EXAMINING THE EFFECTS OF A REPETITIVE TASK PRACTICE PROGRAM AMONG INDIVIDUALS WITH UNILATERAL SPATIAL NEGLECT

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Unilateral spatial neglect (USN) is common after stroke and individuals with USN have greater disability than individuals without USN. Existing interventions for USN must be examined more closely and new interventions should be considered to identify interventions that show the most promise for reducing disability associated with USN. The focus of this dissertation was three-fold. First, we examined the state of the science related to interventions for USN after stroke, and articulated a scientific rationale for examining repetitive task practice. Second, we examined the association between USN and changes in impaired arm function over time. Third, we conducted a Phase II pilot clinical trial examining the feasibility, acceptability, and preliminary efficacy of repetitive task practice among adults with USN after stroke.

The findings highlight the complexities of impairments associated with USN (impaired arm use, impaired arm function, inattention). We proposed a new conceptual model that may be useful in conceptualizing and examining new intervention approaches to USN. We found that individuals with USN have greater impairments in arm function than individuals without USN at the onset of stroke rehabilitation, and that the trajectory of motor recovery is attenuated for individuals with USN in the next 6 months. We also determined that it is feasible to recruit and retain individuals with chronic USN and hemiparesis to participate in an intensive repetitive task practice program and that the intervention was tolerable for participants. Finally, we found that

individuals with USN experience small, yet statistically reliable improvements in arm use, arm function, and attention after participating in a repetitive task practice program.

Future studies should prospectively examine variability in the trajectories of motor recovery, attention, and disability among individuals with USN from the onset of stroke through the first year or two after stroke to inform the refinement of sample selection criteria, intervention design and timing, as well as outcome assessment. These data may be used in future studies to explore additional interventions that address impaired arm use, impaired arm function, and inattention associated with USN.

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PREFACE

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1.0 INTRODUCTION

1.1 BACKGROUND

Stroke is the leading cause of adult disability in the United States and there are 795,000 individuals who have a stroke every year (Go et al., 2014). The economic burden of stroke is staggering. In 2010, the United States spent an estimated 36.5 billion dollars in stroke related medical and disability costs (Go et al., 2014). In addition to the staggering public health costs, there are significant personal costs associated with stroke. Individuals may experience a combination of sensory, motor, cognitive, and affective impairments that contribute to disability. One particularly challenging syndrome that contributes significantly to disability is unilateral spatial neglect (USN). It is critical that USN be studied given the high incidence of USN and the fact that individuals with USN have more significant disability than those without USN (Katz, Hartman-Maeir, Ring, & Soroker, 1999). Although interventions that address USN exist, the effectiveness of these interventions is unclear (Bowen, Lincoln, & Dewey, 2002).

USN has been reported to affect up to 72% of individuals with right hemisphere stroke and 47% of individuals who experience left hemisphere stroke (Katz et al., 1999). USN is characterized by an inattention or disregard to one side of the body or environment (Menon and Korner-Bitensky, 2004). As a result, these individuals with USN, neglect washing one side of their body (personal neglect), miss food on one side of their plate (peripersonal neglect), or walk into obstacles on one side of their field of vision (extra-personal neglect) (Buxbaum et al., 2004) Peripersonal neglect is the most common type of neglect, while personal neglect is the least common type (Buxbaum et al., 2004).

Concurrent with this inattention, individuals with USN experience greater impairments in arm function than individuals without USN after stroke (Paolucci, Antonucci, Guariglia, Magnotti, Pizzamiglio, & Zoccolotti, 1996, Katz et al., 1999). Individuals with USN sustain impairments in strength and motor control, and due to their inattention to the impaired arm or hemispace, they do not use their impaired arm. This non-use may result in greater long term impairments in arm function. However, it is unclear whether the trajectories of motor recovery differ between individuals with and without neglect over time and this should be more closely examined if we are to determine meaningful improvements that can be attributed to intervention.

The combination of impaired arm use, impaired arm function, and inattention has a compounding negative effect on the ability to perform everyday activities. In fact, individuals with USN experience more significant disability than those without USN (Katz et al., 1999). A more recent systematic review reported that USN was predictive of poor functional outcomes in 25 out of 26 studies, and an independent predictor of poor functional outcomes in 11 out of 26 studies (Jehkonen, Laihosalo, & Kettunen, 2006). Given the significant role of USN in post-stroke disability, effective interventions that address USN have the potential to significantly reduce disability and the costs associated with stroke.

At present, repetitive task practice is an intervention that shows promise for addressing all three symptoms: impaired arm use, impaired arm function, and inattention. Repetitive task practice encourages high intensity practice of functional motor tasks using the impaired arm. Robust evidence suggests that repetitive task practice is effective in promoting improved arm use and function after stroke (Taub, Uswatte, King, Morris, Crago, & Chatterjee, 2006; Wolf et al., 2006; Birkenmeier, Prager, & Lang, 2010). These studies, however, have either excluded individuals with USN, or failed to prospectively examine the effects of repetitive task practice on arm use, arm function, and attention in individuals with USN. Nonetheless, there are strong neurobiological, conceptual, and anecdotal reasons to suspect that repetitive task practice may promote improvements in arm use, arm function, and attention in individuals with USN. Evidence from two randomized controlled trials suggest that repetitive task practice, or behavioral therapies quite similar to repetitive task practice, may improve attention in individuals with USN, (Kalra, Perez, Gupta, & Wittink,1997; Robertson, McMillan, MacLeod, Edgeworth, & Brock, 2002; Wu et al., 2013) and two post hoc analyses suggest that repetitive task practice may improve arm use and arm function in individuals with USN (Grattan & Skidmore, 2011; van der Lee et al., 1999). Collectively, these studies suggest that repetitive task practice is promising for addressing the sequalae of USN (impaired arm use, impaired arm function, and inattention). However, no studies have prospectively examined these sequalae simultaneously.

The focus of this dissertation was three-fold. First, we examined the state of the science related to interventions for USN after stroke, and articulated a scientific rationale for examining repetitive task practice. Second, we conducted secondary analyses to examine the association between USN and changes in motor impairment over time. Third, we conducted a Phase II pilot clinical trial examining the feasibility, tolerability, and preliminary efficacy of repetitive task practice among adults with USN after stroke. At the end of this dissertation, we summarize the combined findings from these three foci, and suggest directions for future research.

2.0 CONCEPTUAL OVERVIEW: UNILATERAL SPATIAL NEGLECT AND DISABILITY

Unilateral spatial neglect (USN) is characterized by an inattention to one side of the body or environment and can affect an individual's ability to perform activities of daily living. Individuals with USN may shave only one side of their face, miss food on one side of the plate, or collide with obstacles on the affected side while walking. USN affects individuals with both right hemisphere lesions (13-82%) and left hemisphere lesions (0-76%) (Bowen, McKenna, & Tallis, 1999). USN is not only common after stroke, but it is also a significant predictor of disability (Bowen et al., 1999; Jehkonen, Laihosalo, & Kettunen, 2006; Kalra, Perez, Gupta, & Wittink, 1997; Nijboer, Van de Port, Schepers, Post, & Visser-Meily, 2013). Significant costs are associated with USN. Individuals with USN have longer hospital stays and receive more direct treatment time from physical and occupational therapists than individuals without USN (Bowen, Lincoln, & Dewey, 2007). Despite the high incidence of USN, the high utilization of resources, and the negative outcomes associated with this syndrome, a recent systematic review indicated that no interventions have demonstrated robust effectiveness at reducing disability associated with USN (Bowen et al., 2007). There is a critical need to explore additional interventions that address USN be considered, if clinicians are to be effective in reducing neglect related disability. The purpose of this paper is to discuss a promising intervention (repetitive task practice) for USN. First, we will present a new frame of reference for USN and its association with disability in order to provide a conceptual framework for utilizing repetitive task practice. We will then review evidence that supports the use of repetitive task practice for individuals with USN.

The complexity of impairments associated with the USN syndrome may explain the lack of effective interventions designed to treat USN. Greater emphasis to date has been placed on attentional impairments (i.e., inattention or disregard to one side). USN however, is also associated with significant and persistent motor impairments, often characterized by impaired arm function. Each of these impairments is associated with significant long term disability. A closer look at these linkages may shed new light on mechanisms of disability and potential mechanisms for recovery.

We propose that there are direct (biologically driven) and indirect (behaviorally driven) mechanisms that link inattention to disability (Figure 1).

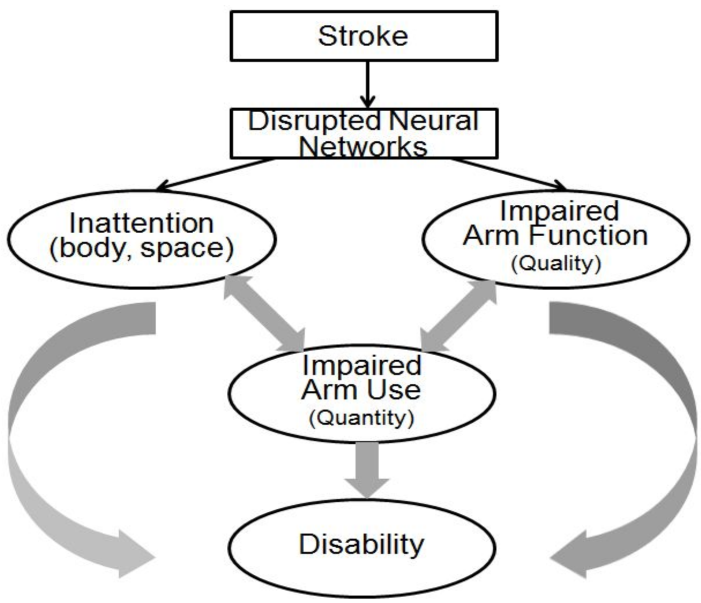

Figure 1. Mechanisms Linking USN and Disability

USN is associated with both cortical (inferior/posterior parietal lobe, temporal-parietal junction, superior/middle temporal gyrus, dorsolateral pre-frontal gyrus) and subcortical (basal ganglia, thalamus) lesions post stroke (Bartolomeo, De Schotten, & Doricchi, 2007). However, USN can occur not only from structural damage to specific areas of the brain, but also from the disruption of distributed neural networks that are involved in controlling attention (Bartolomeo et al., 2007; Corbetta & Shulman, 2011). Evidence indicates that USN can occur as a result of damage to white matter pathways (superior longitudinal fasciculus, frontooccipital fasciculus, arcuate fasciculus) that connect the frontal lobe and parietal lobe (Bartolomeo et al., 2007; Karnath, Rennig, Johannsen, & Rorden, 2011). Thus, the biologically driven mechanism of USN is complex and is not isolated to one focal area of the brain. Rather, lesions to many different areas of the brain can result in inattention to one side of the body or space. This inattention has a direct effect on an individual's ability to complete everyday activities, resulting in disability (Figure 1).

It is common for individuals with USN to also experience motor impairments, characterized by impaired arm function, since the regions of the brain that control attention are in close proximity to regions of the brain that play a critical role in the motor system. When the vascular system is impaired and stroke occurs, these regions of the brain are often affected concurrently since they share a similar blood supply. Lesions to the corticospinal systems (primary and non-primary motor areas) or structures adjacent to the corticospinal tract (basal ganglia and thalamus) cause motor impairments. Therefore, lesions to many different regions of the brain can disrupt the neural networks of the motor system. Although motor impairments after stroke are common and initially affect approximately 85% of individuals with stroke (Nakayama, Jorgensen, Raaschou, & Olsen, 1994), individuals with USN experience significantly greater motor impairment than individuals without USN (Katz et al., 1999; Nijboer, Kollen, & Kwakkel, 2012; Nijboer et al., 2013; Paolucci et al., 1996; Wilkinson, Sakel, Camp, & Hammond, 2012).

This impaired arm function can compound disability for individuals with USN (Figure 1). Although the majority of individuals with USN have concurrent motor impairment, some individuals with USN have normal motor function (normal strength, reflexes) yet they still underutilize the extremity on the affected side (Sampanis & Riddoch, 2013).

Most individuals with USN experience both inattention and impaired arm function that directly results in disability, but there may also be indirect or behaviorally driven mechanisms that contribute to disability (Figure 1). Inattention to the affected side may contribute to a disregard for the affected arm that may lead to non-use of the affected arm. Impaired arm function may also influence arm use because individuals may develop compensatory strategies that rely on use of the unaffected arm because it is frustrating or less efficient to use the affected arm, i.e. “learned non-use” (Taub, 1980; Taub, 2012; Taub et al., 2006, 2002). Learned non-use may contribute to disability. Individuals with learned non-use do not use their affected arm to complete daily activities and therefore do not get the necessary practice needed to improve or even maintain arm function (Taub, 1980; Taub, 2012; Taub et al., 2006, 2002) (Figure 1) (Taub, 1980; Taub, 2012; Taub et al., 2006, 2002). This impaired arm use may also discourage an individual to attend to the affected side. Therefore, impaired arm use may lead to a vicious cycle that exacerbates the severity of impaired arm function and inattention and therefore leads back to disability. By identifying and elucidating these mechanisms, we may be able to consider new approaches to address USN.

Given the complexity of this syndrome, it is logical for therapists to utilize an approach to intervention that addresses both impaired arm function and inattention concurrently. Rehabilitation interventions however, have traditionally focused on impaired arm function and inattention separately in both clinical practice and in research. If we examine the theory and evidence behind interventions utilized to address these impairments, we may be able to identify a more effective and efficient approach for treating USN and subsequent disability.

There are numerous interventions that have been developed to address inattention (Table 1.).

