

REHABILITATION OUTCOME FOLLOWING ACUTE STROKE:
CONSIDERING IDEOMOTOR APRAXIA

Andy J. Wu
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Jeff Radel, PhD (Chairperson)

Winnie Dunn, PhD, OTR, FAOTA

Jianghua He, PhD

Susan Jackson, PhD, CCC-SLP

Catherine Siengsukon, PhD, PT

01/18/2013

Date Defended

The Dissertation Committee for Andy J. Wu certifies that this is the approved version of the following dissertation:

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Jeff Radel, PhD (Chairperson)

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Date Approved

Abstract

Stroke is a leading cause of death and the leading cause of adult disability in the United States affecting approximately 795,000 people yearly. Stroke sequelae often span multiple domains, including motor, cognitive, and sensory subsystems. Impairments can contribute to difficulty participating in activities of daily living (ADLs) and translate into disability – a concern for patients and occupational therapists alike. The role of ideomotor apraxia (IMA) in stroke rehabilitation is unclear. Thus, the purpose of these two studies is to investigate stroke rehabilitation outcome while considering the presence of ideomotor apraxia.

Stroke causes dysfunctional movement patterns arising from an array of potential etiologies. Agreement exists that understanding the patient's functioning serves as the basis for the rehabilitation process and it is insufficient for clinicians simply to determine functional movement problems without knowing how underlying impairments contribute. Stroke-induced paresis is a prevalent impairment and frequent target of traditional rehabilitation. Stroke rehabilitation often addresses paresis narrowly with little consideration for other stroke consequences. Ideomotor apraxia is one such disorder after stroke that could conceivably limit rehabilitation benefit of otherwise efficacious treatment interventions aimed at remediating paresis.

This led us to an initial study of a subject who experienced a single left, ischemic stroke with paresis of his right upper extremity and comorbid ideomotor apraxia. The subject participated in combined physical and mental practice for six consecutive weeks to improve use of his right arm. After intervention, the subject demonstrated clinically significant improvements in functional performance of his more-affected right upper extremity and reported greater self-perception of performance. The subject continued to demonstrate improvements after four weeks with no intervention and despite persistent IMA. This single case report highlights the

importance of recognizing that ideomotor apraxia does present after stroke, and traditional stroke rehabilitation efforts directed at paresis can be efficacious for subjects with IMA.

Traditional beliefs suggested that ideomotor apraxia does not translate to disability in everyday life and that IMA resolves spontaneously. Despite accumulating evidence of the influence of IMA on functional ability, this topic remains relatively neglected. It is unclear how ideomotor apraxia affects the rehabilitation process. The second study reports rehabilitation outcomes of a group of subjects following acute stroke. The Florida Apraxia Battery gesture-to-verbal command test was used to detect IMA in subjects. Level of independence with a set of ADLs and motor impairment of the more-affected upper extremity was documented at admission and discharge. Study subjects participated in standard of care stroke rehabilitation in the inpatient rehabilitation units. A total of fifteen subjects who sustained a left hemisphere stroke participated in this study – ten with IMA and five without IMA. After rehabilitation, subjects with IMA improved ADL independence and displayed decreased motor impairment of their right upper extremity. Subjects with and without IMA exhibited comparable improvements in ADL independence, but subjects with IMA exhibited less ADL independence upon when compared to subjects without IMA. Additional findings suggested that subjects with IMA were not different with respect to motor impairments and length of stay; however, additional studies with larger sample sizes are needed.

In summary, these two studies aid to elucidate the implications of ideomotor apraxia on traditional stroke rehabilitation efforts. Study subjects with ideomotor apraxia after acute stroke still derive benefit from traditional rehabilitation. Because traditional rehabilitation interventions narrowly target motor impairment, these findings support the need for considering IMA as a factor in developing interventions tailored to patients with IMA and possibly as a specific focus for interventions. A step toward addressing this need is to assess whether IMA is present after stroke on a regular basis. This work provides a framework for researchers and clinicians to investigate further how ideomotor apraxia translates into disability. These findings are important

since consideration of ideomotor apraxia could influence selection and design of rehabilitation interventions to optimize patient daily functioning after stroke.

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Table of Contents

Acceptance Page	ii
Abstract	iii
Acknowledgements	vi
Table of Contents	vii
Improved Function After Combined Physical and Mental Practice After Stroke: A Case of Hemiparesis and Apraxia	1
<i>Abstract</i>	2
<i>Introduction</i>	3
<i>Method</i>	5
<i>Results</i>	9
<i>Discussion</i>	10
<i>Table 1. AMAT Composite Scores Before and After Intervention</i>	15
<i>Table 2. COPM Scores Before and After Intervention</i>	16
Rehabilitation Outcome Following Acute Stroke: Considering Ideomotor Apraxia	17
<i>Abstract</i>	18
<i>Introduction</i>	19
<i>Methods</i>	22
<i>Results</i>	26
<i>Discussion</i>	27
<i>Conclusion</i>	33
<i>Table 1. Subject Demographic and Stroke Characteristics</i>	34
<i>Table 2. Within-Group Comparisons for Subjects with IMA for FIM™ and FMA Scores</i>	35
<i>Table 3. Between-Group Comparisons for FIM™, FMA scores and LOS</i>	36
Concluding Remarks	37
Appendix A: Comprehensive Literature Review I	42
Appendix B: Comprehensive Literature Review II	71
Appendix C: Comprehensive Literature Review III	94
Appendix D: Informed Consent Form	112

