: Sections II and III. Section II quantifies self-perceived barriers to UL recovery (e.g. “not enough movement to work with” or “not interested”). Section III includes individual statements that measure belief (I believe further improvement of my [paretic] arm and hand is possible), confidence (I feel confident to do what I need to do to use my [paretic] arm and hand in everyday tasks); and motivation (I want to be able to use my [paretic] arm and hand more in everyday tasks). The individual statements are measured using a 4-point Likert Scale (strongly agree, slightly agree, slightly disagree, and strongly disagree).

4.3.2 Additional study assessments

The Action Research Arm Test (ARAT) was used to measure UL capacity. The ARAT is a valid and reliable measure of UL capacity in adults with UL paresis.⁴⁰⁻⁴³ The ARAT is a 19-item assessment of grasp, grip, pinch, and gross motor function. Individual items are scored using a 0-3 ordinal scale (0= unable to complete the task, 1= partially performed, 2= task completed but with abnormal movement pattern or > 5 seconds, and 3= performed with normal movement in <

5 seconds). Individual item scores are summed, and the final score ranges from 0-57, with higher scores indicating better motor function. Paretic UL strength was quantified using the SAFE (shoulder abduction, finger extension) score.⁴⁴ Cognitive function was screened using The Montreal Cognitive Assessment (MoCA).⁴⁵ The MoCA assesses most cognitive impairment domains commonly observed in cerebrovascular disease⁴⁶ and is more sensitive to change compared to the Mini Mental Status Exam.⁴⁶ Participant demographics were collected via questionnaire.

4.3.3 Statistical analysis

All statistical analyses were completed in R (version 3.3.2),⁴⁷ an open source statistical computing program. Individual change in UL performance over the 12-week study period was tested using hierarchical linear modeling (HLM). HLM is an extension of traditional regression analysis and models individual intercepts and slopes over time in addition to modeling potential moderators of the intercepts and slopes.^{48,49} Group level intercepts and slopes are derived from the individual intercepts and slopes for each accelerometer variable. HLM is the preferred method for these data given it does not require the same number of assessments across participants and can account for missing data,^{48,49} thereby including participants with varying assessment sessions in the analysis. Our dependent variable was change over time (slope values) for each accelerometer variable. The week 2 assessment was the baseline assessment for all accelerometer variables and potential moderators of UL performance over time.

First, we analyzed change in UL performance by testing growth curves across the entire sample with individual change trajectories nested within each participant (Model 1, primary purpose). All nested models were tested using χ^2 goodness of fit tests to identify the best-fit model. When

necessary (e.g. violation of normality assumption), inferences were confirmed via bootstrap analysis. Using Model 1, we then tested for potential moderators of UL performance over time (secondary purpose). Individual belief, confidence, and motivation were introduced separately into the initial model to test for their potential moderating effects on both the intercept and slopes for all accelerometer variables. Participants were dichotomized into two categories (dummy coded), based off their responses on the 4-point Likert scale: strongly agree (group 1) and slightly agree/slightly disagree/strongly disagree (group 2). The decision to dichotomize this scale was two-fold. First, participants who “strongly agree” to these questions are considered to have high, unwavering belief, confidence and motivation to use their paretic UL in daily life. Clinicians would likely not prioritize improving any of these factors with their interventions. Participants in the second category (slightly agree/slightly or strongly disagree), however, lack varying degrees of surety in their belief, confidence, and motivation. Any of these responses could potentially merit intervention in the clinic. The groups were dummy coded and those who indicated they slightly agreed/slightly or strongly disagreed (group 2) served as the reference group in each model.

An additional moderator of interest was baseline UL capacity (week 2 ARAT score). Baseline ARAT scores were grand mean centered and evaluated for their potential moderating effect on both the intercepts and slopes (ARAT x time interaction). The significance level for all HLM models was set to $\alpha < 0.01$ due to multiple predictors across four variables. All moderators were tested separately, however, the more stringent p value was applied to reduce the likelihood of a Type I error.

Lastly, we tested for a relationship between the total number of self-perceived barriers to recovery and UL performance using Spearman's rank-order correlations (third purpose). The total self-perceived barriers reflects the total number of barriers identified at each assessment. We analyzed the relationship between the use ratio and self-perceived barriers at weeks 2 and 12. The significance level for correlation analyses was set at $\alpha < 0.05$.

Visual displays of second-by-second data from the complete 24-hour recording period were examined using density plots.³¹ These density plots display the magnitude ratio (x-axis) and the bilateral magnitude (y-axis) for each assessment. Example density plots for healthy, neurologically intact adults (figure 3, Hayward et al⁵⁰; figure 1, Bailey et al³¹) display several key features to consider when interpreting density plots from adults with UL paresis. First, the density plots from healthy adults are symmetrical, indicating both UL are active nearly the same amount over a 24-hour period. The rounded, bowl-like shape indicates most UL activity is of low intensity. The blue points towards the outer rims of the bowl indicate unilateral UL movement (e.g. one hand is stirring a bowl while the other stabilizes). A center peak represents higher bilateral magnitude values, or more intense UL activity. The color change represents overall frequency of UL movement, with warmer colors indicating increased activity and cooler colors (blue) indicating less frequent UL activity. The color change in the center of the plot indicates majority of UL movement in a 24-hour period is bilateral (magnitude ratio=0) and at low intensity levels (low bilateral magnitude value). The small, individual color bars on both sides of the plot represent unilateral UL movement. These characteristics are stable across neurologically intact, community-dwelling adults.³¹

4.4 Results

Twenty-nine of the 32 enrolled participants had available data for this analysis. The three excluded participants were a result of screen failure, withdrawal prior to completing the week 2 assessment, and inability to return accelerometers after each assessment. Table 1 presents key participant demographics. As expected, the majority of the sample received rehabilitation services across all 12 weeks, with 83% admitted to an inpatient rehabilitation facility at the week 2 assessment. All participants were independent with basic activities of daily living prior to their stroke. At week 2, a large percentage of the sample strongly agreed further improvement of their UL was possible (belief, 87%) and were confident (83%) and motivated (93%) to use their UL in everyday tasks and these numbers stayed high over the duration of the study (Chapter 3). Seven participants dropped out of the study between weeks 2 and 12, due to self-selected withdrawal (n=2), second stroke (n=1), fatal cancer diagnosis (n=1), fall resulting in fractured UL (n=1), and decline in medical status (n=2).

Table 4.1 Participant demographics

	Total sample (n=29)
Age (years)	68.7 ± 9.9
Gender	11 F, 18 M
Race	23 Caucasian 5 African American 1 Asian/ Pacific Islander
Stroke type	29 ischemic
Stroke location	16 cortical 11 subcortical 1 cortical & subcortical 1 posterior circulation/cerebellar
Affected side	19 L, 10 R
Concordance, n (%) ^a	11 (38%)
Prior working status	20 not working 9 working at least part-time
% Independent with ADL prior to stroke	100%
% Living alone prior to stroke	17%
Self-reported comorbidities, median (range) ^b	2 (0,4)
% Receiving rehabilitation services	
Week 2 (n=29)	90%
Week 4 (n=26)	77%
Week 6 (n=25)	68%
Week 8 (n=23)	70%
Week 12 (n=22)	59%
% Admitted to rehabilitation hospital at week 2	83%
Week 2 Values	
Hours of use ^c	2.82 ± 1.8
Use Ratio ^d	0.52 ± 0.26
Magnitude Ratio ^e	-4.5 ± 2.9
Bilateral Magnitude ^f	72.5 ± 16.9
Belief (% who strongly agree)	87%
Confidence (% who strongly agree)	83%
Motivation (% who strongly agree)	93%
Barriers per participant ^g	3.4 ± 2.7
ARAT ^h	25.4 ± 20.8
SAFE score ⁱ	5.2 ± 3.4
MoCA score, median (range) ^j	22 (11, 29)

Values are mean ± SD unless otherwise indicated

^a Dominant limb=paretic limb

^b Median number of self-reported comorbidities per participant

^c Total hours the paretic UL was active during the recording period (referent values: 9.1 hrs/dominant UL, 8.6 hrs/nondominant UL)

^d Hours of the paretic UL divided by hours of nonparetic limb (referent value: 0.95 ± 0.06)

^e Contribution of each limb to an activity for every second of data, 0 indicates equal contribution, negative values indicate greater nonparetic UL movement (referent value= -0.1)

^f Intensity of movement, higher values=greater intensity (referent value=136)

^g Out of 13 possible barriers

^h ARAT=Action Research Arm Test, scores range from 0-57, higher values=better function

ⁱ SAFE=Shoulder abduction, finger extension, calculated using the Medical Research Council muscle grade scores, scored 0-10 where 10=no strength deficits; participants were enrolled, on average, 6.6 ± 3.1 days after stroke

^j MoCA= Montreal Cognitive Assessment, scored 0-30, lower score may also reflect fatigue and communication impairments

There was a significant improvement across all four accelerometer variables over the first 12 weeks post-stroke (purpose 1). Section I of Table 2 reports estimated slope values for the entire sample. These slope estimates represent rate of change per two weeks for the study duration (e.g. participants, on average, increased paretic hours of use by .17 hours, or approximately 10 minutes, every two weeks). Figure 1 presents individual change profiles (spaghetti plots) for each accelerometer variable. Despite overall group improvement, UL performance for the majority of participants was below referent values over the duration of the study. There was a high degree of variability in UL performance across participants for all four accelerometer variables, with some participants fluctuating between weeks, some steadily increasing, and some demonstrating little to no increase in UL performance.