Table 1. Interventions for USN

Unilateral Spatial Neglect (USN) Interventions	Intervention Summary
Limb Activation Training	Activation of impaired extremity to increase awareness and attention to impaired side; Various methods utilized including active movement, passive movement, electrical stimulation
Visual Scanning	Behavioral strategy which involves eye and head movements toward affected side; Use of visual anchors as cues sometimes used to facilitate attention to hemispace
Computerized Training	Scanning exercises completed on computer or virtual reality training with increased stimuli presented in neglected hemispace
Mental imagery Training	Combination of visual and movement exercises to facilitate reduction in left sided representational USN
Neck Muscle Vibration	Vibration of neck muscles using transcutaneous stimulation on impaired side
Head/Neck/Trunk Rotation	Rotation at the head, neck, trunk towards left hemispace to increase attention
Sustained Attention Training	Use of auditory stimuli on impaired side to increase arousal and attention
Optokinetic Stimulation	Movement of stimuli to left on computer screen to modify perception and facilitate optokinetic reflex and nystagmus
Prism Adaptation	Prisms result in right deviating visual feedback which causes adaptation and reduction in left USN

Table 1 (continued)

Eye Patching	Eye patch worn on right eye or right hemi-field to inhibit right gaze
Vestibular Stimulation	Vestibular stimulation to facilitate left nystagmus to decrease inattention to left
Repetitive Transcranial Magnetic Stimulation (rTMS)	rTMS applied to the parietal lobe of non-affected hemisphere to inhibit non-affected hemisphere
Awareness Training	Use of feedback training to increase awareness of impairment and reduce anosognosia; variety of methods utilized including video feedback, guided discovery, visual, verbal feedback
Pharmacological Therapies	Dopamine agonist to alter pre-motor/perceptual components associated with USN; Noradrenergic agonist to modulate and increase attention
Music Therapy	Use of music to facilitate sensory, emotional, and cognitive processes

Note. Information compiled from the following sources: (Audrey Bowen et al., 2002; Luauté, Halligan, Rode, Rossetti, & Boisson, 2006; Manly, 2002; Singh-Curry & Husain, 2010).

The majority of these interventions utilize a behavioral approach designed to increase attention to the affected side. Behavioral approaches facilitate changes in behavior by modifying current behaviors (e.g. inattention) to promote the desired behavior (e.g. scanning to affected side). Limb activation training is one type of intervention for USN and is based on the notion that increased use of the impaired arm provides proprioceptive feedback to the damaged hemisphere. It is hypothesized that use-dependent feedback can improve attention to the impaired side of the body and space and that improved attention promotes reduced disability (Robertson, Hogg, & McMillan, 1998). The majority of these limb activation interventions involve gross motor movement to extinguish an auditory and visual stimulus (buzzer) at various intervals in a session using the affected arm. Other interventions involve tapping of the affected arm in the affected hemispace when cued or passive movement of the affected arm with stretching and electrical stimulation. There is some evidence to suggest these behavioral interventions that promote use of the affected arm can reduce inattention (Priftis, Passarini, Pilosio, Meneghello, & Pitteri, 2013; Robertson et al., 1998; Robertson, McMillan, MacLeod, Edgeworth, & Brock, 2002; Robertson & North, 1992, 1993), and that active use of the impaired arm promotes improved arm function (Fong et al., 2013; O'Neill & McMillan, 2004; Robertson et al., 2002; Wilson, Manly, Coyle, & Robertson, 2000). Therefore, a behavioral intervention program that involves active use of the affected arm may show promise for individuals with USN.

Therapists also employ a wide range of interventions to address impaired arm function after stroke. Overall, these interventions are designed to capitalize on neuroplasticity in order to facilitate motor recovery. Repetition, intensity, and progression of practice have been identified as the critical ingredients needed for neuroplasticity to occur (Birkenmeier, Prager, & Lang, 2010; Bowden, Woodbury, & Duncan, 2013; Ganguly, Byl, & Abrams, 2013; Liepert, Bauder, Miltner, Taub, & Weiller, 2000; Plautz, Milliken, & Nudo, 2000). More specifically, high repetition practice (several hundred repetitions) in a concentrated period is necessary for positive motor cortex reorganization to occur. During practice, the demands of the task must also be increased to ensure that tasks are challenging in order to facilitate change (Plautz et al., 2000). The behavioral interventions (limb activation training) utilized to address inattention that involve use of the affected arm lack these critical ingredients that have been identified to facilitate motor recovery. Therefore, an intervention that utilizes a behavioral approach and combines high repetition, high intensity, and progressive practice may be most effective at reducing impaired arm function and inattention for individuals with USN.

Repetitive task practice is a behavioral intervention that involves high intensity use of the affected arm to complete tasks and may show promise for addressing impaired arm use, impaired arm function, and inattention among individuals with USN. Other terms that are often used interchangeably with repetitive task practice include task specific training and task-oriented training. Although these alternate terms may have slightly different meanings across some professional disciplines or research groups, they represent the same conceptual idea of repeated, challenging practice of functional, goal oriented activities (Lang & Birkenmeier, 2013). Repetitive task practice is a behavioral intervention because it incorporates practice conditions designed to shape behaviors to use the affected arm (Taub, 2012; Taub et al., 1994). Repetitive task practice is tailored to each individual based on their performance and tasks are graded to ensure that an individual is challenged appropriately to allow for progressive task practice (Birkenmeier et al., 2010). Individuals work on meaningful functional motor tasks such as handwriting, opening containers, fastening buttons, or turning pages in a book using the affected arm. Traditionally, the use of a repetitive task practice program has been utilized to address impaired arm function among individuals with hemiparesis post stroke and robust evidence suggests that individuals with impaired arm function after stroke demonstrate significant benefit from repetitive task practice (Taub et al., 2002; Taub, 2004; Wolf et al., 2006). There is also evidence indicating that cortical reorganization can occur as a result of participation in repetitive task practice (Classen, Liepert, Wise, Hallett, & Cohen, 1998; Liepert, Bauder, Miltner, Taub, & Weiller, 2000; Taub, 2004). Thus, there are positive behavioral and biological changes associated with repetitive task practice (Figure 2). The use of a repetitive task practice program has been suggested for individuals with USN (Freeman, 2001; van der Lee et al., 1999), however, studies often exclude individuals with USN and few studies have examined this intervention for individuals with USN or have not systematically examined the effect of the intervention on arm use, arm function, or inattention.

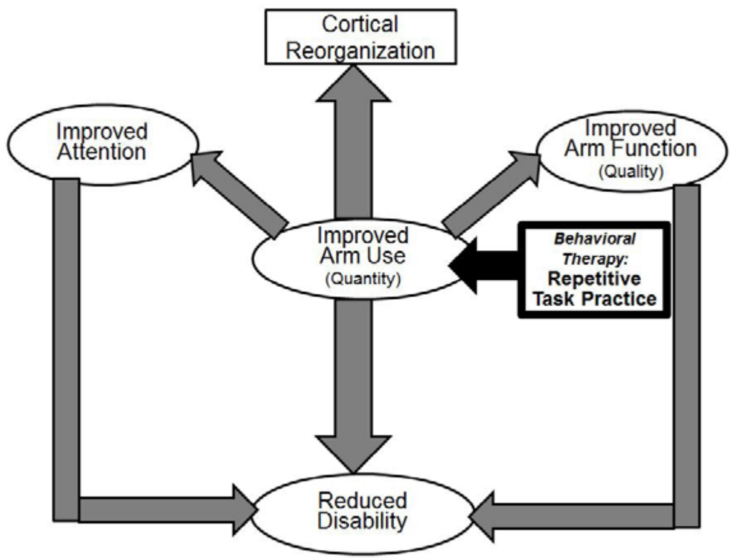

Figure 2. Repetitive Task Practice and USN

Although further research is needed, there is some preliminary evidence supporting the use of a repetitive task practice program specifically with individuals with USN. Two retrospective studies have reported that individuals with USN demonstrated greater improvements (arm use, arm function) after participating in a repetitive task practice program than individuals without USN. Wu et al. (2013) examined the use of a repetitive task practice program for individuals with USN and motor impairment. Researchers found that individuals who participated in the repetitive task practice program demonstrated a more significant improvement in attention while performing functional activities (Catherine Bergego Scale) than those individuals who received traditional occupational therapy for the upper extremity (Wu et al., 2013). Although this study did not investigate changes in arm use or arm function for the impaired arm, these findings suggest that repetitive task practice may be effective for improving attention among individuals with USN. Preliminary evidence from a case study indicated that a repetitive task practice program may have simultaneously improved attention while improving arm use and arm function. An infant with USN and hemiparesis demonstrated improved arm use, arm function, and attention after participating in a repetitive task practice program (Bollea et al., 2007). Although none of this evidence is confirmatory, these findings suggest repetitive task practice may be a promising intervention for improving arm use, arm function, and attention. It remains to be shown whether improving arm use, arm function, and attention impacts disability. Overall, there are strong conceptual reasons and some evidence to suggest that repetitive task practice can reduce impairments and disability associated with USN.

USN is a disabling syndrome and it is common for individuals to not only have impaired attention but also impaired arm function. Therefore, therapists are faced with the challenge of addressing multiple impairments when working with individuals with USN. USN has been described as a multimodal syndrome, so it is logical for therapists to utilize an intervention that is designed to address multiple facets of this disabling syndrome in order to reduce disability (Saevarsson, Halsband, & Kristjánsson, 2011). Repetitive task practice may be a promising intervention for individuals with USN. Repetitive task practice may be able to influence the biological and behavioral mechanisms that link USN and disability. Research is needed to examine the feasibility of a repetitive task practice program for individuals with USN and to examine the effects of a repetitive task practice program on arm use, arm function, and attention among individuals with acute and chronic stroke. Future research should also assess whether participation in a repetitive task practice program reduces disability.

3.0 COMPARING UPPER EXTREMITY MOTOR RECOVERY AMONG INDIVIDUALS WITH AND WITHOUT UNILATERAL SPATIAL NEGLECT

3.1 BACKGROUND

Motor impairment and unilateral spatial neglect (USN) are common after stroke (Bowen, McKenna, & Tallis, 1999; Olsen, 1990) and frequently co-occur (Formisano et al., 1993; Katz et al., 1999; Wilkinson et al., 2012). Individuals with USN have more significant motor impairment in the acute stage of recovery after stroke than individuals without USN and these differences in motor impairment persist for several months (Katz et al., 1999; Paolucci et al., 1996). It is less clear whether USN attenuates motor recovery within the first six months of recovery, since studies report mixed findings (Au-Yeung & Hui-Chan, 2009; Kwakkel, Kollen, van der Grond, & Prevo, 2003). We examined stages of arm and hand recovery (Chedoke-McMaster Stroke Assessment) after stroke and 6 months later among individuals with and without unilateral spatial neglect (USN).

3.2 METHODS

This study is a secondary analysis of data from two prospective longitudinal studies. Participants were recruited upon discharge from acute care or upon admission to inpatient rehabilitation, within the same academic health center. Participants were eligible for study participation if they were able to provide informed consent and had a primary diagnosis of stroke. Participants were excluded if they had: 1) significant pre-morbid cognitive impairment (e.g. Alzheimer's disease), 2) previous stroke or disabling neurological condition, 3) severe aphasia (inability to comprehend and follow one-step directions), 4) alcohol or substance abuse within the previous 6 months, or 5) current untreated major depressive disorder or other psychiatric condition. All procedures were approved by the University's institutional review board and all participants provided informed consent. Descriptive data were obtained from the medical chart and participant interview.

The 18-line version of the Line Bisection Test was administered at baseline to detect the presence of USN (Schenkenberg, Bradford, & Ajax, 1980). Participants were presented with a piece of paper with a series of horizontal lines varying in length (100-200 mm) placed to the left, right, and center of the page. Participants placed a pencil mark through the center of each line. To score, the deviation from the center (either direction) was measured for each line and the number of unmarked lines were recorded. The mean percent deviation was calculated using the following formula: sum of deviation/lines completed. Participants were determined to have USN if they made 2 or more omissions or their performance was more than 2 standard deviations from the mean percent deviation for control (Schenkenberg et al., 1980).

The Chedoke-McMaster Stroke Assessment Impairment Inventory (CMA) was administered at baseline and 6 months later to classify the stage of arm and hand recovery after stroke (Gowland et al., 1993). Scores range from 1 (flaccid paralysis) to 7 (normal movement patterns).[10] The CMA is a valid and reliable measure (Gowland et al., 1993).

3.3 DATA ANALYSIS

Data were analyzed using SPSS Version 20.0 (Chicago, IL). Eligible participants were dichotomized based on USN status (present or absent based on the Line Bisection Test). The study examined differences between groups using *t*-tests and χ^2 tests. Data were not normally distributed, so the Kruskal-Wallis test was conducted to examine differences in arm and hand recovery between groups (USN+, USN-) at baseline and follow-up.

3.4 RESULTS

Forty-three participants met criteria and 10 participants had USN (Table 2). There were no significant differences between groups (USN +, USN-) at baseline, except for the hemisphere affected by stroke. Individuals with USN were more likely to have right hemisphere stroke than those without USN ($\chi^2_{1=}6.60$, $p=.04$).

There were no significant differences between groups for CMA arm or hand scores at baseline (Table 2). On average, participants were at stage 3 of motor impairment for arm and hand, indicating that spasticity and synergy patterns were present, but some volitional movement was apparent. At 6 months, there were significant differences between groups for arm ($\chi^2_1=6.90$, $p\leq.01$) and hand scores ($\chi^2_1=7.25$, $p\leq.01$). Individuals with USN had significantly lower arm (stage 3) and hand scores (stage 4) than individuals without USN (arm, stage 5; hand, stage 6), indicating less arm and hand recovery (Figures 3, 4). Thus, those with USN continued to demonstrate significant spasticity and synergy patterns that were challenging to overcome. However, individuals without USN were at a stage 5 of motor impairment, emerging to a stage 6, for arm and hand. This indicates that individuals without USN either no longer had spasticity or had very weak spasticity and that movement and coordination were close to normal.

Table 2. Demographic and Baseline Characteristics

	Sample (n=43)	USN – (n=33)	USN+ (n=10)	Test Statistic
Age, years, *M (SD)*	63.9 (15.3)	64.6 (16.0)	61.7 (13.4)	t_{41}= 1.16
Male, *n* (%)	26 (60.5)	21 (63.6)	5 (50.0)	χ^2_1= 0.60
Caucasian, *n* (%)	39 (90.7)	29 (87.9)	10 (100)	χ^2_1= 1.34
Ischemic, *n* (%)	34 (79.1)	28 (84.8)	6 (60.0)	χ^2_1= 2.83
Right Hemisphere, *n* (%)	19 (44.2)	11 (34.4)	8 (80.0)	χ^2_2= 6.60*
Subcortical, *n* (%)	24 (57.1)	18 (56.3)	6 (60.0)	χ^2_2= 1.02
Visual Field Impairment, *n* (%)	7 (18.9)	5 (17.9)	2 (22.2)	χ^2_1= 0.09
Dominant Limb Affected, n (%)	22 (51.2)	18 (54.5)	3 (30.0)	χ^2_1= 1.85
Chronicity, days, *M (SD)*	10.0 (10.3)	8.6 (9.8)	14.5 (11.4)	t_{41}= 0.22
Baseline CMA				
Arm, *M (SD)*	3.51 (1.6)	3.73 (1.66)	2.89 (1.40)	χ^2_{42}= 2.58
Hand, *M (SD)*	3.77 (1.9)	4.00 (1.91)	3.10 (1.79)	χ^2_{42}= 1.50
Follow-up CMA				
Arm, *M (SD)*	5.28 (1.8)	5.73 (1.57)	3.80 (1.99)	χ^2_{42} = 6.90*
Hand, *M (SD)*	5.53 (1.5)	5.94 (1.17)	4.20 (1.87)	χ^2_{42} = 7.25*

Note. USN+, Unilateral spatial neglect present; USN-, Unilateral spatial neglect absent; CMA, Chedoke-McMaster Stroke Assessment Impairment Inventory; *p<.05

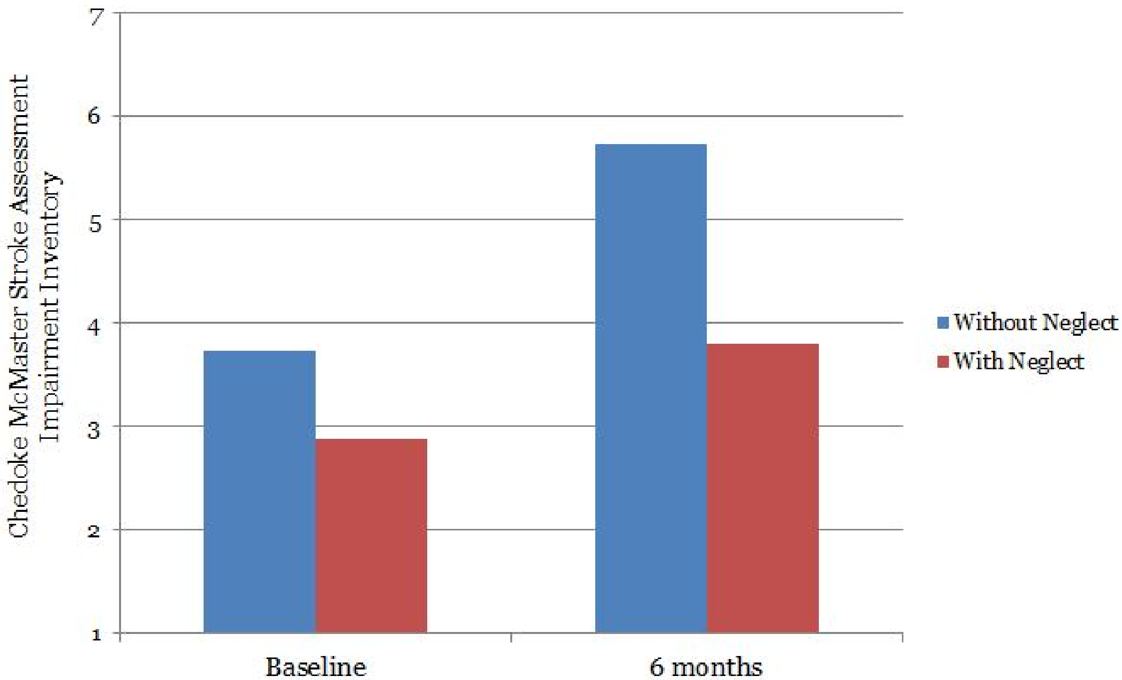

Figure 3. Chedoke McMaster Stroke Assessment Impairment Inventory Arm Recovery

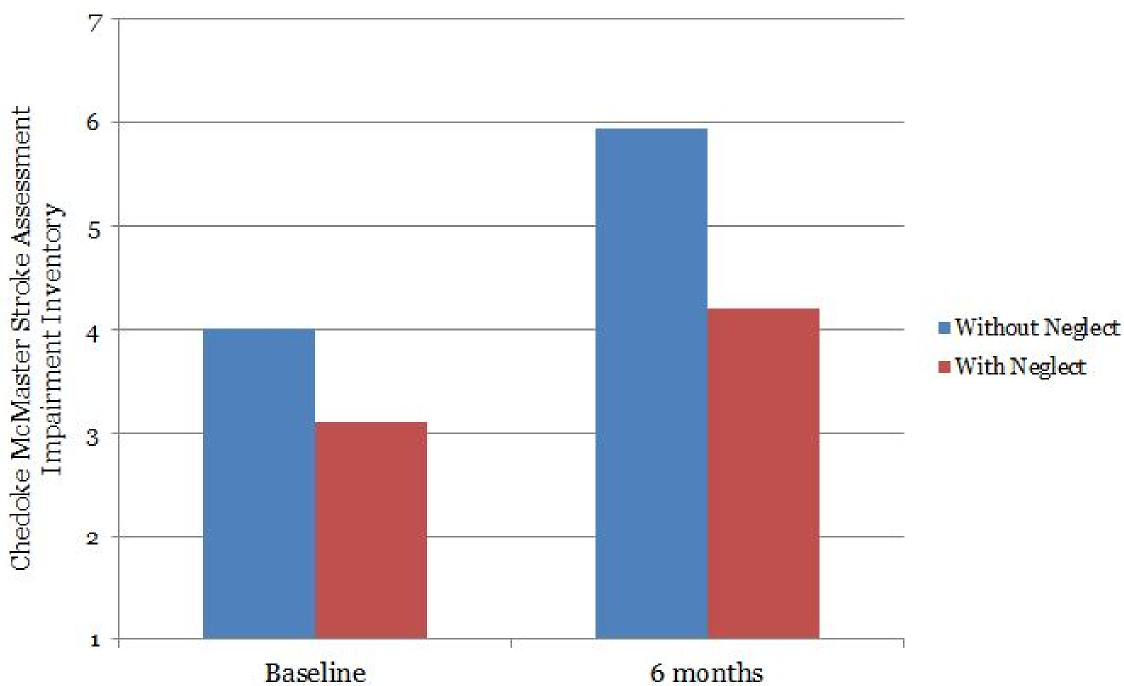

Figure 4. Chedoke McMaster Stroke Assessment Impairment Inventory Hand Recovery

3.5 DISCUSSION

Findings suggest that individuals with USN have less arm and hand recovery in the first 6 months than individuals without USN despite similar levels of motor impairment immediately after stroke. One potential explanation for these findings is that individuals with USN may develop a greater non-use of the affected upper limb over time which leads to less motor recovery. If individuals with USN are not attending to their affected side, they may not practice using the affected upper limb outside of therapy in daily life unless cues are provided.

These findings differ from previous studies that report significant differences in motor impairment in the acute stage after stroke between individuals with and without USN (Katz et al., 1999; Paolucci et al., 1996; Wilkinson et al., 2012). Our findings suggested that stage of motor recovery in the arm and hand, is not different between individuals with and without USN during the acute stages post stroke. However, previous research indicated left USN was positively associated with spasticity when comparing the occurrence of spasticity between individuals with and without USN who were admitted to inpatient rehabilitation (Wilkinson et al., 2012). Wilkinson et al. (2012) specifically assessed muscle tone and used dichotomous outcomes (spasticity present, spasticity absent) to characterize participant's muscle tone which differs from the approach used in the present study. In this study, the CMA characterized the stages of motor recovery, focusing on the influences of spasticity on functional movements, but did not directly measure spasticity. Not only did the measures differ, but the samples also differed from one another. The present study examined both left and right USN, rather than only left USN.

This sample (with exception of race) was typical of individuals who experience stroke. While USN is more common with right hemisphere stroke (13-82%), it can occur with left hemisphere stroke (0-76%) (Bowen et al., 1999).

These findings were derived from a secondary analysis and are useful for hypothesis development and designing future prospective studies. Studies designed to examine mechanisms that influence rates of motor recovery in individuals with and without USN may provide insights to support treatment approaches. Future research should utilize a more extensive battery or an assessment that evaluates the impact of USN on daily living and use of the affected upper limb during activities of daily living. Rehabilitation history should also be examined to determine if there are differences in the treatment that individuals with and without USN receive.

3.6 CONCLUSION

This study examined stages of arm and hand recovery over time among individuals with and without USN. Despite similar arm and hand impairment immediately after stroke, individuals with USN experienced less motor recovery over the first 6 months. Although preliminary, these findings suggest the importance of additional investigations examining hemiparesis among individuals with USN.

4.0 FEASABILITY AND PRELIMINARY EFFICACY OF A REPETITIVE TASK PRACTICE PROGRAM FOR UNILATERAL SPATIAL NEGLECT

4.1 INTRODUCTION

In the previous chapters, we established that USN and impaired motor function co-occur and that repetitive task practice may be a promising intervention for individuals with USN. However, research is needed to examine the use of repetitive task practice for USN.

We conducted the first prospective pilot study examining the feasibility, tolerability, and preliminary efficacy of a 6 week repetitive task practice program on arm use, arm function, and attention in individuals with USN after stroke. The pilot study addressed two specific aims:

AIM 1: Establish feasibility and tolerability of a repetitive task practice program for USN after stroke as indicated by:

- Recruitment and retention of ≥95% of targeted sample size for the entire protocol
- Tolerability in terms of little or no adverse effects (i.e., pain) reported by ≥90% of participants and acceptable to high satisfaction scores reported by ≥90% of participants

AIM 2: Examine improvements in symptoms associated with USN syndrome after treatment. Using a single-group repeated-measures design, we predicted that:

H1: Individuals would demonstrate significant improvements in use of the affected arm (measured by Motor Activity Log Amount of Use Scale) after treatment.

H2: Individuals would demonstrate a significant improvement in arm function (measured by Action Research Arm Test) after treatment.

H3: Individuals would demonstrate a significant improvement in attention (measured by the Catherine Bergego Scale) after treatment.

4.2 METHODS

4.2.1 Participants

This study was a collaborative effort between the University of Pittsburgh and Washington University in St. Louis. In Pittsburgh, participants were recruited through referrals from the UPMC Rehabilitation Institute, Centers for Rehab Services, UPMC Department of Physical Medicine and Rehabilitation Research Registry, the University of Pittsburgh Stroke Rehabilitation Research Network, and Forbes Regional Hospital. Participants were also recruited through local stroke support groups. In St. Louis, participants were recruited through referrals from the Brain Recovery Core Database and therapist referral.

After receiving a referral, participants were contacted to arrange a study visit. Participants who provided informed consent or proxy consent were screened for eligibility. Participants were eligible to participate if they met the following criteria: 1) age 18 years or older; 2) primary diagnosis of unilateral hemiparesis due to stroke at least 6 months prior to the study; 3) presence of unilateral spatial neglect (impairment on at least one of the conventional subtests of the Behavioral Inattention Test); 4) mild to moderate impairment of arm function (defined by Motricity Index scores of 48 – 92); 5) English speaking. Participants were excluded if they had severe aphasia (as indicated by the inability to follow 1-step directions at least 80% of the time) or were receiving concurrent therapy for the affected upper extremity. Screening methods are presented in Table 3.

Table 3. Screening and Assessment Procedures

Screening Assessments	(Screening Only)
Medical Record Review	Past medical history and history of present illness
Behavioral Inattention Test	USN: impairment on ≥1 subtest of BIT
Motricity Index	Arm function: score of 48 – 92 on the affected side
Participant Interview	Aphasia screen: able to follow 1-step commands 80% of the time
Descriptive Assessments	**(Pre-Intervention Only)**
Participant Interview	Age, gender, race, education, medical and rehabilitation history
Repeatable Battery of Neuropsychological Status	Cognition (for descriptive analyses)
National Institutes of Health Stroke Scale	Stroke severity (for descriptive analyses)
Patient Health Questionnaire, 9-item Version	Mood symptoms (for descriptive analyses)
Feasibility Assessments	
Wong Baker FACES Pain Rating Scale	Tolerability of intervention
Client Satisfaction Questionnaire (8 item)	Satisfaction with intervention
Outcome Assessments	**(Pre and Post-Intervention)**
Motor Activity Log	Arm use (surrogate measure of disability)
Action Research Arm Test	Arm function (surrogate measure of disability)
Chedoke Arm and Hand Activity Inventory	Arm function (surrogate measure of disability)
Catherine Bergego Scale	Attention (surrogate measure of disability)
Behavioral Inattention Test	Attention (surrogate measure of disability)
Stroke Impact Scale	Disability/Stroke-specific health outcome

Rationale for Study Criteria: We decided to include participants who were at least 6 months post-stroke based on the evidence regarding the natural trajectory of arm function attention recovery for individuals with USN (Appelros, Nydevik, Karlsson, Thorwalls, & Seiger, 2004; Cherney & Halper, 2001; Farne et al., 2004). By 6 months post-stroke, natural recovery of arm function and attention is largely complete and these deficits are stable without intervention (Appelros et al., 2004; Cherney & Halper, 2001; Farne et al., 2004). The determination of USN is based on the presence of extrapersonal neglect measured by the Behavioral Inattention Test (Halligan, Wilson, & Cockburn, 1991). The criteria for mild to moderate impairment in arm function is derived from previous studies (Birkenmeier et al., 2010; Dromerick et al., 2009; Lang & Beebe, 2007).

4.2.2 Measures

A battery of assessments was administered pre-intervention and post-intervention. All assessments were administered by an independent evaluator trained to competency in the administration and scoring of each measure. At the Pittsburgh site, we elected to administer exploratory measures that were not administered at the St. Louis site. An overview of the screening measures, descriptive measures, feasibility measures, and outcome measures is provided in Table 3.

4.2.2.1 Recruitment and Retention

We planned to recruit 20 participants to have 80% power to detect a moderate effect size (d=.60) on the primary (Motor Activity Log). We also needed 20 participants to detect a moderate effect on the secondary outcome measures (Action Research Arm Test, Catherine Bergego Scale). We assessed Aim 1 by examining our success in recruitment and retention.

4.2.2.2 Descriptive Measures

We administered a battery of measures at baseline to describe the sample (Table 3). Demographic information was collected via interview. We administered the Repeatable Battery for the Assessment of Neuropsychological Status to assess baseline cognition. The Repeatable Battery for the Assessment of Neuropsychological Status is a battery of neuropsychological tests designed to assess attention, immediate recall, delayed recall, language and visuospatial/constructional processing. The Repeatable Battery for the Assessment of Neuropsychological Status is a reliable and valid measure and has been used with individuals with stroke (Gontkovsky, Beatty, & Mold, 2004; Larson, Kirschner, Bode, Heinemann, & Goodman, 2005; Randolph, Tierney, Mohr, & Chase, 1998; Wilde, 2006). We used age-adjusted total and domain index scores to describe the sample. Age adjusted scores have a mean of 100 and a standard deviation of 15 (Randolph et al., 1998). Therefore, age adjusted scores below 85 indicate impairments in cognition.