Table 4.2: Values are slope estimate \pm SE

	Hours of use	Use ratio	Magnitude ratio	Bilateral magnitude
I. Entire Sample^a				
	0.17 \pm 0.04**	0.02 \pm 0.004**	0.23 \pm .05**	1.46 \pm 0.49*
II. Psychosocial modifiers				
Belief				
<i>Reference^b</i>	0.16 \pm 0.07	0.02 \pm 0.007	0.18 \pm 0.09	0.62 \pm 0.82
<i>Strongly agree^c</i>	0.01 \pm 0.08	0.004 \pm 0.008	0.07 \pm 0.1	1.05 \pm 0.87
Confidence				
<i>Reference^b</i>	0.22 \pm 0.08	0.02 \pm 0.008	0.23 \pm 0.1	1.94 \pm 0.87
<i>Strongly agree^c</i>	-0.07 \pm 0.09	0.004 \pm 0.009	0.005 \pm 0.11	-0.63 \pm 0.92
Motivation				
<i>Reference^b</i>	0.006 \pm 0.11	0.003 \pm 0.01	-0.05 \pm 0.13	-1.3 \pm 0.25
<i>Strongly agree^c</i>	0.18 \pm 0.12	0.02 \pm 0.01	0.27 \pm 0.14	3.1 \pm 1.1*
III. Additional modifiers				
Baseline ARAT				
<i>Grand Mean^d</i>	0.17 \pm 0.04**	0.02 \pm 0.003**	0.22 \pm 0.04**	1.48 \pm 0.47*
<i>Respect to grand mean^e</i>	-0.001 \pm 0.002	-0.0003 \pm 0.0002	-0.007 \pm 0.002*	-0.004 \pm 0.02

**p < 0.001; *p < 0.01

^aSlope estimate for entire sample; significance indicates significantly different from zero

^bReference group=participants who slightly agreed, slightly disagreed, or strongly disagreed

^cParticipants who strongly agreed; slope estimate is modifier x time interaction; slope value is with respect to the reference group (e.g. slope estimate for reference group for belief x hours of use is 0.16, slope for those who strongly agreed is 0.16 + 0.01 = 0.17); if significant here, slope is significantly different from the reference group

^dSlope estimate for participants at the grand mean (25.4 points), significance indicates significantly different from zero.

^eBaseline ARAT x time interaction; estimate for every 1 point increase above the grand mean (i.e. the ARAT x hours of use slope is attenuated -0.001 for every point above the grand mean);significant effect here indicates that the slope changes significantly with changes in baseline ARAT

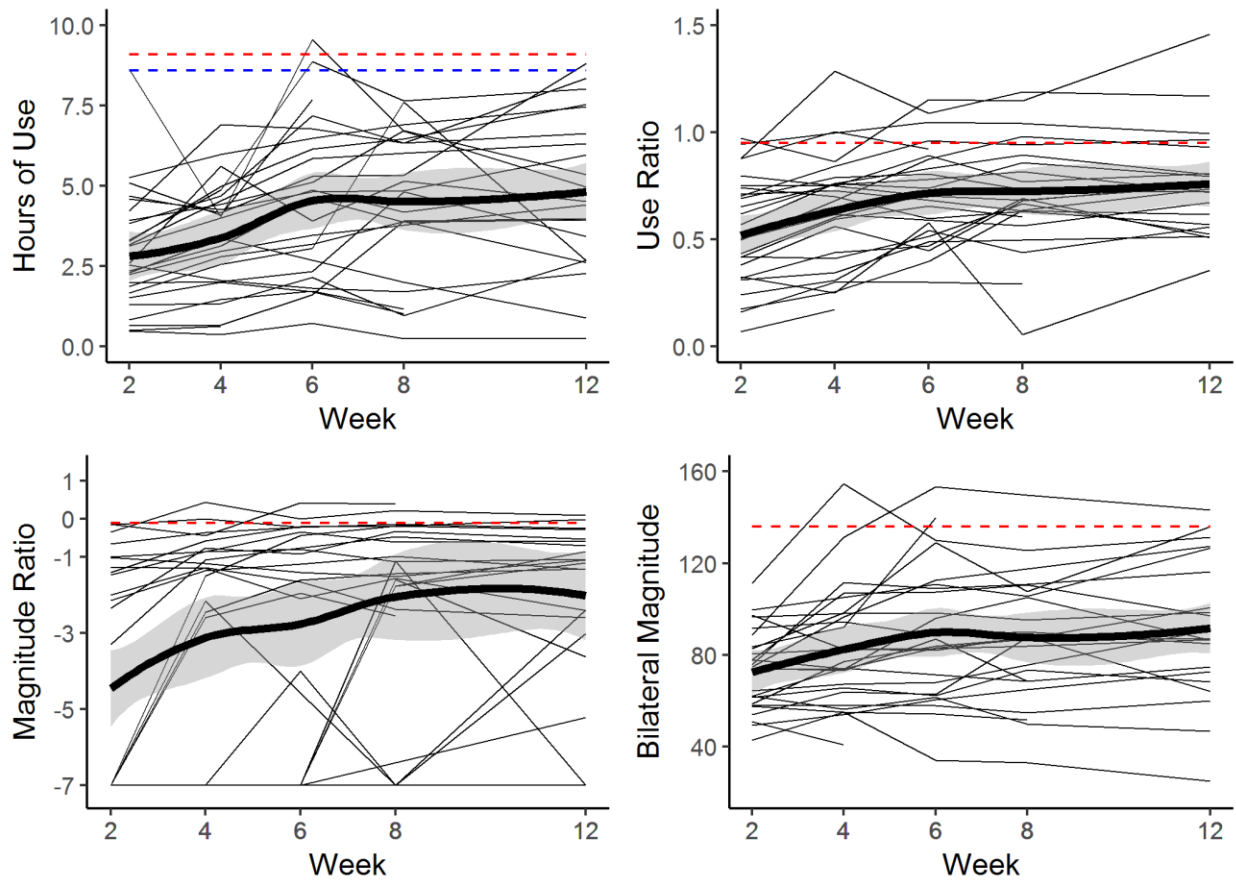


Figure 4.1 Change profiles for every participant (spaghetti plots). Each line represents a study participant with the thick black line representing the mean \pm SE shading. The dashed lines represent referent values from a healthy, community dwelling adult population. For hours of use, the dashed red line represents referent hours for the dominant UL and the blue line represents referent values for the nondominant UL.

Belief, confidence, and motivation did not significantly modify UL performance over the first 12 weeks post-stroke (Table 2, section II, purpose 2). Compared to the reference group (i.e. those who slightly agreed, slightly or strongly disagreed), participants who strongly agreed further improvement of their paretic UL was possible (belief), and were both confident and motivated to use their paretic UL did not demonstrate greater change over time. The single, moderating effect

of motivation on the bilateral magnitude is notable, but should be interpreted with caution given the lack of moderating effect on the other accelerometer variables. Figure 2 visually displays the predicted slope values for the confidence by time interaction. There was no difference in rate of change over time (slope value) in participants who strongly agreed compared to those who slightly agreed or disagreed (reference group). Belief, confidence, and motivation did not significantly modify the intercepts of any accelerometer variable.

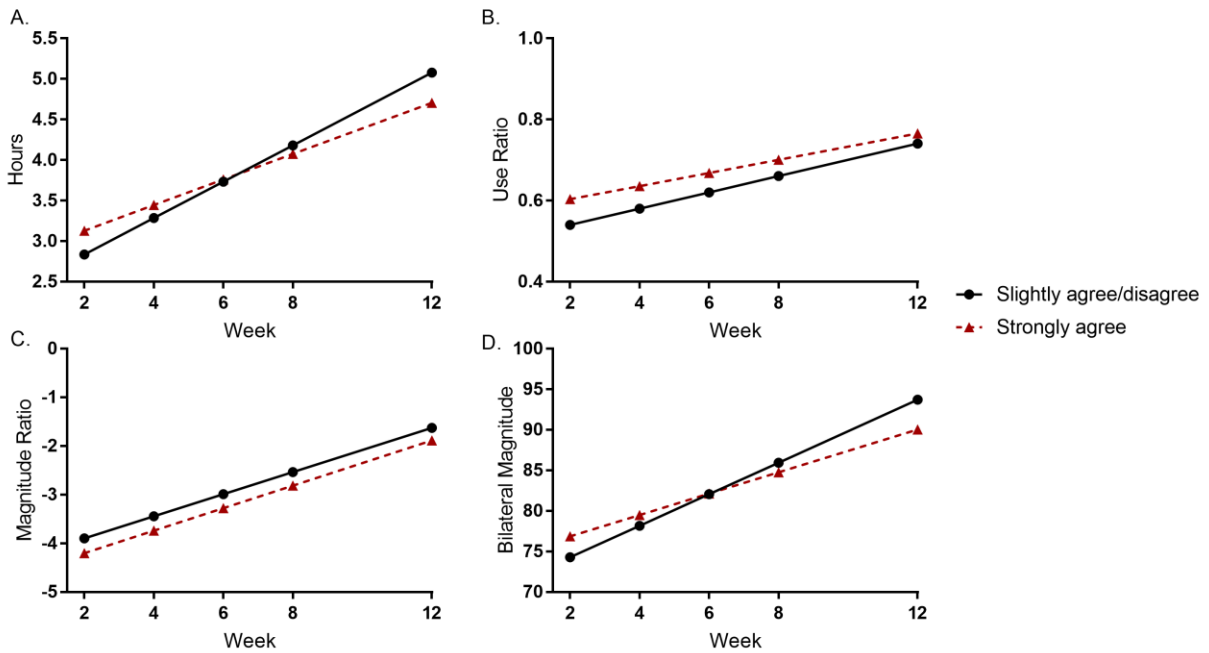


Figure 4.2 Predicted slopes for confidence x time interaction. The black line represents the reference group (participants who slightly agreed, slightly disagreed, or strongly disagreed) and the red line represents participants who strongly agreed. Participants who strongly agreed did not differ from the reference group in rate of change over time.

There was a single, significant interaction between baseline ARAT and time for the magnitude ratio (Table 2, section III). The significant interaction for the magnitude ratio indicates that for every one-point increment above the grand mean, the slope is attenuated by 0.007. There was not a significant interaction between baseline ARAT and time for the remaining accelerometer variables. The significant slope at the grand mean indicates that participants who were at the grand mean (25.4 points) had a significant change over time. Baseline ARAT significantly modified the intercept for hours of use (intercept= $3.16 \pm .02$, modified by $0.06 \pm .01$, $p < .001$), use ratio (intercept= $0.57 \pm .02$, modified by $0.01 \pm .001$, $p < .001$), magnitude ratio (intercept= $-3.90 \pm .28$, modified by $0.12 \pm .01$, $p < .001$), and the bilateral magnitude (intercept= 77.3 ± 2.9 , modified by $0.63 \pm .14$, $p < .001$). This significant intercept indicates that for every point increase in baseline ARAT, the intercept increased by the modified value listed above (e.g. hours intercept increased by .02 hours for every point above the grand mean).

For illustrative purposes, Figure 3 presents individual data for the entire sample grouped by baseline ARAT score. Participants were categorized into mild (ARAT between 46-57 points), moderate (ARAT between 20-45 points), or severe (ARAT between 0-19 points) UL capacity levels for better visualization. Both the intercept and attenuating slope estimates are visually represented in Figure 3. Overall, participants with higher UL capacity started with greater UL performance (intercepts) but demonstrated less change in UL performance (slopes), compared to those with less UL capacity (lower ARAT scores).