The National Institute of Health Stroke Scale was used to measure stroke severity. There are 13 items on the National Institutes of Health Stroke Scale and higher scores indicate greater stroke impairment. Evidence indicates that the National Institutes of Health Stroke Scale is a valid and reliable measure (Adams et al., 1999; Goldstein & Samsa, 1997; Schlegel et al., 2003). We used the summed total score to describe the sample. In addition, the visual field item was used to determine whether participants had a visual field impairment, and the sensory item provided information regarding the presence or absence of sensory impairment.

The Patient Health Questionnaire-9 was used to measure depressive symptoms and severity (Kroenke, Spitzer, & Williams, 2001). The Patient Health Questionnaire-9 has nine items and each item is scored on a scale from 0-3. A total score is derived from the nine items to determine depressive severity. Higher scores on the Patient Health Questionnaire-9 indicate greater depressive severity. Items on the Patient Health Questionnaire-9 are based upon the criteria for depression according to the Diagnostic and Statistical Manual Fourth Edition (Kroenke et al., 2001). The diagnostic validity of the Patient Health Questionniare-9 has been established (Kroenke et al., 2001).

4.2.2.3 Tolerability and Satisfaction Measures

Tolerability: The number, type, and severity (measured with Wong-Baker FACES Pain Rating Scale) of side effects was collected by interviewing the participant at the beginning and end of each intervention session (Williamson & Hoggart, 2005). The Wong-Baker FACES Pain Rating Scale has been established as a valid measure of pain (Garra et al., 2010; Wong & Baker, 2001). Side effects were identified by comparing participant responses pre and post intervention. We calculated the percentage of participants who reported side effects and descriptive data regarding the number, type, and severity. For individuals who reported an increase in pain in any session, we categorized their pain using the following categories: Score 0-2, no/mild pain; Score 3-6, Moderate Pain; Score 7-10, Severe Pain (Kelly, 2001). We examined each session to determine whether participants experienced an increase in pain and whether the increase in pain was an adverse event. We defined an adverse event as a participant switching from one pain category to another (no/mild pain, moderate pain, severe pain).

We also calculated the total percentage of sessions that participants attended, the mean number of repetitions completed, and the mean number of minutes that participants were actively engaged during the each intervention session. The mean number of task changes, task upgrades, task downgrades, and the percentage of bilateral tasks over the 18 intervention sessions were calculated.

Satisfaction: The Client Satisfaction Questionnaire-8 was used to evaluate participants' satisfaction with the repetitive task practice program (Nguyen, Attkisson, & Stegner, 1983). There are 8 items on the questionnaire. Each item is scored on a scale from 1-4. Higher scores indicate greater satisfaction. A total score is derived from the 8 items to indicate participant satisfaction. Total scores on the Client Satisfaction Questionnaire-8 range from 8-32. The Client Satisfaction Questionnaire-8 has been established as a valid measure of satisfaction (Attkisson & Zwick, 1982; Larsen, Attkisson, Hargreaves, & Nguyen, 1979). We used the total score to assess tolerability by calculating the percentage of participants who reported acceptable to high satisfaction total scores.

4.2.2.4 Primary and Secondary Outcome Measures

Arm Use Measure: We used the Motor Activity Log to measure use of the affected arm. The Motor Activity Log was the primary outcome measure for AIM 2. The Motor Activity Log measures the amount of use and quality of movement of the impaired upper extremity during activities of daily living. In this study, the amount of use will be utilized as the primary measure and the quality of use will be used as the secondary measure. Individuals were asked to report on the amount of use and quality of use for thirty items (Uswatte, Taub, Morris, Light, & Thompson, 2006). Each item is scored on two scales which range from 0-5 (Amount Scale, 0=did not use weaker arm for activity, 5=used weaker arm as much as did pre-stroke; Quality Scale, 0=weaker arm was not used at all for activity, 5=ability to use weaker arm for an activity was a good as before stroke). For each scale, total scores are derived from a mean of scores;

higher scores indicate better quality of movement and greater use of the arm. The Motor Activity Log has been utilized extensively in research as an outcome measure in constraint induced movement therapy trials and is a valid and reliable measure (Hammer & Lindmark, 2010; Taub, Uswatte, & Pidikiti, 1999; van der Lee, Beckerman, Knol, De Vet, & Bouter, 2004; Wolf et al., 2006, 2010). The Motor Activity Log Quality of Use was only administered at the Pittsburgh site.

Rationale for Primary Outcome Measure: Previously, we presented our hypothesis that participation in repetitive task practice will directly increase arm use and that as a result of increased arm use, individuals will experience a reduction in inattention and impaired arm function. In accordance with our hypothesis, we chose to use the Motor Activity Log as the primary outcome measure for Aim 2. Furthermore, we chose the Motor Activity Log as the primary outcome measure, because the Motor Activity Log was used in previous studies that examined repetitive task practice and was utilized in the post hoc analysis that provided evidence to suggest that repetitive task practice may improve arm use in individuals with USN (van der Lee et al., 1999). Arm function and attention served as a secondary outcome measures for Aim 2.

Arm Function Measure: The secondary outcome measure was the Action Research Arm Test which measures upper extremity grasp, grip, pinch, and gross movement. The Action Research Arm Test includes 19 items to evaluate arm function (Lyle, 1981). Each item is assigned a score ranging from 0-3, yielding a total score of 0–54. Higher scores on the Action Research Arm Test indicate normal movement. The Action Research Arm Test is established as a valid and reliable measure and has been studied extensively (Lang, Wagner, Dromerick, & Edwards, 2006; Nijland et al., 2010; Platz et al., 2005; van der Lee, Beckerman, Lankhorst, & Bouter, 2001). We used the summed total score for hypothesis testing.

We also explored arm function using The Chedoke Arm and Hand Activity Inventory. The Chedoke Arm and Hand Activity Inventory-9 assesses arm function while completing nine task oriented activities (Barreca, Stratford, Lambert, Masters, & Streiner, 2005; Barreca, Stratford, Masters, Lambert, & Griffiths, 2006; Barreca et al., 2004). A seven point scale is used to score each item and the scale ranges from total dependence to complete independence. A higher score on the Chedoke Arm and Hand Activity Inventory indicates greater independence (total score range 7 – 63). The Chedoke Arm and Hand Activity Inventory is a valid and reliable measure of arm function (Barreca et al., 2005). We used the summed total score as a secondary outcome in exploratory analyses. The Chedoke Arm and Hand Activity Inventory was only administered at the Pittsburgh site.

Attention Measure: In order to assess attention we utilized the Catherine Bergego Scale as a secondary outcome measure. The Catherine Bergego Scale measures personal, peripersonal, and extrapersonal neglect through observation of 10 activities which include: knowledge of the limbs, dressing, mobility, grooming, oral care, eating, gaze orientation, auditory attention, spatial orientation, and locating personal belongings on left side of environment (Azouvi, 1996; Azouvi et al., 2003). This assessment is unique from other assessments since it is the only assessment which measures the three hemispaces (Menon & Korner-Bitensky, 2004). This assessment was also used to evaluate anosognosia as an exploratory measure and was only administered at the Pittsburgh site. The scale has been administered to patients to self-assess difficulty on these same 10 items using a similar scoring method. The difference between the participant's score and the rater's score indicates the anosognosia score (Azouvi, 1996). A four point scale is used for each item and higher scores indicate greater neglect and anosognosia. We used the summed total score for hypothesis testing.

The Catherine Bergego Scale has good inter-rater reliability and all items have fair to good internal consistency (Azouvi, 1996) Performance on the Catherine Bergego Scale has been significantly correlated (Spearman rho=.50–.74, $P<.001$) to performance on commonly used measures of neglect including cancellation, reading, and drawing tasks. The Catherine Bergego Scale has also been significantly correlated to performance on the Barthel Index (Spearman rho=−.63, $P<.0001$) when administered to individuals with acute and chronic stroke (Azouvi, 1996). The Catherine Bergego Scale has also demonstrated that it is more sensitive at detecting neglect than traditional paper and pencil measures (Azouvi, 1996; Azouvi et al., 2006).

We also explored attention using the conventional subtests of the Behavioral Inattention Test. The conventional items of the Behavioral Inattention Test include six paper pencil subtests which include line crossing, letter cancellation, star cancellation, line bisection, figure and shape copying, and representational drawing (Wilson, Cockburn, & Halligan, 1987). Scores are derived for each subtest by counting the number of omissions on the test and subtracting the omission from the total number of stimuli. The subtests are weighted differently but together provide a maximum score of 146 points (Hartman-Maeir & Katz, 1995; Wilson et al., 1987). Cut-off scores for each subtest have been established to determine if an individual demonstrates neglect (Halligan, Cockburn, & Wilson, 1991). The Behavioral Inattention Test has been established as a valid and reliable measure of neglect (Halligan, Marshall, & Wade, 1989; Halligan et al., 1991; Wilson et al., 1987). We used the total score as a secondary outcome for exploratory analyses.

Disability Measure: We used the Stroke Impact Scale 3.0 as an exploratory measure of disability (Duncan, Bode, Min Lai, & Perera, 2003). The Stroke Impact Scale is a stroke specific health outcome measure. It is a self-report measure and each item is scored on a 5 item Likert scale. There are a total of 59 items that assess the following 8 domains: strength, hand function, mobility, physical and instrumental activities of daily living (ADL/IADL), memory and thinking, communication, emotion, and social participation. We administered items from the ADL/IADL domain and used the domain score to describe the sample (Duncan et al., 1999). Domain scores range from 0-100 and higher scores reflect less disability.

4.2.3 Intervention

Intervention sessions were delivered by an occupational therapist or physical therapist with experience working in stroke rehabilitation. The intervention was an existing protocol developed to provide rigorous and standardized repetitive task practice program to individuals with chronic stroke (Birkenmeier et al., 2010; Lang & Birkenmeier, 2013). The repetitive task practice program involved high doses of repetitive training for the impaired arm in the context of functional tasks, and were administered 1 hour/day, 3 days/week for 6 weeks. Missed sessions were not re-scheduled if a participant did not notify the therapist to cancel and reschedule the session prior to the appointment and was not present at the time of the scheduled session.

The Canadian Occupational Performance Measure (Law et al., 1994) was used to generate individual participant goals and identify functional tasks that were meaningful to practice during therapy sessions. Each of the tasks selected required participants use their impaired arm to address a minimum of two components of arm function such as grasp, reach, or fine motor coordination. The research therapist graded the tasks for each participant throughout the 6 week intervention period as appropriate to increase or decrease the task complexity based on the participant's improved arm function (Birkenmeier et al., 2010).

In each one hour session, the research therapist selected three tasks with the goal of having the participant achieve a total of 300 repetitions of practice. Each movement of the impaired arm counts as a repetition (Birkenmeier et al., 2010; Lang & Birkenmeier, 2013). The research therapist documented each task, the grading utilized for the task, and the number of repetitions for each task in each session. If a participant achieved mastery of a task or became uninterested in a task, a new task was selected.

4.2.4 Analyses

Data were entered and stored in REDCap. We analyzed data using IBM® SPSS® Statistics for Windows, Version 21.0 (Armonk, NY). Descriptive data were analyzed using Chi-square tests, *t*-tests, and Mann-Whitney *U* tests as appropriate. To assess the feasibility of the repetitive task practice program (**AIM 1**), we calculated the number of referrals, number of eligible participants enrolled, number of participants who completed the study, and provided descriptive reasons for early termination. We calculated the percentage of the targeted sample recruited and retained in the study. To assess the of the repetitive task practice program (**AIM 1**), we analyzed the data using the following indicators: the number, type, and severity (measured with Wong Baker Faces Pain Rating Visual Scale) (Wong & Baker, 1998) of side effects associated with the repetitive task practice program, and the participants' satisfaction with the repetitive task practice program (measured with the Client Satisfaction Questionnaire-8) (Nguyen, Attkisson et al. 1984). We calculated the percentage of participants who reported side effects and generated descriptive data regarding the number, type, and severity of side effects. We calculated the percentage of participants who reported acceptable to high satisfaction total scores.

To assess the preliminary effects of the repetitive task practice program (**AIM 2**), we conducted a series of analyses. We started by examining the distributions of scores on each of the measures. We tested stated hypotheses for measures of arm use (Motor Activity Log, primary outcome measure), arm function (Action Research Arm Test, secondary outcome measure), and attention (Catherine Bergego Scale, secondary outcome measure), by conducting *t*-tests and/or non-parametric Wilcoxon Signed Ranks tests with Bonferroni corrections. We also conducted exploratory analyses for a measure of disability (Stroke Impact Scale ADL/IADL). We determined the magnitude of the change and standard deviation of change with Cohen's D effect sizes calculations. Effect sizes were interpreted as follows: 0.2=small effect, 0.5=moderate effect, 0.8=large effect (Cohen, 1988). Exploratory analyses were used to examine associations between descriptive, primary outcome, and secondary outcome measures to identify critical variables that should be included in the statistical model of the next study.

4.3 RESULTS

4.3.1 Recruitment and Retention

We received 174 referrals between the two sites. Eighty-eight individuals provided informed consent and were screened for eligibility. Sixty-eight participants were ineligible and 20 participants met the eligibility criteria and were enrolled. All participants completed the intervention, but 1 participant was lost to follow-up due to a change in medical status. We enrolled 100% of the targeted sample and retained 95% of enrolled participants. These results are outlined in Figure 5.

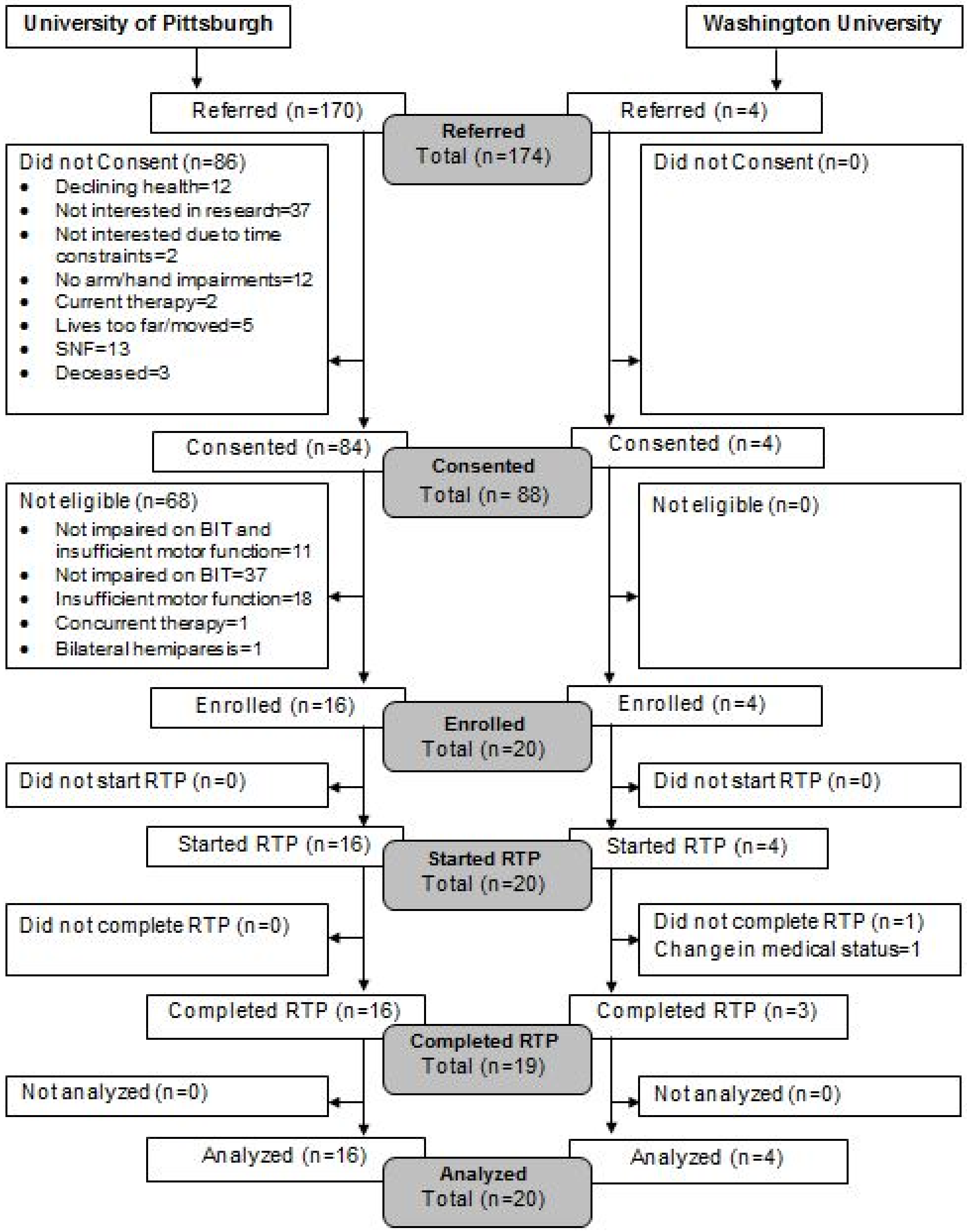

Figure 5. Flow Diagram

We recruited participants from a number of different sources (Table 4). The majority of the 88 participants who consented to the study were recruited from local support groups (n=28) and the UPMC Department of Physical Medicine & Rehabilitation Research Registry (n=29). Participants who were referred by the Washington University Brain Recovery Core Database were well characterized and therefore had a high likelihood of meeting the eligibility criteria. This is evident by the fact that 100% of the referrals from this source met the eligibility criteria and were enrolled. Although we had a fewer number of participants from other recruitment sources consent, we enrolled a higher percentage of these participants.

Table 4. Recruitment Sources

	University of Pittsburgh Stroke Rehabilitation Research Network	Local Support Groups	UPMC Department of Physical Medicine & Rehabilitation Research Registry	Therapist Referrals	Flyers	Washington University Brain Recovery Core Database
Consented, n	16	28	29	7	5	3
Enrolled, n	5	5	4	2	1	3
Enrolled/Consented, %	31.3%	17.9%	13.8%	28.6%	20.0%	100%

Sixty-eight participants were ineligible to participate in the study. Descriptive data for these participants is displayed in Table 5. Forty-eight participants who were screened did not have USN, but the majority (n=37) of these participants without USN met the motor criteria. Conversely, 20 participants with USN were ineligible but the majority (n=18) of these participants did not meet the motor criteria.

Table 5. Characteristics of Ineligible Participants

	USN + Motor - n=18	USN + Motor + Other n=2	USN – Motor - n=11	USN – Motor + n=37
Age, years	61.0 (12.7)	77.0 (2.8)	62.4 (14.7)	65.9 (17.7)
Male, % male	55.5	50.0	54.5	56.7
Race, % Caucasian	94	100	81.8	78.3
Chronicity, years	7.0 (8.0)	1.1 (0.5)	6.0 (6.2)	3.3 (3.2)
Hemisphere, % right	83	-	63.6	51.3
BIT subtests impaired, n	3.5 (2.0)	3.5 (2.1)	0 (0)	0 (0)
BIT total score, mean (SD)	118.2 (28.3)	134.5 (10.6)	144.5 (1.6)	143.1 (3.4)
MI total score, mean (SD)	34.8 (8.8)	65 (17.0)	41.6 (19.2)	73.1 (11.7)

Note. USN+, Neglect present; USN-, Neglect absent, Motor +, Motor criteria met; Motor -, Motor criteria not met; Other, met neglect and motor criteria but ineligible for other reasons; BIT, Behavioral Inattention Test.

4.3.2 Descriptive Data

The descriptive data for this study are summarized in Table 6.

Table 6. Demographic and Descriptive Data

	n=20
Age, years, *M (SD)*	66.7 (11.7)
Male, *n* (%)	10 (50.0)
Caucasian, *n* (%)	14 (70.0)
Stroke Etiology	
Ischemic, *n* (%)	17 (85.0)
Stroke Hemisphere	
Right hemisphere, *n* (%)	11 (55.0)
Stroke Location, *n* (%)	
Cortical	13 (65.0)
Subcortical	1 (5.0)
Cortical/Subcortical	5 (25.0)
Posterior Circulation	1 (5.0)
Chronicity, months, median, (interquartile range)	19.0 (9.8-67.3)
Number of strokes, *n* (%)	
One	13 (65.0)
Two	5 (25.0)
Three or more	2 (10.0)
Number of co-morbidities, *M (SD)*	4.1 (1.6)
Education (>12 years), *n* (%)	10 (50.0)
Assistance with Basic ADLs, *n* (%)	13 (65.0)
Employed, *n* (%)	0 (0.0)
Dominant limb affected, *n* (%)	7 (35.0)
Visual Fields	
Quadrantopsia, *n* %	4 (20.0)
Homonymous Hemianopsia, *n* (%)	5 (25.0)

Table 6 (continued)

Sensory impairment*, *n* (%)	
Mild to moderate	7 (43.8)
Severe to total	3 (18.8)
Motricity Index, *M (SD)*	68.3 (13.6)
RBANS Index Scores, *M (SD)*	
Immediate Memory	74.1 (21.9)
Visuospatial/Constructional	72.3 (17.9)
Language	82.6 (15.5)
Attention	62.9 (13.4)
Delayed Memory	76.3 (17.9)
Total Scale	68.6 (13.1)
National Institutes of Health Stroke Scale*, *M (SD)*	7.2 (3.6)
Patient Health Questionnaire-9, *M (SD)*	6.9 (5.9)
Wong Baker FACES Pain Rating Scale-Pre-Intervention, *M (SD)*	1.0 (2.3)

Note. RBANS, Repeatable Battery for the Assessment of Neuropsychological Status. *n=16

The mean age of the sample was 66.7 years and the median time since stroke was 19.0 (*IQR*=9.8-67.3 months) months. The sample included an equal number of males and females. The majority of the participants in the sample were white (70.0%) and sustained ischemic strokes (85.0%). Approximately 60% of participants had right hemisphere strokes, and 65% were in the cortical regions. Half of the participants in the sample had more than 12 years of education. Stroke symptoms at baseline ranged from mild to moderate (National Institutes of Health Stroke Scale, mean 7.2, SD=3.6) and 65% of participants required assistance to complete basic ADLs. Participants had moderate depressive symptoms (Patient Health Questionnaire-9, mean 6.9, SD=5.9) and demonstrated severe cognitive impairment scoring more than two standard deviations below age adjusted means on the Repeatable Battery for the Assessment of Neuropsychological Status (Total Scale Index Score, mean 68.6, SD= 13.1). On average, participants reported low levels of pain pre-intervention (Wong Baker FACES Pain Rating Scale, mean 1.0, SD=2.3).

4.3.2.1 Tolerability and Satisfaction

Data regarding the side effects experienced during the intervention are presented in Table 7 and Table 8. Eight participants (40%) experienced an increase in pain in one or more sessions. Seven (35%) participants experienced a reduction in pain during one or more sessions. Overall, participants experienced an increase in pain 5% of the sessions and a reduction in pain 4% of the sessions. Five participants experienced an adverse event in one or more sessions. There were a total of 9 (3%) adverse events over all treatment sessions (Table 7). Three participants reported reductions in pain, switching pain categories in at least one session (Table 8). No other adverse events (e.g. injuries) occurred.

Table 7. Adverse Events

Category Change Occurrences, *n*	9
No/Mild Pain to Moderate Pain, *n*	4
No/Mild Pain to Severe Pain, *n*	3
Moderate Pain to Severe Pain, *n*	2
% Sessions with Adverse Events	3
% Session with Increase Pain	5

Table 8. Reductions in Pain

Category Change Occurrences, *n*	6
Moderate Pain to No/Mild Pain, *n*	4
Severe Pain to Moderate Pain, *n*	2
% Sessions with Category Change	2
% Sessions with Reductions in Pain	4

Intervention data are presented in Table 9. Collectively, participants attended almost all (99.4%) of the scheduled sessions. Two participants received 17 intervention sessions instead of 18. On average, participants completed close to 300 repetitions per session (total repetitions, mean 5152.9, SD=515.9) although there was a wide range of repetitions completed among participants. Participants spent the majority of the sessions actively completing repetitions (total minutes, mean 889.6, SD=133.8). Tasks were switched, downgraded, and upgraded throughout the course of the 18 intervention sessions. Participants completed both unilateral and bilateral tasks during the sessions, but on average participants completed more bilateral tasks (mean 0.58, SD=0.2).

Table 9. Intervention Data

% of sessions attended	99.4%
Total repetitions completed	
M (SD)	5152.9 (515.9)
Range	3459-5807
Total minutes active during sessions	
M (SD)	889.6 (133.8)
Range	735-1076
Tasks over sessions	
Number of tasks switched, *M (SD)*	4.5 (1.5)
Number of upgrades, *M (SD)*	8.8 (6.5)
Number of downgrades, *M (SD)*	3.4 (2.9)
% bilateral tasks, *M (SD)*	0.58 (0.2)

Participants expressed high satisfaction (Client Satisfaction Questionnaire-8, mean 29.5, SD=3.1) with the intervention, with 95% of the sample reporting moderate to high satisfaction.

4.3.2.2 Primary and Secondary Outcomes

The primary and secondary outcomes are plotted in Figures 6–9 exhibiting the distribution of scores on the study measures. At baseline, participants reported using their affected arm rarely to half as much as before their strokes (Motor Activity Log Amount of Use, mean 2.5, SD=1.3) and rated the quality of use as poor to fair (Motor Activity Log Quality of Use, mean 2.7, SD=1.4) (Table 10.) Participants had moderate impairments in arm function (Action Research Arm Test, mean 31.2, SD=15.7; Chedoke Arm and Hand Activity Inventory, mean 31.3, SD=16.2). Participants had mild USN (Catherine Bergego Scale, mean 6.1, SD=4.6; Behavioral Inattention Test, mean 118.5, SD=26.2) and had some awareness of their inattention (Catheine Bergego Scale-Self Assessment, mean 4.4 SD=4.2). Participants also reported difficulty completing activities of daily living and instrumental activities of daily living (Stroke Impact Scale ADL/IADL Subscale, mean 65.8, SD=17.8).