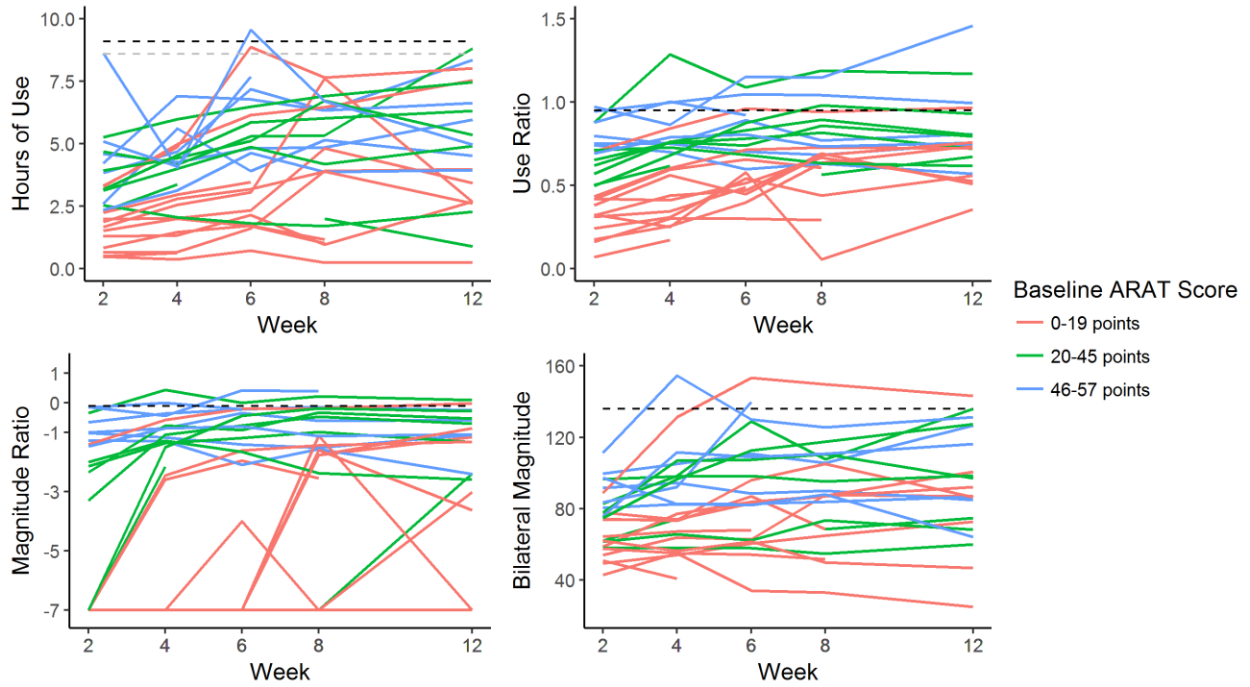


Figure 4.3 Individual change profiles by week 2 ARAT score. The dashed lines represent referent values. For hours of use, the black line represents the dominant UL and the gray line represents the nondominant UL. Participants with limited UL capacity at week 2 (low ARAT score) demonstrated greater change compared to participants with mild UL paresis.

There was a significant, moderate, negative relationship between total self-perceived barriers and UL performance at week 2 ($r_s = -0.45$, $p=0.01$, third purpose). This relationship declined by week 12 ($r_s = -0.29$, $p=0.19$), indicating total self-perceived barriers to UL recovery were associated with UL performance early after stroke, but not later.

To better visualize changes in UL performance over time, Figure 4 presents density plots from three study participants, each with varying degrees of UL capacity at week 2. Participant #1 (figure 4A) had severe UL paresis at week 2 (ARAT= 0 points), but consistently improved in both UL capacity and UL performance across the 12-week study period. Compared to week 2, the improved symmetry of the plot indicates an overall increase in paretic UL movement and the color change indicates increased overall UL activity (week 12). Participant #2 had moderate UL paresis at week 2 (ARAT =24) and increased UL performance between weeks 2 and 12. Similar to participant #1, participant #2 increased paretic UL performance (symmetry) and overall UL activity (color change) over the study period. Participant #2 demonstrated increased intensity of UL movement (bilateral magnitude, center peak) over the study period as well. Lastly, participant #3 had mild UL paresis (ARAT = 54). Their paretic UL performance was closer to normal, compared to the other participants, at week 2 (less asymmetry), and fell within normal range by week 12.

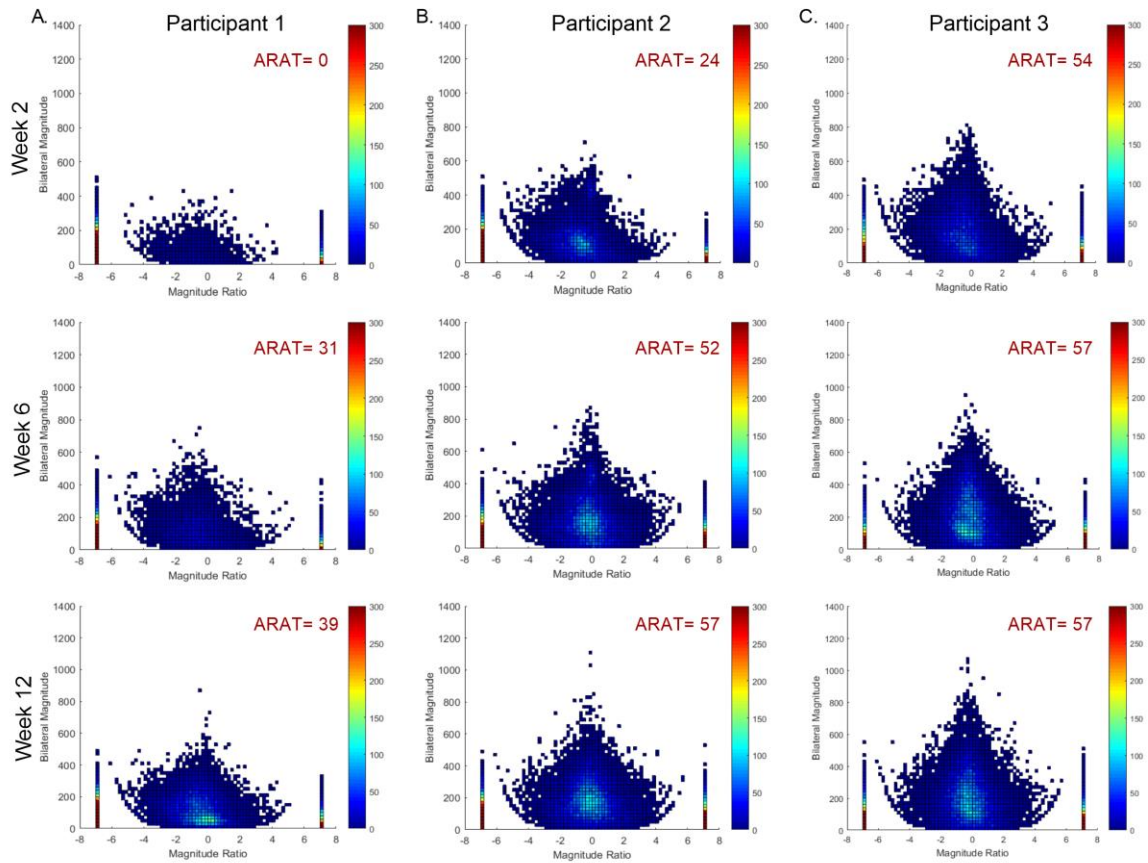


Figure 4.4 Examples of individual density plots. Density plots show UL activity for both upper limbs, for every second of data. The magnitude ratio, which quantifies the contribution of each limb to an activity, is on the x-axis. The y-axis represents the intensity of UL activity (bilateral magnitude). At week 2, participant 1 (Fig. 4A) had severe UL paresis, participant 2 (Fig. 4B) had moderate UL paresis, and participant 3 (Fig. 4C) had mild UL paresis. Across all three participants, there was an increase in UL performance from week 2 to week 12, as observed in the improved symmetry, appearance or increase of the center peak (bilateral magnitude), and improved overall frequency of UL activity (color change). For all three participants, the majority of UL activity occurred bilaterally (magnitude ratio value of 0) and of low intensity, consistent with healthy, neurologically intact adults.

4.5 Discussion

To our knowledge, this is the first study to examine the natural trajectory of sensor-measured UL performance early after a stroke and characterize the relationship between psychosocial factors, self-perceived barriers, and UL performance during the period of time when majority of UL motor recovery occurs. Our results show that UL performance can improve early after a stroke. It is well-established UL impairment and capacity spontaneously improve after stroke,^{22,23,51} to varying degrees, and these are the first results to suggest this is also true for sensor-measured UL performance. This increase in UL performance is not moderated by individual belief, confidence, and motivation over the first 12 weeks post-stroke. Our results also showed a moderate, negative relationship between self-perceived barriers and UL performance (use ratio) 2-weeks after a stroke. By week 12, this relationship weakens. Together, these findings provide novel insight into the interconnections of UL performance in daily life and the psychosocial factors that may underscore improvements early after a stroke.

The most salient finding was that UL performance increased early after a stroke, which is in contrast to previous work in chronic stroke survivors.^{18,20} The participants who demonstrated the greatest increase in UL performance were more impaired at week 2 (low ARAT scores, low performance values). These participants had more room to improve, compared to participants who were mildly impaired. The increase in UL performance, however, is modest over the 12 weeks, and the group change was below referent values across all four accelerometer variables. Participants likely had variable UL use prior to their stroke. While ratio values are consistent in healthy adults, there is a wide range of total hours of UL use and intensity of movement.^{30,31}

Improvements in UL performance after a stroke, therefore, may be related to pre-stroke activity levels.

As expected, there was a high degree of variability in the change profiles of participants. This mirrors the well-documented variability in the recovery of UL impairment and capacity.⁵²⁻⁵⁴

Some participants demonstrated a steady, positive increase over the duration of the study while some were more variable between weeks, and others did not change or slightly worsened. The degree of heterogeneity varied across the four accelerometer variables. This variability is likely influenced by biological, personal, environmental, and compensatory factors. Future studies could explore these factors in greater detail to possibly develop a predictive algorithm for UL performance, similar to the PREP2 algorithm for UL impairment outcomes.⁵¹ To date, the prognostic indicators of UL performance are relatively unexplored, leaving the field vulnerable to developing a uniform, one-size-fits-all intervention.