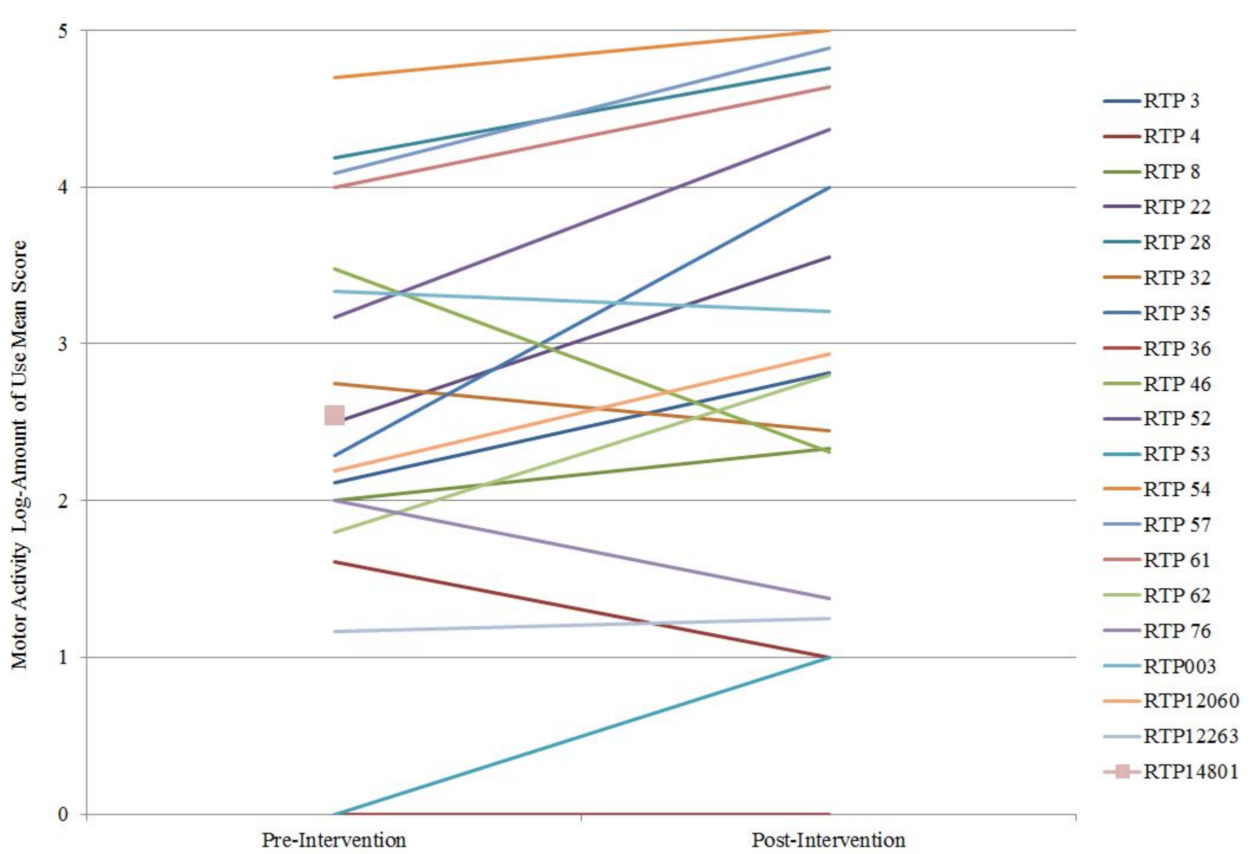

Figure 6. Motor Activity Log Reflecting Arm Use Over Time

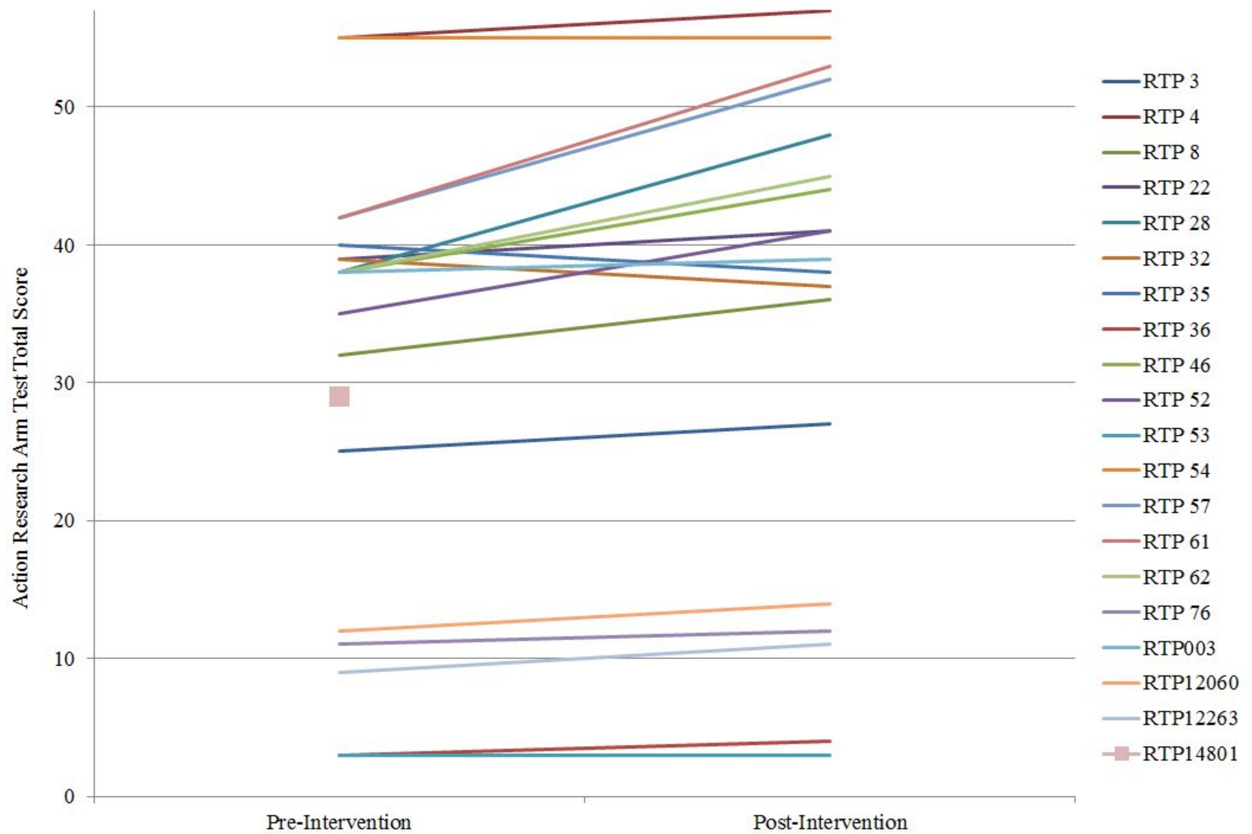

Figure 7. Action Research Arm Test Reflecting Arm Function Over Time

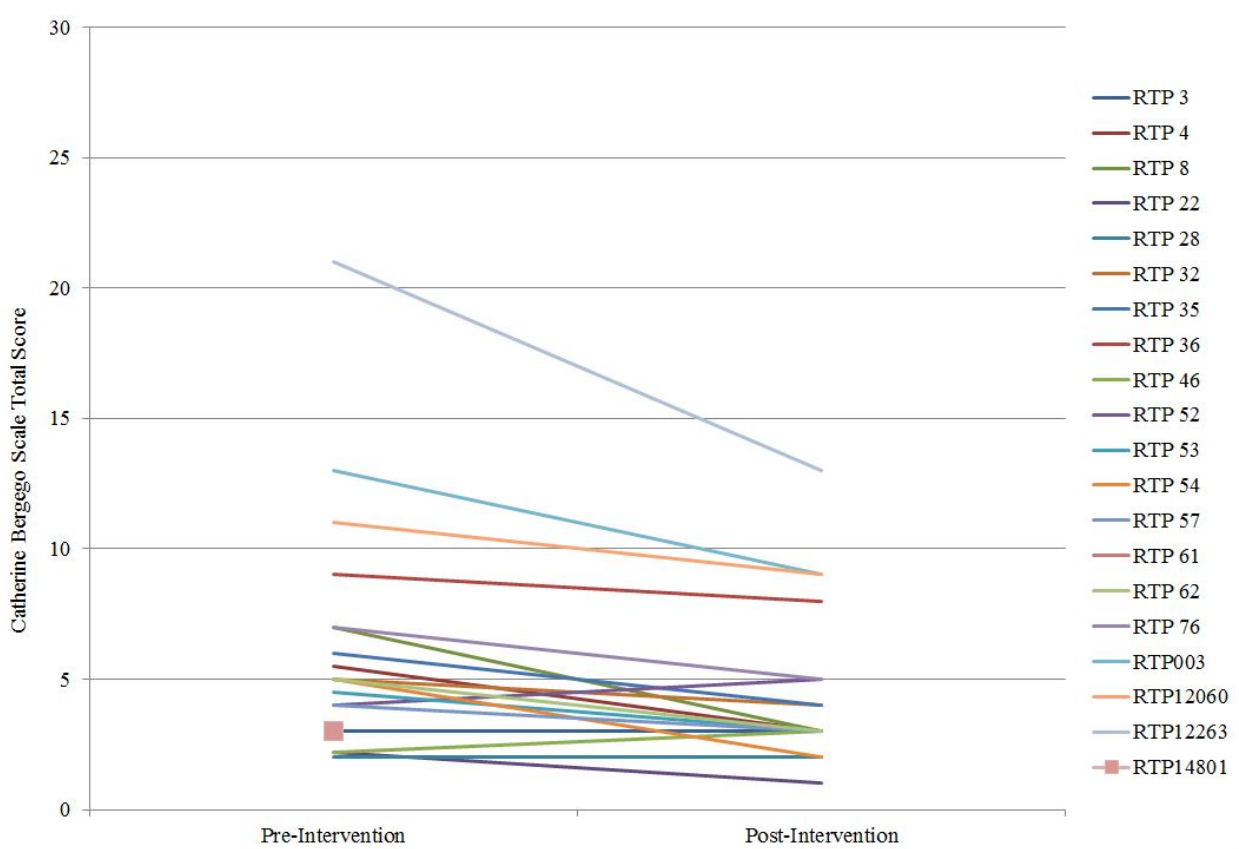

Figure 8. Catherine Bergego Scale Reflecting Inattention Over Time

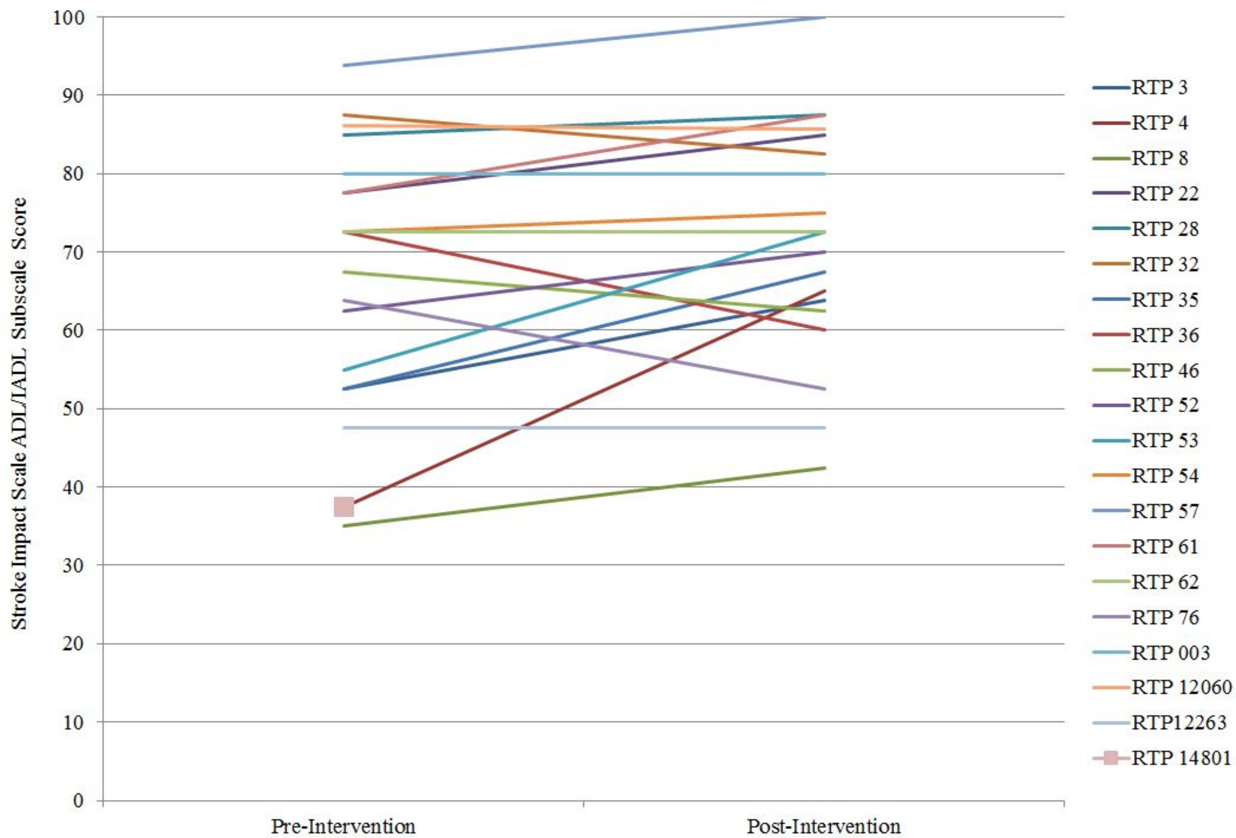

Figure 9. Stroke Impact Scale ADL/IADL Subscale Reflecting Disability Over Time

Table 10. Primary and Secondary Outcomes

	Scale	Baseline (n=20)	Follow-up (n=19)	Test Statistic	Effect Size
Catherine Bergego Scale*, *M (SD)*	0-30				
Performance observation		6.1 (4.6)	4.4 (3.2)	$t_{19=}$-3.4‡	*d*=-0.44
Self-evaluation		4.4 (4.2)	3.1 (3.8)	$t_{16=}$-1.6	*d*=-0.33
Behavioral Inattention Test, *M (SD)*	0-146	118.5 (26.2)	128.6 (30.6)	$t_{18=}$-3.1‡	*d*=0.36
Action Research Arm Test, *M (SD)*	0-57	31.2 (15.7)	34.6 (17.6)	$t_{19=}$-3.0‡	*d*=0.20
Chedoke Arm and Hand Activity Inventory, *M (SD)*	0-63	31.3 (16.2)	37.3 (16.6)	$t_{16=}$-3.3‡	*d*=0.37
Motor Activity Log, *M (SD)*	0-5				
Amount of Use		2.5 (1.3)	2.9 (1.5)	$t_{19=}$-2.1†	*d*=0.30
Quality of Use		2.7 (1.4)	2.9 (1.4)	$t_{15=}$-1.3	*d*=0.09
Stroke Impact Scale ADL/IADL subscale *M (SD)*	0-100	65.8 (17.8)	71.6 (15.0)	$t_{19=}$-1.7	*d*=0.35
Client Satisfaction Questionnaire-8, *M (SD)*	0-32	-	29.5 (3.1)	-	-

Note. *Lower scores=better performance; †, $p<.05$; ‡, $p<.01$.

Baseline correlations are presented in Table 11. The Action Research Arm Test and Chedoke Arm and Hand Activity Inventory-9 (arm function measures) had a good to excellent association ($r=.78$, $p<.01$). The Catherine Bergego Scale and Behavioral Inattention Test (attention measures) had a moderate to strong association ($r=-.55$, $p<.05$).

Table 11. Baseline Correlations

	Age	Chronicity	NIHSS	PHQ-9	MI	ARAT	CAHAI	MAL-A	MAL-Q	CBS	CBS Self	BIT	SIS ADL
Age	1.0	.09	.03	-.13	.12	.00	-.09	-.21	-.06	.12	-.26	-.20	-.08
Chronicity	.09	1.0	.16	.13	.07	.06	-.03	.11	.24	-.09	-.15	.11	.39
NIHSS	.03	.16	1.0	-.14	-.40	-.26	-.30	-.38	-.36	.08	-.04	-.28	-.25
PHQ-9	-.13	.13	-.14	1.0	.07	-.14	-.25	-.19	.04	.23	-.19	-.08	-.31
MI	.12	.07	-.40	.07	1.0	.76†	.62*	.73†	.82†	-.52*	-.20	.56*	.19
ARAT	.00	-.06	-.26	-.14	.76†	1.0	.78†	.62†	.66†	-.31	-.41	.54*	.28
CAHAI	-.09	-.03	-.30	-.25	.62*	.78†	1.0	.72†	.67*	-.42	-.29	.32	.42
MAL-A	-.21	.11	-.38	-.19	.73†	.62†	.72†	1.0	.85†	-.51*	-.06	.71†	.53*
MAL-Q	-.06	.24	-.36	.04	.82†	.66†	.67†	.85†	1.0	-.51	-.29	.76	.61*
CBS	.12	-.09	.08	.23	-.52*	-.31	-.42	-.51*	-.51*	1.0	-.09	-.55*	-.14
CBS-Self	-.26	-.15	-.04	-.19	-.20	-.41	-.29	-.06	-.29	-.09	1.0	.00	-.37
BIT	-.20	.11	-.28	-.08	.56*	.54*	.32	.71†	.76†	-.55*	.00	1.0	.44
SIS ADL	-.08	.39	-.25	-.31	.19	.28	.42	.53*	.61*	-.14	-.37	.44	1.0

Note. *p<.05; †p<.01; NIHSS, National Institutes of Health Stroke Scale; PHQ-9, Patient Health Questionnaire; MI, Motricity Index; ARAT, Action Research Arm Test; CAHAI, Chedoke Arm and Hand Activity Inventory-9; MAL-A, Motor Activity Log Amount Scale; MAL-Q, Motor Activity Log Quality Scale; CBS, Catherine Bergego Scale; BIT, Behavioral Inattention Test; SIS, Stroke Impact Scale.

At follow-up, small improvements in arm use (Motor Activity Log Amount of Use, mean 2.9, SD=1.5) were seen on the primary outcome measure, the Motor Activity Log Amount of Use Scale (*t*=-2.1, *p*=.04, *d*=0.30), but were not seen on the Motor Activity Log Quality of Use Scale (mean 2.9 SD=1.4, *t*=-1.3, p<.20, *d*=0.09). There was not a significant change in the amount of use or the quality of use reported after applying a Bonferroni correction to adjust for multiple comparisons. Participants continued to report using their affected arm approximately half as much as before stroke and that the quality of arm use was fair. Participants had persistent impairments in arm function (Action Research Arm Test, mean 34.6, SD= 17.6; Chedoke Arm and Hand Activity Inventory-9, mean 37.3 SD=16.6) and showed small but significant improvements in arm function on the Action Research Arm Test (*t*=-3.0, *p*<.01, *d*=0.20) and on the Chedoke Arm and Hand Activity Inventory-9 (*t*=-3.3, *p*<.01, *d*=0.37), which was used as an exploratory measure. Participants continued to have mild to moderate USN (Catherine Bergego Scale, mean 4.4, SD=3.2; Behavioral Inattention Test, mean 128.6, SD=30.6), but experienced a small but statistically significant improvement in attention on the Catherine Bergego Scale (*t*=-3.4, *p*<.01, *d*=-0.44). No changes were seen on the Catherine Bergego Scale self-assessment (*t*=-1.6, *p*=.10, *d*=-0.33). Participants also demonstrated a small but statistically significant improvement in attention on the Behavioral Inattention Test (*t*=-3.1, *p*<.01, *d*=0.36) which was an exploratory measure in this study. Participants continued to report difficulty completing ADLs/IADLs (Stroke Impact Scale ADL/IADL subscale, mean 71.6, SD=15.0), but experienced a small reduction in disability (*t*=-1.7, *p*=.08, *d*=0.35). However, this reduction was not statistically significant. Effect sizes were small on all measures.

Variability in response to treatment was detected among measures of motor function (Table 12). We examined these differences by comparing changes scores for each outcome measure that had a minimally clinically important difference established in the literature. There was considerable variability among participants and many participants demonstrated improvement on some measures but not on others. Variability was seen particularly on the Action Research Arm Test and Chedoke Arm and Hand Activity Inventory-9 (arm function assessments). These findings suggest that different measures may pick up different aspects of arm use and arm function.

Table 12. Measures of Change, By Participant

ID	MAL A (MCID=0.5)	MAL Q (MCID=0.5)	ARAT (MCID=5.7)	CAHAI-9 (MDC=4.4)
RTP 3	0.70*	-	2	10*
RTP 4	-0.61	0.32	2	12*
RTP 8	0.33	0.90*	4	12*
RTP 22	1.1*	0.72*	2	20*
RTP 28	0.57*	-0.94	10*	2
RTP 32	-0.30	-2.10	-2	10*
RTP 35	1.71*	0.17	-2	6*
RTP 36	0	0.00	1	0
RTP 46	-1.17	-0.32	6*	8*
RTP 52	1.2*	0.80*	6*	0
RTP 53	1	0.00	0	2
RTP 54	0.30	0.33	0	8*
RTP 57	0.80*	1.11*	10*	2
RTP 61	0.64*	0.32	11*	2
RTP 62	1.0*	0.6*	7*	2
RTP 76	-0.63	0.5*	1	1
RTP003	-0.13	-	-5	-
RTP12060	0.74*	-	2	-
RTP12263	0.08	-	2	-
RTP14801	†	†	†	†
Participants achieved MCID or exceeded MDC, n	9	6	6	8

Table 12 (continued)

Note. MCID=Minimally clinically important difference; MCD=Minimal Detectable Change; MAL-A, Motor Activity Log Amount of Use; MAL-Q, Quality of Use; ARAT, Action Research Arm Test; CAHAI-9, Chedoke Arm and Hand Activity Inventory; References for MCID/MCD: Lang, Edwards, Birkenmeier, & Dromerick, 2008; van der Lee et al., 2001; *MCID achieved or MDC exceeded; †Participant lost to follow-up.

We examined differences in performance on the Action Research Arm Test and Chedoke Arm and Hand Activity Inventory-9 more closely for participants (University of Pittsburgh, n=16) who were assessed on both arm function measures (Table 13). We used minimal clinical important difference (and in one case minimal detectable change) estimates to characterize differences between measures, merely as a means to compare measures. These estimates are not to be considered clear indicators of improvement, but are presented here merely for exploration. Only 1 participant made clinically meaningful changes on both the Action Research Arm Test and Chedoke Arm and Hand Activity Inventory-9. Five participants made clinically meaningful changes on the Action Research Arm Test and 7 participants made clinically meaningful changes on the Chedoke Arm and Hand Activity Inventory-9. Participants with changes on the Chedoke Arm and Hand Activity Inventory-9 had lower baseline Chedoke Arm and Hand Activity Inventory-9 scores than participants who only made changes on the Action Research Arm Test. Baseline Action Research Arm Test scores for these two groups were comparable. There were 3 participants who demonstrated no changes on either measure. These individuals had the most severe impairments in arm function.

Table 13. Comparison of Changes on ARAT and CAHAI-9

	Improvement on ARAT Only (n=5)	Improvement on CAHAI Only (n=7)	Improvement on both ARAT/CAHAI (n=1)	No Improvement on ARAT/CAHAI (n=3)
Age, Years				
M (SD)	68.6 (13.2)	66.9 (11.8)	56.0	73 (13.5)
Range	49-84	54-88	-	59-86
Motricity Index				
M (SD)	75.6 (9.8)	72.7 (11.3)	75.0	49.0 (1.7)
Range	65-85	51-85	-	48-51
ARAT Pre				
M (SD)	39.0 (3.0)	40.7 (11.1)	38.0	5.7 (4.6)
Range	35-42	25-55	-	3-11
ARAT Post				
M (SD)	47.8 (5.0)	41.6 (10.8)	44.0	6.3 (4.9)
Range	41-53	27-57	-	3-12
CAHAI Pre				
M (SD	44.8 (9.0)	29.4 (15.1)	38.0	10.7 (2.1)
Range	35-57	11-55	-	9-13
CAHAI Post				
M (SD)	46.4 (9.5)	40.6 (14.4)	46.0	11.7 (2.1)
Range	35-59	23-63	-	10-14
MAL Pre				
Amount, *M (SD)*	3.4 (1.0)	2.6 (1.0)	3.5	0.7 (1.2)
Amount, Range	1.8-4.2	1.6-4.7	-	0-2
Quality *M (SD)*	3.5 (0.5)	3.2 (1.0)	2.9	0.7 (1.2)
Quality, Range	2.8-4.0	2.0-4.9	-	0-2
MAL Post				
Amount *M (SD)*	4.3 (0.9)	3.0 (1.3)	2.3	0.8 (0.7)
Amount Range	2.8-4.9	1.0-5.0	-	0-1.4
Quality *M (SD)*	3.9 (0.8)	3.1 (0.7)	2.5	0.8 (1.4)
Quality Range	2.8-4.9	1.9-4.1	-	0-2.5
CBS Pre				
M (SD)	3.6 (2.8)	4.8 (1.7)	2.2	6.8 (2.3)
Range	2.0-5.0	2.2-7.0	-	4.5-9.0
CBS Post				
M (SD)	2.8 (1.5)	2.9 (1.1)	3.0	5.3 (2.5)
Range	1.0-5.0	1.0-4.0	-	3.0-8.0
BIT Pre				
M (SD)	131.4 (4.0)	127.7 (9.9)	131	104.7 (36.2)
Range	125-135	106-135	-	63-128
BIT Post				
M (SD)	141.2 (3.6)	140.5 (2.9)	133	122.3 (34.3)
Range	138-140	136-145	-	83-136

Note. ARAT, Action Research Arm Test; CAHAI, Chedoke Arm and Hand Activity Inventory; MAL, Motor Activity Log; CBS, Catherine Bergego Scale; BIT, Behavioral Inattention Test.

4.4 DISCUSSION

This study demonstrated the feasibility of recruiting and retaining individuals with USN with hemiparesis in the chronic stage of stroke. We found small changes in amount of use, arm function, and attention (reliable for arm function and attention). The findings in this pilot study will help to guide future research and better inform our understanding of the use of repetitive task practice for individuals with USN.

4.4.1 Recruitment and Generalizability

We were able to recruit 100% of the targeted sample (n=20), however this required screening a large number of individuals (n=88) to identify eligible participants. Although estimates of chronic USN range considerably (33-87% of individuals with acute neglect have chronic USN), we found that 45% of individuals we screened had USN (Appelros et al., 2004; Karnath et al., 2011; Ringman, Saver, Woolson, Clarke, & Adams, 2004). This was a community based sample. The percentage of individuals with USN in our sample will differ since some participants were referred by clinicians who suspected that individuals had USN. It is also possible that our screening measure, the Behavioral Inattention Test, was not sensitive enough to detect USN in all individuals with USN and that we excluded some individuals who actually did have USN. It has been well cited in the literature that different measures of USN vary considerably in sensitivity and that behavioral assessments of USN are most sensitive (Azouvi et al., 2006; Bowen et al., 1999). We selected the Behavioral Inattention Test because it includes a battery of subtests and is one of the most widely used assessments. We also chose to use the Behavioral Inattention Test rather than the Catherine Bergego Scale, which examines behavioral USN, since the Catherine Bergego Scale was one of our primary outcome measures. Nonetheless, the relatively high number of participants we identified with USN should be noted. Although clinicians are often more aware of acute USN, this study highlights the prevalence of USN in chronic stroke and emphasizes that individuals beyond the first several months post stroke may struggle with USN and may be at risk for USN related disability.

Although a large percentage of individuals who were screened had USN, only 53% of individuals with USN met the motor criteria and were eligible to participate. Thus, approximately half of individuals with chronic USN may not be able to participate in a repetitive task practice program due to severe hemiparesis. Other interventions should be explored for these individuals.

Our sample of enrolled participants was composed primarily of individuals with mild neglect (85%) which limits the generalizability of the findings. However, it is unclear from the literature how common moderate to severe USN (measured by the Catherine Bergego Scale) is in the chronic stage post stroke so we are unable to draw a comparison. Interestingly, ineligible participants (had USN but insufficient motor function) had similar Behavioral Inattention Test scores (Mean 118.2, SD=28.3) as individuals who were enrolled in the study (Mean 118.5, SD=26.2) (had USN and had sufficient motor function). If we infer that these individuals would also demonstrate similar performance on the Catherine Bergego Scale then, this would suggest that the majority of individuals screened had mild USN. However, we are not able to make this conclusion based on the available data. It is possible that individuals with more severe USN are not living in the community (e.g., Skilled nursing facilities) and are therefore under-represented.

4.4.2 Tolerability and Satisfaction

We also examined the tolerability of the intervention and satisfaction with the intervention. We found that the majority of individuals (95%) provided positive feedback regarding the intervention on the Client Satisfaction Questionnaire-8. Although anecdotal, participants frequently reported improvement in their affected arm to the therapist during intervention sessions and satisfaction with their improved ability to perform various activities that were important to them (e.g. handwriting). We also found that only a few adverse events (i.e., change in pain) occurred during the course of the intervention sessions. Although many participants had pain in their affected arms at baseline, participants tolerated the sessions well without substantial increases in pain. The goal of our sessions was to provide high doses of repetitive task practice (target goal=300 reps) and for participants to complete as many repetitions as possible in each session. We were able to provide high doses of repetitive task practice over the intervention sessions (Mean 5152.9, SD=515.9) but only 50% of participants were able to achieve an average of 300 reps per session. Participants in a different pilot study examining repetitive task practice for individuals without neglect found that participants were able to complete slightly more repetitions (Mean 5476, SD=1088) (Birkenmeier et al., 2010). However, these findings suggest that the presence of neglect may not prohibit participants from achieving a large number of repetitions. It is unclear what the best dose of repetitive task practice is for individuals with hemiparesis post stroke and whether differences in dose impacts outcomes, particularly for individuals with USN.

4.4.3 Preliminary Efficacy

In Chapter 2, we presented a conceptual model (Figure 2) highlighting how repetitive task practice may be able to improve arm use, arm function, and attention and therefore reduce disability. We examined the preliminary efficacy of repetitive task practice and found that participants made small improvements in arm use, arm function, and attention and experienced small reductions in disability (Figure 10). However, the effect sizes were small, indicating that the changes may not be meaningful. These improvements were significant for arm function and attention after applying a Bonferroni correction indicating that the results were reliable for arm function and attention. Although our model indicates that repetitive task practice may also facilitate positive changes in cortical reorganization, it is unclear whether the intervention results in cortical reorganization since this was not examined in our study. At this time, we do not have sufficient evidence to validate the model, but these preliminary findings suggest that the intervention may have the largest effect on attention.