There are likely several hypotheses as to why individual belief, confidence, and motivation did not modify UL performance over the first 12 weeks post-stroke. The lack of moderating effect is likely a result of very high levels of belief, confidence, and motivation across the study duration (Chapter 3). More than 80% of the sample strongly agreed they were motivated to use their paretic UL in daily life at every assessment session. In the event where participants did not strongly agree to these questions, they often slightly agreed. This is an intriguing finding, given the current push to incorporate motivation and confidence into clinical interventions.^{29,55} Early after a stroke, it appears these factors are very high and may not merit direct intervention until much later (≥ 6 months) in the recovery process. Efficacy expectations are vulnerable to failures,

level of task difficulty, and incentives to perform, all of which vary over time and circumstance.²⁷ It is reasonable to presume these factors are high early after stroke because most survivors possess a strong desire to return to pre-stroke abilities and are willing to engage in rehabilitation efforts as a means to meet their recovery goals. Over months and years, belief, confidence, and motivation may decline and thus, become more appropriate therapy targets.

Instead, the moderate, negative relationship between self-perceived barriers to recovery and UL performance may be an early target of clinical intervention. In-clinic interventions could aim to reduce self-perceived barriers that may limit UL performance. Some barriers are appropriate clinical targets while some are outside the scope of direct therapy intervention. However, addressing barriers, whether through an acknowledgement or a controlled intervention such as strategy training⁵⁶ could help participants increase UL use in daily life.

Several limitations influence the interpretation of these data. The small sample size limits generalizability. A larger study, quantifying UL performance over 24-weeks, is currently underway to verify these findings. This larger, longer study will allow advanced analyses to test for non-linear change in UL performance over a 24 week period. Additionally, belief, confidence, and motivation are complex constructs and the survey used in this study was not capable of quantifying every aspect of these factors. Currently, there are no validated UL specific assessments that probe these factors in-depth. The survey used here was specific to the paretic UL, an important detail given that belief, confidence, and motivation are often situation specific and vary across tasks.⁵⁷ Future research could explore individual belief, confidence, and

motivation using a mixed methods approach to dissect the different components of these broad constructs.

4.5.1 Conclusions

Upper limb performance can improve early after a stroke. The participants who changed the most had limited UL capacity at week 2 (low baseline ARAT). Participants with higher UL capacity (high baseline ARAT scores) started with higher values, compared to those with limited UL capacity, and had a narrower range for improvement. The lack of moderating effect of individual belief, confidence, and motivation on UL performance suggests improving these factors may matter less early after stroke. These factors may vary or decline with increased time and personal circumstance. Early after stroke, clinical interventions could address self-perceived barriers to UL recovery in effort to increase overall UL performance in daily life. Understanding the time course and factors influencing UL performance will ultimately lead to a more integrated approach for optimizing UL performance outcomes, a top priority for people post-stroke.

4.6 Acknowledgements

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Chapter 5: Summary of Major Findings

5.1 Major Findings

In Chapter 2, we tested the assumption that improved UL capacity translates to increased UL performance in daily life in a chronic stroke cohort (≥ 6 months). We hypothesized that individuals with significant UL capacity gains would demonstrate increased UL performance. Additionally, we hypothesized there would be no dose-response relationship to UL performance in daily life and that concordance (dominant UL = paretic UL) would not modify UL performance. Contrary to our first hypothesis, we found that improved UL capacity does not translate to increased UL performance in daily life. There was no dose-response relationship to UL performance. Lastly, concordance did not moderate UL performance in daily life. Three additional moderators (stroke chronicity, baseline UL capacity, and independence with activities of daily living), previously shown to moderate UL performance at a single time point, did not moderate change in UL performance over time. The lack of improved UL performance in daily life was observed at the group and individual level. Indeed, across all 78 participants, not one participant improved their UL performance on two or more accelerometry-derived variables. These somewhat surprising results led to several new questions that we explored in Chapters 3 and 4.

In Chapter 3, we examined how psychosocial factors evolve over the first 24 weeks, or 6 months, post-stroke. The three psychosocial factors examined were belief further improvement of the paretic UL was possible, confidence, and motivation to use the paretic UL in everyday activities. We hypothesized that belief, confidence, and motivation would be high immediately after stroke and persist over the 24-week study period. Additionally, we quantified the total number of self-perceived barriers to UL recovery over the same 24-week period. We posited that the total

number of self-perceived barriers to UL recovery would be highest immediately after stroke and decline over 24 weeks. Our third hypothesis was that depressive symptomatology (CES-D) and cognitive impairment (MoCA) would have a negative association with belief, confidence, and motivation. Our first hypothesis was supported. Our results showed a remarkably high level of belief further improvement of the paretic UL was possible, and confidence and motivation to use the paretic UL in everyday activities across the 24-week study period. Very few participants indicated low levels of belief, confidence, and motivation at any assessment session. The second and third hypotheses were not supported. There was not a significant difference in the total self-perceived barriers to UL recovery between weeks 2 and 24 and there was no relationship between depressive symptomatology, cognitive function, and belief, confidence, and motivation.

In Chapter 4, we characterized the natural trajectory of UL performance over the first 12 weeks post-stroke. We then examined if belief, confidence, and motivation significantly moderated UL performance over the 12 week period. Lastly, we explored the relationship between self-perceived barriers and UL performance (use ratio). First, we hypothesized that UL performance would significantly increase over the first 12 weeks. Second, we posited that belief, confidence, and motivation would significantly moderate UL performance in daily life. Our third hypothesis was that a greater number of self-perceived barriers would result in less UL use in daily life (negative association). Our first hypothesis was supported. We found that upper limb performance significantly improved early after a stroke (≤ 12 weeks). Contrary to our second hypothesis, belief, confidence, and motivation did not moderate UL performance over the first 12 weeks post-stroke. Our third hypothesis was supported, but only at week 2. We found a

moderate, negative relationship between total number of self-perceived barriers to UL recovery and the use ratio at Week 2, but this relationship did not persist at Week 12.

5.2 Limitations

The primary, shared limitation across studies is the sample size. A discussion of the limitations associated with sample size, accelerometry, and quantifying belief, confidence, and motivation is included in this section. A more detailed discussion of the specific limitations associated with each study is included at the end of each chapter.

The small sample size for each study limits the generalizability of these results. In Chapter 2, the sample size (n=78) is consistent with a moderately sized clinical trial in stroke rehabilitation. The moderate sample size and corroborating cross-sectional data from other research groups^{1,2} aids with the generalizability of our results. We recruited a smaller cohort for the studies reported in Chapters 3 and 4 due to the observational, exploratory design. This smaller cohort, however, limits the generalizability of these results as well. A larger study is required prior to extending these findings to the UL stroke rehabilitation community at large. Conveniently, a larger study (n=100) is currently underway to validate the findings reported in Chapters 3 and 4.

Accelerometers are valid and reliable instruments for quantifying UL performance³⁻⁸ but are not without limitations. Indeed, accelerometers cannot distinguish between activities with similar kinematic profiles (e.g. chopping vegetables or typing on a computer), or the purpose of activities, and do not provide information about the quality (i.e. presence or absence of compensatory movement patterns) of UL movement. Accelerometers record all UL movement, including arm swing associated with walking and unintentional UL movement. Previous work

has unsuccessfully attempted to distinguish between intentional and unintentional UL movement⁹⁻¹¹ and also failed to reliably identify accelerations associated with walking in adults with stroke.¹² The recording of unintentional UL movement and arm swing while walking, if anything, results in a slight overestimation of UL movement in daily life. Given that the majority of participants in these studies were well below referent values, it is unlikely that even a slight overestimation positively biased our results.

Belief, confidence, and motivation are complex constructs and the results reported in Chapters 3 and 4 should be interpreted with caution. These studies were not designed to probe the full extent of each construct. It is recommended that future research explore these constructs in more detail in order to make definitive conclusions regarding the potential role of belief, confidence, and motivation in UL performance recovery. Currently, the field is limited by a lack of standardized psychosocial assessments that are specific to UL performance after stroke. The Stroke Self-Efficacy Scale,¹³ for example, is a general measure that emphasizes walking and life roles, not UL performance. Self-efficacy, and its related components, are situation specific and often vary across individual tasks.¹⁴ This warrants the development of an UL-specific outcome measure to explore the full extent of belief, confidence, and motivation in addition to other potential psychosocial factors of interest (e.g. self-regulation).

5.3 Innovation, significance and impact

These studies are significant for several reasons. First, Chapter 2 includes the first study to show that what someone is capable of doing with their paretic UL in the clinic does not translate to increased UL performance in daily life in the chronic phase of stroke recovery. The failure to increase UL performance in daily life at ≥ 6 months post-stroke is likely due to several factors.

First, recovery of UL impairment and capacity has plateaued by 6 months post-stroke. Individuals have likely established new habits or routines that may exclude the paretic UL, which contributes to the learned non-use phenomenon.¹⁵ The lack of rehabilitation services in the chronic phase of recovery reduces access to healthcare providers who may assist with addressing barriers to UL performance. Lastly, the changes observed in UL capacity may not have been sufficient to increase UL performance in daily life. Indeed, there may be a specific threshold for UL capacity to exceed in order to increase UL performance in daily life.

Chapter 3 includes the first study to characterize the evolution of belief, confidence, and motivation to use the paretic UL in daily life during the early weeks and months post-stroke. Prior to this study, cross-sectional data in cohorts 4-7 years post-stroke provided our limited knowledge of these psychosocial factors and self-perceived barriers to UL recovery.¹⁶⁻¹⁸ Quantifying these factors across the early weeks after stroke captured their inherent dynamic nature during the time when majority of stroke recovery occurs and rehabilitation services are delivered.¹⁹

This thesis includes the first study to map the natural trajectory of sensor-measured UL performance over the first 12 weeks post-stroke. This is significant for several reasons. First, mapping the natural trajectory of UL performance during the same period of time when the majority of recovery of UL impairment and capacity occurs affords future opportunities to compare the recovery trajectories of these three domains. Second, this was the first study to show that UL performance in daily life naturally improves during the period of time when UL capacity and impairment improvement occurs. Lastly, to our knowledge, this was the first study to test the

moderating role of three psychosocial factors on UL performance. In the wake of discovering that improved UL capacity does not translate to increased UL performance, psychosocial factors, such as confidence and motivation, emerged as possible clinical targets to improve UL use in daily life. This was the first study to test if these factors moderated UL performance in daily life. The results reported in Chapter 4 suggest that belief, confidence, and motivation may not be appropriate mechanisms to target when trying to increase UL performance early after stroke. This begins what will likely be a long, informative pursuit of understanding how UL use in daily life changes over the early weeks and months post-stroke and what factors may moderate this change.