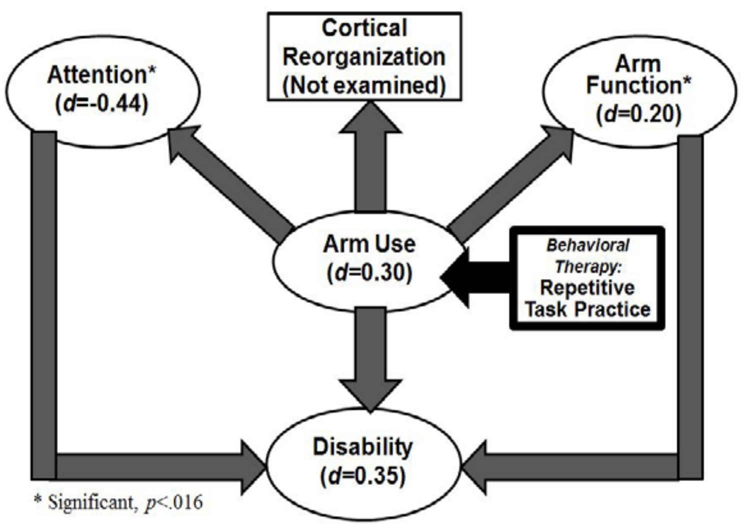

Figure 10. Preliminary Effects of Repetitive Task Practice for Individuals with USN

Few studies have been conducted with individuals with chronic USN or utilizing repetitive task practice, so it is challenging to compare the effect sizes in this study to other studies. Our study found smaller changes in arm use and arm function than a study conducted with individuals with chronic stroke (10% of sample had USN). van der Lee et al. (1999) found a moderate effect of the intervention (unilateral repetitive task practice program) on arm use (Motor Activity Log Amount of Use, d=0.7). Although our intervention differed (unilateral and bilateral training vs. unilateral training; 18 hours of training vs. 60 hours of training) and the majority of participants did not have USN in the study conducted by van der Lee (1999), these findings provide at least some reference to compare the outcomes and suggest that our intervention had less of an effect on arm use. It is possible that a higher dose of the intervention is needed for individuals with USN to benefit. With respect to arm function, we found the intervention had a small effect (Action Research Arm Test, d=.20). This effect was much smaller than in a study conducted by Birkenmeier et al. (2010) with individuals with chronic stroke who did not have neglect (Action Research Test, d=1.85). Participants in the study by Birkenmeier et al. (2010) had much lower baseline Action Research Arm Test scores (Mean 21.7 SD=3.3) than our sample (Mean 31.2 SD=15.7) which may contribute partially to the differences seen between studies. However, it should be noted that the same intervention protocol was used in these studies. This suggests that the intervention may not be as potent at reducing impaired arm function for individuals with USN or that a higher dose may be needed for individuals with USN. It is also possible that individuals with less impairment may also benefit less. Wu et al. (2013) found a large effect (d=-0.87) of treatment (repetitive task practice) on inattention (measured by the Catherine Bergego Scale) in a small sample (n=8) of individuals with subacute and chronic stroke (Mean 10.1 SD=10.4, months). We found a small effect (Catherine Bergego

Scale, d=-.44) in our sample, but it is difficult to compare these effects given differences in chronicity.

We assessed disability to conduct exploratory analyses. Although there was not a statistically significant reduction in disability (Stroke Impact Scale ADL/IADL subscale), there was a small effect (d=.35). It is possible that a more comprehensive performance based measure of disability would be more appropriate to use.

In examining the data more closely at the participant level, we found that there were many individuals who demonstrated what is considered clinically meaningful change on several of the outcome measures (Table 12) which suggests that the intervention may be effective for some individuals. We examined participant's scores on the arm function measures and noted that individuals who did not respond on either the Action Research Arm Test or the Chedoke Arm and Hand Activity Inventory-9 were those with the greatest impairments in arm use, arm function, and attention. These participants demonstrated severe impairments in arm function on the Action Research Arm Test and were much more impaired than those individuals in the study by Birkenmeier et al. (2010). This suggests that the intervention may not be beneficial for individuals with USN who have more severe impairments and should be considered when designing future studies.

We also noted that many participants demonstrated changes in arm function, but that these changes were only seen on either the Action Research Arm Test or the Chedoke Arm and Hand Activity Inventory-9 (Table 13). At baseline, the two subgroups of participant's scores were similar on the Action Research Arm Test but the Chedoke Arm and Hand Activity Inventory-9 scores were lower for the individuals who saw clinically meaningful changes on the Chedoke Arm and Hand Activity Inventory-9. The Chedoke Arm and Hand Activity Inventory-

9 is an assessment that examines the ability and contribution of the affected arm completing bilateral tasks. It is possible that individuals who scored lower at baseline incorporated their affected arm into the tasks much less and utilized it more at follow-up. This hypothesis aligns when comparing baseline scores on the Motor Activity Log Amount of Use Scale. Individuals who demonstrated improvement on the Chedoke Arm and Hand Activity Inventory-9 reported less use than individuals who only improved on the Action Research Arm Test. However, it remains unclear exactly why discrepancies on these two assessments of arm function exist in our study. It is possible that differences in the items on the assessments (e.g., unilateral vs. bilateral tasks; greater emphasis on fine motor vs. gross motor skills) contributed to these discrepancies.

We used a variety of measures in our battery including several self-report measures (Motor Activity Log Amount of Use, Motor Activity Log Quality of Use, Stroke Impact Scale ADL/IADL Domain), but the accuracy of self-report measures in a population of cognitively impaired (>2 SD from age adjusted total score on Repeatable Battery for the Assessment of Neuropsychological Status) individuals may be questioned and is a potential limitation of our study. Upper extremity accelerometers may provide a more accurate measure of arm activity and use. However, we selected these measures because they are commonly used in repetitive task practice trials and have informed the conception and design of the current study. We also recognized the importance of including patient reported outcomes. Previously, we touched on the issue associated with assessment of USN and the fact that different measures seem to detect different aspects of this complex syndrome. We used the Catherine Bergego Scale as one of our primary outcomes (inattention) which is one of the only assessments that examines USN in the context of activities of daily living. Although we feel that this assessment is more relevant than the majority of USN assessments that are paper and pencil based, we believe that the Catherine

Bergego Scale may not contain sufficiently difficult items and that more complex instrumental activities of daily living may be more relevant --- particularly for community dwelling individuals with chronic USN. For example, locating an item on a shelf during meal preparation or navigating the aisles of a crowded store are likely more challenging activities for individuals with neglect than more basic activities of daily living such as eating and grooming. This may be a limitation of our study. Future studies should examine the ability of the Catherine Bergego Scale to comprehensively measure USN particularly for individuals with chronic USN.

4.4.4 Limitations

There are several other limitations to our study. We found that that there appears to be a large percentage of individuals with chronic USN who have severe motor impairment, and therefore are not able to participate in repetitive task practice programs. This limits the generalizability of the intervention and of our findings, and suggests the need for additional investigations of alternative interventions. This was also a pilot study with a small sample and requires replication to confirm the findings. The design of the study did not include a control group, so we are unable to attribute the changes seen to the intervention per se. It is also unclear what the long term effects of the intervention are and whether the effects are stable since we did not conduct multiple follow-up assessments. Future studies should examine the long term effects of the intervention on arm use, arm function, and attention.

Although there were not large effects seen in this study, there was a small signal present to suggest that the intervention did have some reliable effect. It is possible that individuals with acute USN may benefit more from participation in a repetitive task practice program since the potential for neurological reorganization is greater during the acute stage after stroke, but this has not been examined. A randomized controlled trial would be needed to control for natural recovery. In summary, we demonstrated the feasibility and tolerability of repetitive task practice for individuals with chronic USN and that participants may benefit from small improvements in arm use, arm function, and attention.

5.0 CONCLUSION

USN is associated with poor outcomes including greater disability after stroke. This project intended to clarify concepts surrounding USN. The purpose of this project was also to examine an intervention for individuals with USN. This project encompasses a thorough review of the literature, a retrospective study, and a prospective pilot study.

5.1 AIMS

This dissertation study had the following aims:

1) To review the evidence and provide the scientific rationale for examining repetitive task practice for individuals with USN.
2) To examine the association between USN and motor impairment over time
3) To conduct a Phase II pilot clinical trial:
   a) To establish feasibility and tolerability of a repetitive task practice program for USN after stroke as indicated by:
      - Recruitment and retention of ≥95% of targeted sample size for the entire protocol
      - Tolerability in terms of little or no adverse effects reported by ≥90% of participants and acceptable to high satisfaction scores reported by ≥90% of participants

b) Examine improvements in symptoms associated with USN syndrome after treatment. Using a single-group repeated-measures design, we predicted that:

H1: Individuals would demonstrate significant improvements in use of the affected arm (measured by Motor Activity Log Amount of Use Scale) after treatment.

H2: Individuals would demonstrate a significant improvement in arm function (measured by Action Research Arm Test) after treatment.

H3: Individuals would demonstrate a significant improvement in attention (measured by the Catherine Bergego Scale) after treatment.

5.2 SUMMARY OF FINDINGS

In Chapter 2, we presented a new frame of reference for USN and its association with disability. Specifically, we highlighted potential mechanisms that link USN to disability and discussed the complexity of impairments associated with USN (inattention and impaired arm function). We then reviewed evidence that suggests that repetitive task practice may be able to alter these mechanisms and reduce disability for individuals with USN.

In Chapter 3, we examined motor recovery among individuals with and without USN. We found that individuals with USN had less arm and hand recovery at 6 months than individuals without USN despite similar patterns of recovery after stroke. These findings highlight the importance of investigating interventions to address motor impairment for individuals with USN since they may be at greater risk for long term impairments.

In Chapter 4, we reviewed the findings of our prospective pilot study that examined repetitive task practice for individuals with USN. We demonstrated the feasibility of recruiting and retaining individuals with chronic USN. We also found that the intervention was tolerable for participants. Finally, we found that participants had small yet significant improvements in arm use, arm function, and attention.

5.3 LIMITATIONS

Although the findings of this project provide greater insight into USN and potential interventions to address USN, there are a number of limitations. We developed a conceptual model linking USN to disability based on available evidence. However, additional research is necessary to be able to support this model. In our prospective study (Chapter 4), we examined the effects of repetitive task practice on arm use, arm function, and attention. We also administered the Stroke Impact Scale as an exploratory measure of disability. However, we did not have a comprehensive performance based measure of disability. Thus, it remains to be shown whether improvements in arm use, arm function and attention translate to reductions in disability.

Another limitation of our project was that we conducted a retrospective study rather than a prospective study examining arm and hand motor recovery (Chapter 3). We used the Line Bisection Test (Schenkenberg et al., 1980) to classify participants (presence or absence of USN), but it is possible that additional individuals with USN went undetected by this single assessment. Variable performance on paper and pencil based assessments has been shown. A more comprehensive battery of USN measures would have provided a more reliable classification of participants. Also, we used the Chedoke Arm and Hand Activity Inventory to describe the stages of motor recovery which provides a broader examination of motor recovery than more specific impairment measures may provide. It would also have been interesting to examine USN recovery over time and the relationship between USN and motor recovery had these data been available.

Our prospective pilot study also had a number of limitations including the small sample size. The majority of our sample included individuals with mild USN. Therefore, it is unclear what the effects of the intervention would be for individuals with more severe USN and whether their experience in the program would be similar to those in our sample. We also found that many individuals with USN did not have sufficient motor function to participate in our study. Therefore, we must consider how generalizable the intervention is for individuals with chronic USN. Self-report measures were used in our study to examine arm use. However, it is possible that these reports were inaccurate and do not reflect how much or how well individuals were truly using their affected arm. We also do not know whether the effects of the intervention were maintained since we did not include additional follow-up assessments. This study did not include a control group either, so we are unable to attribute the changes seen to the intervention with certainty.

5.4 FUTURE DIRECTIONS

Future investigations should focus in three areas: improvement in the assessment of USN and associated sequalae, expanded investigations of interventions for USN, and identification of participants most likely to benefit from selected interventions.

Long term longitudinal studies are also needed to examine the trajectory of USN recovery, motor recovery, and disability for individuals with USN after stroke using a comprehensive battery of assessments from the acute onset to chronic phase of recovery. Future studies should examine optimal outcome measures for all sequalae, including arm use, arm function, attention, and disability. For example, technology may be used to assist in monitoring and measuring arm use, in addition to self-report measures such as the Motor Activity Log. With respect to arm function, we found that the Chedoke Arm and Hand Activity Inventory-9 was better able to detect changes in arm function for this population than the Action Research Arm Test. More rigorous evaluation of measures of attention is warranted, to ensure scalability of measures across the continuum of severity. We also recommend a performance based measure of disability should also be used to determine the effects of the intervention on an individual's ability to complete activities of daily living.

Optimal intervention programs for individuals with USN at various stages in recovery are unclear. Our scoping review suggest that no intervention has demonstrated robust effects, as of yet. In our pilot study, we found that individuals demonstrated significant, yet small changes after participating in a repetitive task practice program and that the intervention was both feasible to utilize and tolerable for participants. It may be that this particular intervention program did not provide a sufficient dose, or that additional active ingredients are necessary to improve gains. Future studies may examine the addition of cognitive behavioral components to aid generalization of repetitive tasks practice, thus potentially enhancing improvements over time for individuals with cognitive impairments. Additional interventions must also be explored for individuals with USN who have more severe impairments in motor function who are unable to participate in repetitive task practice programs. These interventions may include a refinement of scanning or similar intervention protocols, perhaps combined with haptic or technologically-supported movement of the affected limb.

There are several considerations for future studies with respect to the selection of participants. One approach would be to refine the eligibility criteria in future studies n to focus on participants who are most likely to benefit from the intervention. This may require) exclusion of individuals with severe impairments in arm function who did not respond to intervention. Another approach may be to focus on participants in the acute or subacute stage post stroke, who are more likely to benefit from participation in the program. In order to control for natural recovery in the acute or subacute phases, studies examining this subpopulation would need to have a randomized comparison group.

In summary, USN is complex. To date, there are no robust interventions that result in large reductions in impairments or disability associated with USN. Future studies can build on lessons learned in this dissertation to refine assessment, intervention, and sample selection.

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