Together, the results from Chapters 2, 3, and 4 are important for the stroke rehabilitation community. Assuming improvements in what someone is capable of doing in the controlled clinical environment is no indication of what that individual will actually do at home. The purpose of rehabilitation is to improve performance in daily life. Until now, UL performance was often a secondary outcome, quantified via self-report. The results reported here make a compelling case for including UL performance as a primary outcome, quantified with a direct measure (i.e. sensors). Increasing UL performance in daily life will likely require a complex intervention. Future research can use the results reported in Chapters 2, 3, and 4 to help design interventions that primarily target UL performance in the early months post-stroke.

5.4 Future Directions

There are several implications for future research from the results reported in this thesis. Upper limb performance in daily life continues to be a relatively unexplored area, compared to UL impairment and capacity.²⁰ To better understand the recovery of UL performance, there are five

directions for future research. First, future studies can explore the components of belief, confidence, motivation and other factors beyond the motor system that may influence UL performance in daily life. Second, future research could explore biomarkers of recovery that predict who improves UL performance early after stroke. Third, future interventions can pilot novel behavioral techniques to increase UL performance in daily life. Fourth, piloting strategy training techniques to reduce self-perceived barriers to UL recovery may be worthwhile. Lastly, there are no minimal clinically importance difference (MCID) values for the accelerometry-derived variables. Future work may want to establish clinically meaningful change scores for the accelerometer variables to allow for a more robust interpretation of change over time.

5.4.1 Components of belief, confidence, and motivation.

Belief, confidence, and motivation are complex, dynamic constructs. Given the stability of belief over several years post-stroke,^{16,17} perhaps the priority for future studies is exploring the different dimensions and sources of motivation and confidence. There are two key sources of motivation.²¹ People are motivated to act by intrinsic sources (e.g. value an activity, personal commitment to a goal) or extrinsic sources (e.g. a bribe, fear of being watched or disappointing others).²¹ People who are intrinsically motivated to perform a task have greater interest, confidence, persistence, and higher overall vitality over time than those who are extrinsically motivated.²¹⁻²³ It is possible some individuals who are receiving rehabilitation are motivated by external sources such as fear of disappointing their therapist/loved ones, obligation, or rewards. Other individuals may be intrinsically motivated, or a combination of both. These extrinsic and intrinsic sources are not static and therefore will change across the recovery period, making the need for well-designed longitudinal studies apparent. Understanding the sources of an individual's motivation after a stroke is important for understanding long-term outcomes. While

extrinsic sources of motivation are common, intrinsic sources of motivation lead to better long-term behavioral outcomes (e.g. medication adherence,²⁴ weight loss maintenance²⁵), persistence, and enhanced subjective well-being.²¹ Similarly, confidence is influenced by many factors, namely prior successes and failures with the specific or related tasks.^{26,27}

Quantifying the contributing sources of motivation and confidence will require mixed-methods research that queries a large sample of stroke survivors over time. Information from mixed-methods research will contribute to the development of more robust standardized assessments. Additionally, future research could explore the role of self-regulation,^{21,28,29} outcome expectation,²⁹ and perceived control²⁷ in moderating UL performance in daily life. Investigating these additional factors as potential moderators of UL performance may help identify other salient mechanisms to target with performance-based interventions.

5.4.2 Biomarkers of recovery

The recovery of UL impairment and capacity are highly variable across individuals post-stroke.

³⁰⁻³² Recent work has identified clinical and neurological biomarkers that predict, with an exceptionally high degree of accuracy, the expected recovery of UL capacity post stroke.³³⁻³⁵

Together, the individual biomarkers were combined to form a predictive algorithm for the recovery of UL functional capacity at 6 months post-stroke. This predictive algorithm improves the efficiency of rehabilitation services, identifies the recovery potential of each individual, and provides stratification parameters for researchers to help control for the variability in UL recovery.³⁵ To date, no research has explored potential predictors for the recovery of UL performance. Without this information, researchers and clinicians do not know who will improve their UL use in daily life and by how much. This leaves the field vulnerable to implementing a

uniform, one-size-fits-all intervention. Future research could explore potential biological (e.g. initial UL impairment, apathy), personal (e.g. personality factors), psychosocial (e.g. self-regulation), and environmental factors (e.g. home environment) that may predict the recovery potential of UL performance that will ultimately lead to more individualized, comprehensive interventions.

5.4.3 Piloting novel behavioral change techniques

Changing behavior (here, UL performance) in the free-living environment is difficult and likely requires novel techniques not currently implemented in routine rehabilitation interventions. The few stroke rehabilitation studies designed to improve performance in daily life defaulted to educational training or therapist coaching techniques and failed to consistently incorporate principles of behavior change such as feedback, social comparisons, and incentives.³⁶ The skill transfer package, created as part of constraint-induced UL movement therapy (CIMT), is an exception. A skill transfer package includes behavioral components such as a behavioral contract, daily logs of UL activity, addressing perceived barriers, phone calls with clinicians (accountability), and written homework to help increase UL use in daily life.³⁷ A transfer package has previously shown to improve self-reported UL performance in daily life,³⁷ but has yet to demonstrate efficacy for improving sensor-measured UL performance. Of note, the individualized, intensive task-specific intervention delivered in Chapter 2 included some components of a transfer package but failed to increase sensor-measured UL performance. Future studies can incorporate principles of behavior change such as feedback, social comparison, or incentives to help increase UL performance in daily life in the early months post-stroke. The high levels of belief, confidence, and motivation early after stroke will be an asset to these future UL interventions.

A small number of stroke rehabilitation studies have tested feedback as a means to change performance. The SIRROWS trial provided feedback on gait speed during inpatient rehabilitation. The results showed that feedback about performance, compared to no feedback, significantly improved discharge gait speed.³⁸ Two studies are currently underway in Europe testing if real-time feedback increases daily UL performance in individuals with stroke using a smartphone application.^{39,40} Exploring the potential role of feedback, delivered in real-time as opposed to several days or weeks after wearing the sensors, is a critical next step in UL performance research.

Social comparisons are powerful techniques that provides not just feedback about individual performance but also how individual performance compares to peer performance.⁴¹ Social comparison feedback significantly increased the total daily steps in a healthy adult population.⁴² For individuals with stroke, real-time feedback could include peer comparison (i.e. feedback includes how individual UL performance compared to other individuals receiving therapy at the same clinic) to help increase UL use in daily life. Borrowing from behavioral science, future research may employ a team approach to help increase UL performance in daily life. The individual with stroke can couple with another person (e.g. marital partner, adult child, close friend), form a team, and collectively work towards achieving a daily UL performance goal. The feedback would include how each team's UL performance ranks amongst other teams in the study or rehabilitation clinic. Social comparison feedback via a team approach has demonstrated positive results with weight loss interventions⁴¹ and improving overall physical activity⁴³ and may also reduce the negative effects of social isolation after a stroke. Additionally, future studies

designed to increase UL performance in daily life may want to pilot the use of financial incentives to increase UL use, as financial incentives serve as powerful motivators and help increase steps per day in adult populations.^{44,45}

5.4.4 Strategy training to reduce barriers

Cognitive strategy training techniques may help address the negative relationship between self-perceived barriers and UL performance reported in Chapter 4. Strategy training interventions use meta-cognitive strategies to help individuals observe, assess, and alter behaviors in effort to improve participation in everyday life roles.^{46,47} A key feature of strategy training includes teaching individuals to identify barriers to different activities and actively problem solve through the identified activity limitations.⁴⁸ Global strategy training (e.g. “Goal-Plan-Do-Check”) is feasible early after stroke⁴⁸ and can improve outcomes in adults with cognitive impairment.^{47,48} Given the significant relationship between self-perceived barriers to UL recovery and UL performance at 2 weeks post-stroke, applying global strategy training techniques to reduce self-perceived barriers in an effort to increase UL use in daily life may be worthwhile.

5.4.5 Detecting meaningful change with accelerometers

Detecting a statistically significant change in the accelerometry-derived variables is likely different from a clinically meaningful change. The minimal clinically important difference (MCID) score represents the minimum change score on a measure (here, accelerometry) that is detectable by an individual that may lead to an updated treatment plan.⁴⁹⁻⁵¹ While flawed, the MCID score provides helpful information that allows clinicians and researchers to interpret change scores as meaningful to individuals. Previous research has established MCID values for measures of UL capacity^{52,53} and UL impairment.^{54,55} To date, only one study has attempted to define an MCID score with accelerometer data, using total activity counts.⁵⁶ Future work may

want to pursue establishing MCID values for the clinically relevant accelerometer variables, such as the use ratio and hours of paretic UL use. Establishing the MCID values will help researchers and clinicians interpret meaningful individual and group change over time.

5.5 Conclusions

The goal of rehabilitation post-stroke is to improve performance in everyday life. The results reported in this dissertation suggest that improving performance in everyday life is complex and perhaps one of the next big challenges in the stroke rehabilitation field. Increasing UL performance in daily life will require novel interventions that extend beyond in-clinic protocols that only improve UL capacity. To the field's benefit, however, are the high levels of belief, confidence, and motivation that individuals with stroke possess during the period of time when the majority of motor recovery occurs. Future interventions can leverage these high levels to help increase UL performance. Together, these results will contribute to the larger discussion and provide valuable data for future, larger studies of UL performance.

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Appendix A

The figure below provides a visual representation of some of the data reported in Chapter 2 (Table 2.2). These figures were not included in the publication but visually illustrate the slope values for the entire sample, participants with a significant change in UL capacity, and participants who were concordant (dominant limb = paretic limb).

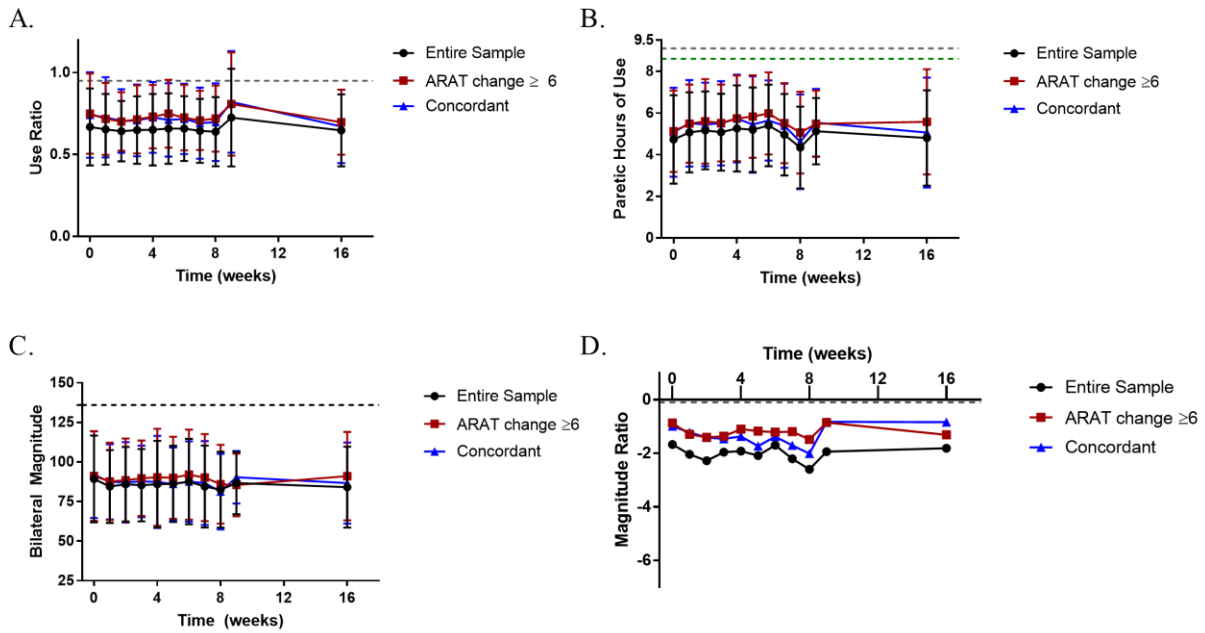


Figure A.1 Means \pm SD for the use ratio (A), hours of paretic limb use (B), bilateral magnitude (C), and median values for the magnitude ratio (D) over the study duration. Dashed lines represent referent values. For hours of use, the gray dashed line is the referent value for the dominant limb and green dashed line is the referent value for the nondominant limb. There was no change in UL performance across the entire sample (black line), participants with a clinically meaningful change in UL capacity (red line), and participants who were concordant (blue line).

Appendix B

This was a sub-analysis exploring the potential role of cognition on the reporting of each psychosocial factor, depressive symptomatology (CES-D), and overall health state (EuroQol-5D-3L). The CES-D and EuroQol are two additional self-report measures collected in this study. Exploring additional self-report measures affords a more comprehensive evaluation of the potential role of cognition on reporting abilities of the sample.

The submission for publication did not include these figures but they may be of interest to the committee given the high prevalence of cognitive impairment after stroke.

Overall, there were no substantial reporting differences between participants who were cognitively intact (MoCA score ≥ 26) or cognitively impaired (MoCA score ≤ 25). Using established thresholds, participants who were cognitively impaired are either mildly (MoCA score between 19-25 points) or severely impaired (MoCA score < 19 points).

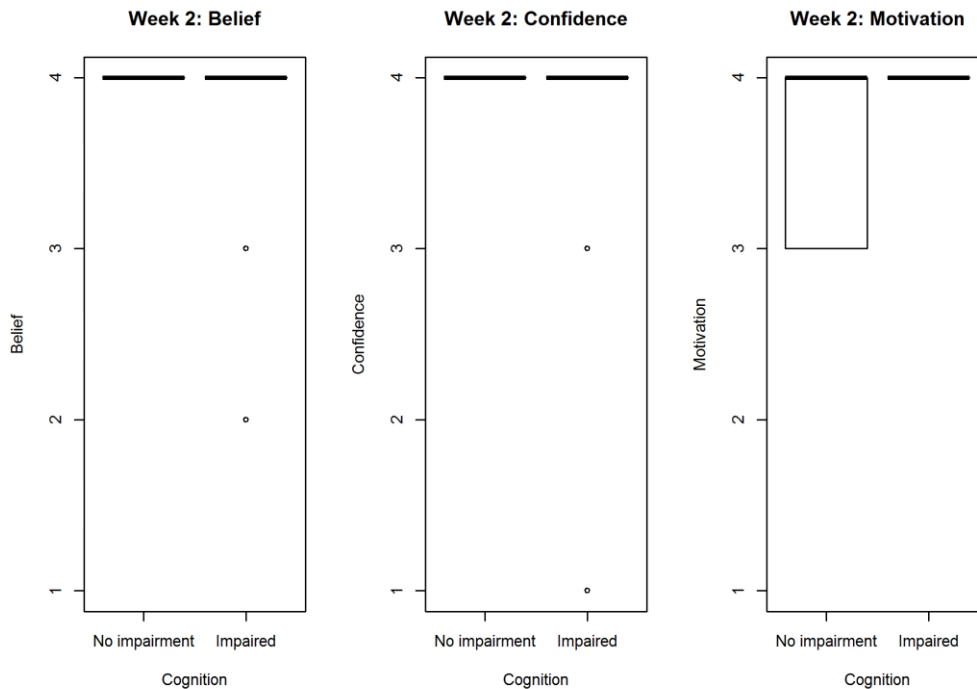


Figure B.1 Belief, confidence, and motivation values at the week 2 assessment by cognitive level. The boxplots show median values (solid black line) and interquartile range. The median value is 4 (strongly agree) for both groups, with no concerning differences noted. Five participants had no cognitive impairment, and 23 participants were considered cognitively impaired (mild impairment, n=14; severe impairment, n=9).

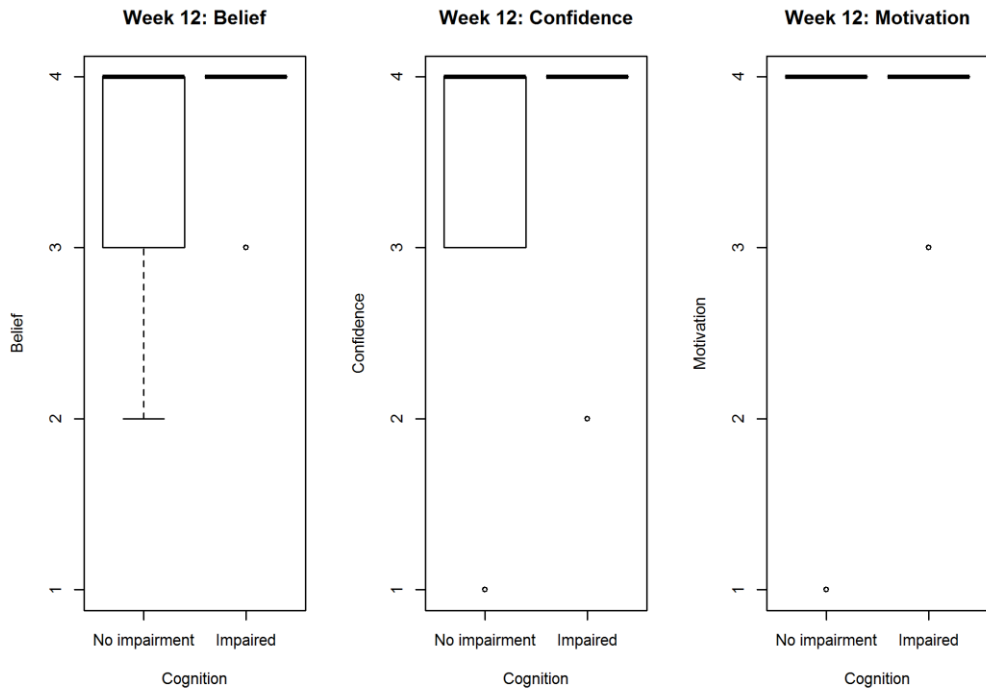


Figure B.2 Belief, confidence, and motivation values at the week 12 assessment by cognitive level. The boxplots show median values (solid black line) and interquartile range. At week 12, the median value remains at 4 (strongly agree) for both groups. As expected, cognitive abilities improved at week 12 with more participants presenting with no impairment (n=8). Of those who were cognitively impaired, the majority were mildly impaired (n=12), with an overall decrease in the number of severely impaired participants (n=2).

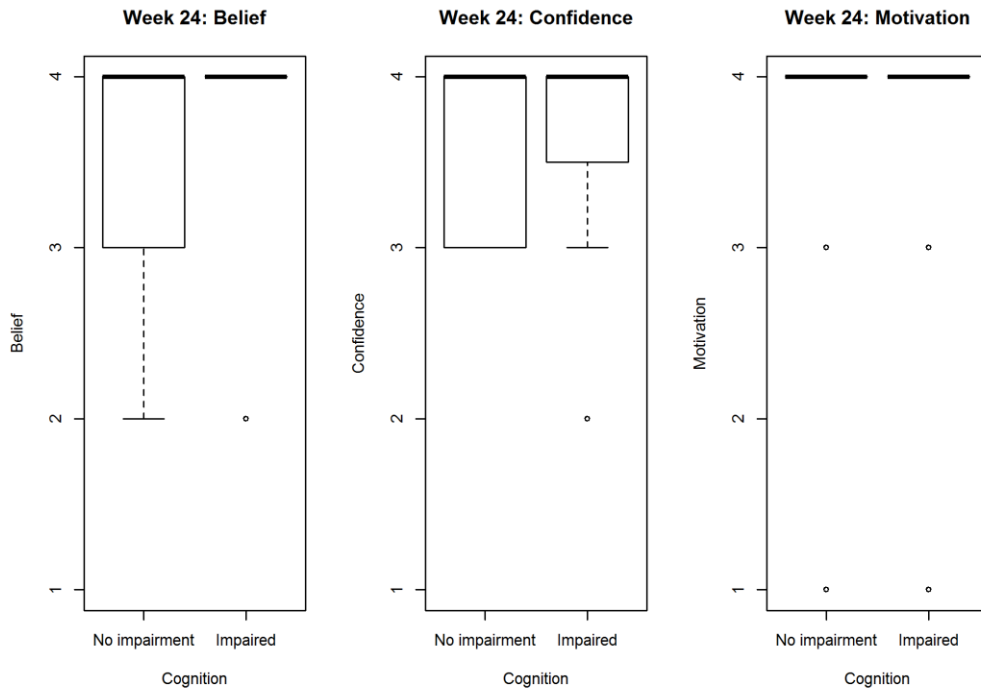


Figure B.3 Belief, confidence, and motivation values at the week 24 assessment by cognitive level. The boxplots show median values (solid black line) and interquartile range. The median value remains at 4 (strongly agree) with no observable differences that would suggest a reporting bias in the cognitively impaired group. Cognitive function continued to improve by week 24 with more participants presenting with no impairment (n=9). Of those who were cognitively impaired, the majority were mildly impaired (n=9) compared to severely impaired (n=3).

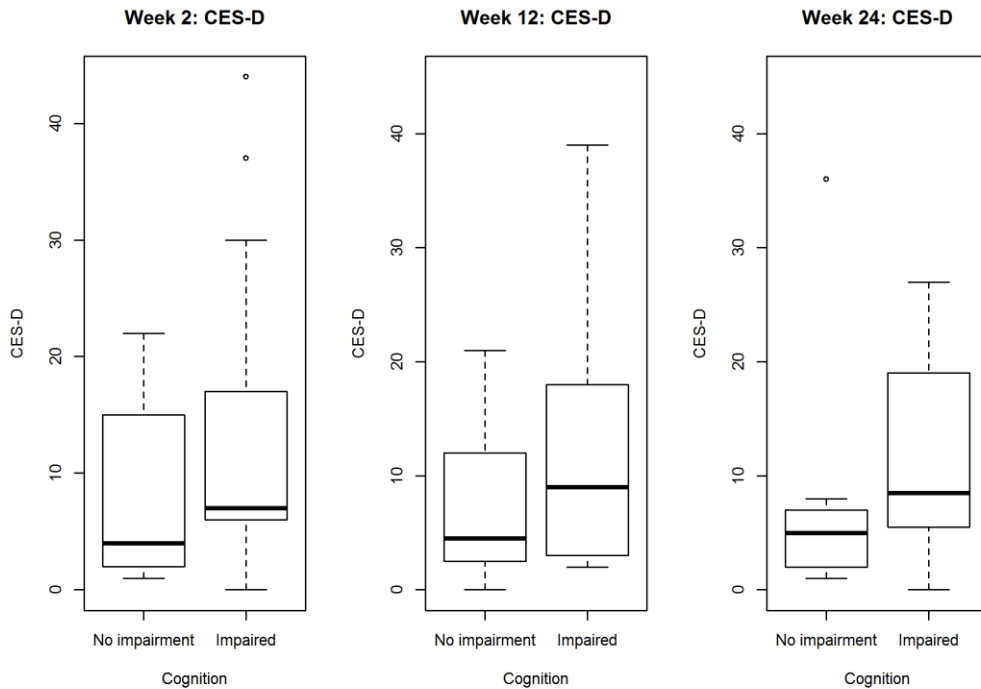


Figure B.4 Total score on the Centers for Epidemiological Studies Depression Scale (CES-D) at weeks 2, 12, and 24 by cognitive level. Total scores range from 0-60, with higher scores indicating the presence of more depressive symptomatology. A total score > 16 points may indicate a depressive episode. Here, the median value for both cognitive groups was below the 16-point threshold, indicating low depressive symptoms in our sample. There is no clear evidence that cognitive function biased the reporting of depressive symptomatology.

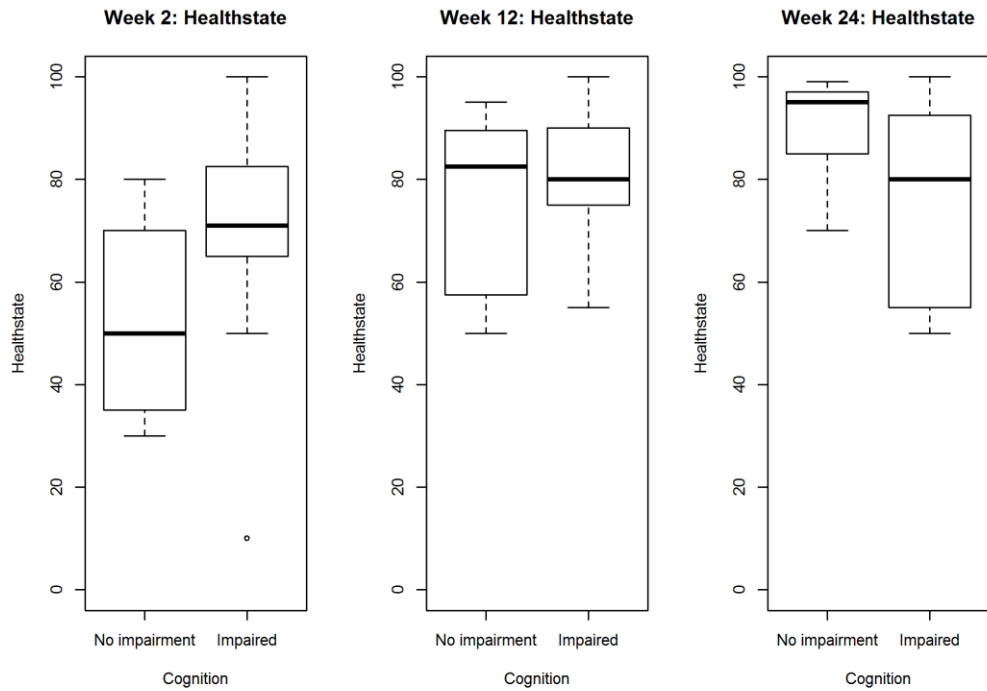


Figure B.5 Participant self-reported health state (EuroQol-5D-3L¹) by cognitive level at weeks 2, 12, and 24. Self-reported health state scores range from 0-100, with higher scores indicating a better overall health state. There is no evidence that cognitive abilities biased the reporting of overall health state across weeks 2, 12, and 24.

¹ Brooks R, Group E. EuroQol: the current state of play. *Health policy*. 1996;37(1):53-72;

Group TE. EuroQol-a new facility for the measurement of health-related quality of life. *Health policy*. 1990;16(3):199-208.

Appendix C

This study fulfilled the degree requirement for the Masters of Science in Clinical Investigation (MSCI) degree. These results show a high degree of variability and inconsistency between self-reported and sensor-measured UL performance after stroke (Chapter 1) and may be of interest to the committee.

This study has been published:

Waddell KJ. Lang CE. Comparison of self-report versus sensor-based methods for measuring the amount of upper limb activity outside the clinic. *Archives of Physical Medicine and Rehabilitation*, September 2018; 99(9): 1913-1916.

C.1 Abstract

Objective: To compare self-reported with sensor-measured upper limb (UL) performance in daily life for individuals with chronic (≥ 6 months), UL paresis post-stroke. Design: Secondary analysis of 64 participants enrolled in a Phase II randomized, parallel, dose-response UL movement trial. This analysis compared the accuracy and consistency between self-reported UL performance and sensor-measured UL performance at baseline and immediately post an 8-week intensive UL task-specific intervention. Setting: Outpatient rehabilitation. Participants: Community dwelling individuals with chronic (≥ 6 months) UL paresis post-stroke. Main outcome measures: Motor Activity Log- Amount of Use Scale and the sensor-derived use ratio from wrist-worn accelerometers. Results: There was a high degree of variability between self-reported UL performance and the sensor derived use ratio. Using sensor-based values as a reference, three distinct categories were identified: accurate reporters (reporting difference ± 0.1), over reporters (difference > 0.1), and under reporters (difference < -0.1). Five of 64 participants accurately self-reported UL performance both pre and post-intervention. Over half of participants (52%) switched categories from pre-to post-intervention (e.g. moved from under reporting pre-intervention to over reporting post-intervention). For the consistent reporters, no participant characteristics were found to influence whether someone over- or under-reported performance compared to sensor-based assessment. Conclusions: Participants did not consistently or accurately self-report UL performance when compared to the sensor-derived use ratio. While self-report and sensor-based assessments are moderately associated and appear similar conceptually, these results suggest self-reported UL performance is often not consistent with sensor-measured performance and the measures cannot be used interchangeably.

C.2 Introduction

Individuals with stroke are referred for rehabilitation services to improve performance in daily life. Performance, defined as what a person actually does in his/her current environment, outside of a rehabilitation clinic or laboratory,¹ is difficult to measure for the upper limb (UL).

Performance is most commonly quantified by amount, with other aspects (e.g. quality or efficiency) being more difficult to measure *during* everyday life. Researchers must choose between self-report measures of UL performance, which provide critical information about patient perception of abilities but are subject to inherent biases such as social desirability and recall bias,^{2,3} or sensor-based methods, such as accelerometry. Accelerometry is a valid, reliable, quantitative measure of UL performance in daily life^{4,5} and is not subject to the same biases as self-report measures, but cannot determine the specific activities someone performs and will capture functional as well as non-functional movements.

Of note, a recent physical activity review indicates self-report and sensor quantifications of physical activity can vary widely and unsystematically, with correlations ranging from -0.7 to 0.7 across studies.⁶ The purpose of this brief report, therefore, was to compare self-report and sensor-based measures of UL performance in daily life in a clinical trial cohort of persons with chronic stroke. While self-report and sensor-based UL performance measures are moderately correlated,⁵ it is critical to know the accuracy and consistency between the two measures.

C.3 Methods

This was a secondary analysis from a Phase II, randomized, parallel, dose-response trial of intensive, task-specific UL motor training (see⁷ for comprehensive assessment battery).⁷ Data from the baseline and post-intervention assessment time points were used for this analysis. The

trial was approved by the Washington University Human Research Protection Office and all participants provided informed consent.

C.3.1 Assessments

Our sensor-based measure of UL performance in daily life was derived from bilateral, wrist-worn accelerometers (wGT3X+, Actigraph, Pensacola, FL). Accelerometers record movement in terms of acceleration across three axes in activity counts. Participants wore the accelerometers for 24 hours pre-intervention and again for 24 hours post-intervention during all daily activities, including bathing and walking.⁸ The variable of interest for this comparison was the use ratio, an established metric of UL performance in daily life post-stroke.^{4,9} The use ratio quantifies the amount of time the paretic UL is active relative to the non-paretic UL and ranges from 0-1. A use ratio value of 1 indicates both UL were active the same amount of time throughout the recording period and a use ratio of 0.5 indicates the paretic limb was active 50% of the time the non-paretic UL was active. Healthy, non-disabled adults have a use ratio value of 0.95 (SD = 0.06).⁹

The self-report measure of UL performance was the Motor Activity Log (MAL) amount of use (AOU) scale.¹⁰ Participants reported how much they used the paretic UL across 28 representative functional activities, with scores from 0 = did not use the paretic UL to 5= used the paretic UL as often as before the stroke. Because the use ratio is near unity and highly consistent in neurologically-intact adults, then a score of 3 on the AOU scale (used paretic UL half as much as before the stroke) is comparable to a sensor-derived use ratio of 0.5, where the paretic UL is active half as much relative to the non-paretic limb, and a use ratio of 1 is analogous to a 5 on the MAL.⁹

C.3.2 Statistical Analysis

Using the sensor-derived use ratio and the final MAL AOU value, correlation analyses were completed pre and post-intervention to examine the association between the two measures. Each individual's total MAL AOU values were scaled from 0-1 to match the range of the use ratio. The use ratio was subtracted from the individual scaled AOU values at each time point to create a difference score. Participants whose difference score was ± 0.1 ($\pm 10\%$) were classified as "accurate" reporters. Participants whose difference score was $> +0.1$ were classified as "over reporters" and those whose difference score was < -0.1 were "under reporters." This classification scheme was determined separately for the two time points.

To examine the accuracy and consistency between the two measures, frequencies of the different categories were first calculated. Second, consistency of classification was examined by computing frequencies of individuals who were in the same category at both time points (e.g. accurate at baseline and post-intervention) vs. those who switched categories (e.g. accurate at baseline and under-reported post-intervention). And third, of the participants who were consistent, we explored characteristics that may explain their classification accuracy. Because of small, imbalanced group numbers, 95% confidence intervals of potential exploratory characteristics of age, memory (i.e. Short Blessed Test), depressive symptomatology (i.e. Centers for Epidemiologic Studies Depression Scale [CES-D]), baseline UL motor capacity (i.e. Action Research Arm Test [ARAT] score), and concordance (dominant limb = paretic limb) were examined across the three categories.

C.4 Results

Sixty-four of 85 clinical trial participants had available data for this analysis. The 21 excluded participants had either accelerometer recording errors, missing self-report data, or withdrew from the study. Participant demographics (Table 1) were not different from the large clinical trial cohort.⁷ This cohort of persons with mild to moderate UL paresis was enrolled at similar time points post-stroke.⁸ The MAL-AOU (2.73 ± 0.94) and the use ratio (0.66 ± 0.22) were not different from the total cohort. Consistent with previous reports⁵, the MAL and use ratio were moderately associated at baseline ($r=0.31$, 95% CI [0.07, 0.51], $p = 0.014$) and post-intervention ($r = 0.52$, 95% CI [0.32, 0.68], $p < 0.001$).

Table C.1 Participant demographics. Values are means \pm SD or median (min, max)

	Entire sample (n=64)
Age	61.2 \pm 11.1
Gender	22 F, 42 M
Race	37 Caucasian 26 Afr American 1 Multi-race
Type of stroke	47 ischemic 6 hemorrhagic 11 unknown
Months post-stroke	11.5 (6, 180)
Affected side	35 R, 29 L
% Concordance ^a	52%
% Independent with ADL	81%
Baseline ARAT ^b score	32 \pm 10.9
Baseline Use Ratio	0.66 \pm 0.2
Baseline MAL AOU ^c	2.73 \pm 0.9

a= Concordance = dominant side is paretic side; value here indicates the percentage of the sample who identified their dominant UL as the paretic UL

b= Action Research Arm Test; scores range from 0-57 points with higher scores indicating more normal movement. Here, participants had mild to moderate UL paresis at baseline.

c= Motor Activity Log, Amount of Use scale; scores range from 0-5 where 0= did not use the paretic UL to 5= used the paretic UL as often as before the stroke.

The main finding in this study is the high degree of variability between self-reported and sensor derived UL performance, as indicated by the difference scores (Figure 1A baseline; Figure 1B post-intervention). The majority of participants under-reported their UL performance (negative difference scores) at both time points.

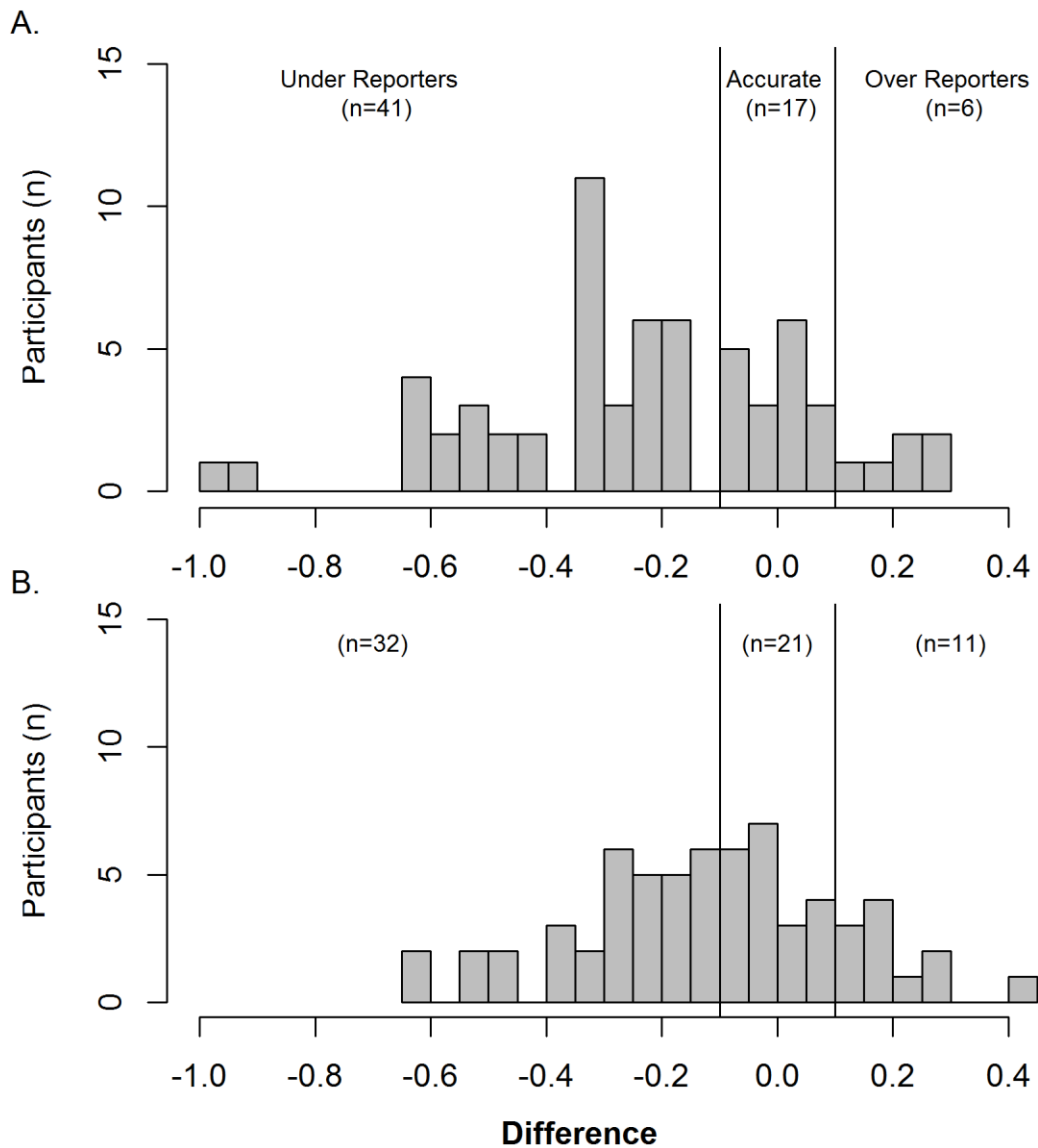


Figure C.1 Reporting differences (MAL-Use Ratio) across the sample for (A) baseline and (B) post-intervention. Accurate reporters were defined as a difference value of ± 0.1 ; under-reporters were < -0.1 and over-reporters were > 0.1 . There was a high degree of variability between self-reported and sensor-derived performance at both time points.

Thirty-one of 64 participants (48%) were consistent in their category, with the remaining 33 participants (52%) being inconsistent (i.e. switching categories). Table 2 explores the 31 consistent reporters, divided into consistently accurate, under-reporting, and over-reporting. Only five participants were classified as consistently accurate. In this small sample, we could see no differences in age, cognitive function, depressive symptomatology, UL functional capacity, and concordance (dominant limb = paretic limb) across categories to explain these reporting differences.

Table C.2 Potential modifiers of reporting accuracy across *consistent* reporters. Values are means \pm SD (95% CI) or n (%).

Modifier	Accurate (n = 5)	Under reporters (n=24)	Over reporters (n=2)
Age	63.8 \pm 7.3	60.7 \pm 10.2	56 \pm 11.3
Cognition (Short Blessed Test) ^a	3.2 \pm 4.1 (0, 6.8)	3.4 \pm 6.1 (0.9, 5.8)	5 \pm 7.1 (0, 14.8)
Depressive Symptomatology (CES-D) ^b	11.4 \pm 9 (3.5, 19.3)	16.5 \pm 11.9 (11.7, 21.3)	11 \pm 9.9 (0, 24.7)
UL functional capacity (ARAT) ^c	33.8 \pm 16 (19.8, 47.8)	31.4 \pm 10.5 (27.2, 35.6)	37 \pm 1.4 (35, 38.7)
Concordance ^d (n (%))	2 (40%)	12 (50%)	2 (100%)

a= Cognitive screen for memory, orientation, and concentration with scores ranging from 0-28; lower scores indicate better cognitive function (0-4 = normal cognition)

b= Center for Epidemiologic Studies Depression Scale; Scores range from 0-60 with higher scores indicating greater depressive symptomatology

c= Action Research Arm Test; Scores range from 0-57 with higher scores indicating better function. All individuals across groups had moderate UL paresis.

d= Concordance is when the dominant limb is the affected, paretic limb

C.5 Discussion

Despite moderate correlations, we found a high degree of variability and inconsistency between self-reported and sensor-measured UL performance measures post-stroke. Half of our sample consistently reported UL performance from pre to post-intervention, but only five individuals accurately reported at both time points. Many UL clinical trials include an outcome measure of UL performance in daily life. The high degree of variability and inconsistencies between self-reported and sensor-measured performance indicate the measures cannot be used interchangeably. If a tested intervention is intended to improve self-perceptions of UL performance, then a self-report measure is the better choice. If a tested intervention is intended to improve actual arm use in daily life, then using a quantitative measure of UL performance is the better choice.

The inconsistency across time points seen here is concerning. As with the physical activity literature,⁶ reporting inconsistency could compromise the results of research studies testing the efficacy of interventions to improve UL performance post-stroke. If individuals are not consistent and/or accurate in their reporting of UL performance, their change scores will contain a large degree of error and it will be difficult to draw conclusions about whether or not an UL intervention can drive change outside of the clinic or laboratory.

C.5.1 Limitation

A key limitation of this brief report is the modest sample size. The sample analyzed cannot generate definitive conclusions regarding self-report and sensor-measured UL performance. Instead, these data serve to initiate a critical dialogue amongst researchers regarding the most appropriate UL performance outcome measure for each individual research study.

C.5.2 Conclusions

While self-report and sensor-based assessments are moderately associated and appear similar conceptually,⁵ these results indicate self-reported UL performance is often not consistent with sensor-measured UL performance. It is recommended that clinicians and researchers measure outcomes via self-report if improved perception of UL performance is the primary outcome of interest and measure outcomes via sensors if improvements in actual UL performance is the primary outcome of interest.

C.6 References

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