Appendix E: Screening Form	116
Appendix F: Functional Independence Measure	117
Appendix G: Fugl-Meyer Assessment	118
Appendix H: Florida Apraxia Battery gesture-to-verbal command subtest	120
Appendix I: Florida Apraxia Battery pantomime-to-photograph matching subtest	121
References	122

Improved Function After Combined Physical and Mental Practice After Stroke: A Case of Hemiparesis and Apraxia

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Abstract

This study describes change in functional performance and self-perception after participation in combined training with physical practice followed by mental practice. The subject was a 44-yr-old White man who experienced a single left ischemic stroke 7 mo before enrollment in the study. He engaged in physical and mental practice of two functional tasks: (1) reaching for and grasping a cup and (2) turning pages in a book with the more-affected arm. Practice took place 3 times per week during 60-min sessions for 6 consecutive wk. Primary outcome measures were the Arm Motor Ability Test (AMAT) and the Canadian Occupational Performance Measure (COPM). An abbreviated version of the Florida Apraxia Battery gesture-to-verbal command test approximated severity of ideomotor apraxia. After intervention, the subject demonstrated increased functional performance (AMAT) and self-perception of performance (COPM) despite persistent ideomotor apraxia. The results of this single-case report indicate functional benefit from traditional rehabilitation techniques despite comorbid, persisting ideomotor apraxia.

Key Words: activities of daily living, ideomotor apraxia, mental processes, paresis, stroke, task performance and analysis

Introduction

Stroke is the third most common cause of death and a leading cause of disability in the United States: It is estimated that 795,000 people experience new or recurrent stroke each year (Lloyd-Jones et al., 2009). Upper-extremity hemiparesis after stroke is a significant disabling consequence of stroke and the condition most commonly treated by occupational therapists (Radomski & Trombly, 2008), because it compromises the ability to perform valued activities of daily living (ADLs). Most studies to date have directed treatment efforts toward hemiparesis, with little consideration given to comorbid disorders that may influence potential rehabilitation benefit.

Ideomotor apraxia (IMA) is a common disorder after left hemisphere stroke, and it has implications for functioning in everyday life. It has been defined as a disorder of learned skilled movements that cannot be attributed to other common stroke deficits, such as primary motor or sensory impairments or language comprehension difficulties (De Renzi, 1989; Rothi & Heilman, 1997). Indirect evidence has suggested that IMA influences functioning in everyday life, as revealed in a positive association between severity of IMA and dependence in daily living skills (Bjørneby & Reinvang, 1985; Hanna-Pladdy, Heilman, & Foundas, 2003; Sundet, Finset, & Reinvang, 1988). Patients with IMA after left hemisphere stroke display spatial and temporal errors in movement trajectories that subsequently affect efficient manipulation of objects in the environment that is required for independence (Foundas et al., 1995; Hanna-Pladdy et al., 2003). Few studies, however, have examined rehabilitation of apraxia. Although studies have shown efficacy in the treatment of apraxia (Smania et al., 2006; Smania, Girardi, Domenicali, Lora, & Aglioti, 2000), most have used single-case designs (Butler, 2000; Maher, Rothi, & Greenwald, 1991; Pilgrim & Humphreys, 1994), and little evidence has indicated that treatment generalizes in the natural environment beyond the training paradigm. Systematic reviews of apraxia treatment have suggested that evidence is insufficient to support or refute treatment of apraxia and that development of treatment paradigms is in its infancy (Buxbaum et al., 2008;

West, Bowen, Hesketh, & Vail, 2008). Despite evidence of the influence of apraxia on daily functioning, few studies have considered the impact of apraxia on motor rehabilitation efforts.

Mental practice is a technique used to enhance physical performance in which a person rehearses a motor task cognitively, in the absence of physical movements. Early studies with healthy people have reported increases in strength (Shelton & Mahoney, 1978; Tynes & M., 1987), endurance (Lee, 1990), and precision and aim (Murphy & Woodfolk, 1987; Wrisberg & Anshel, 1989) when mental practice and physical practice are used in combination. Within the past decade, mental practice has been suggested for use in rehabilitative settings (Jackson, Lafleur, Malouin, Richards, & Doyon, 2001; Page, 2001; Sharma, Pomeroy, & Baron, 2006).

Research involving mental practice has focused on people with stroke, and several earlier studies have suggested that mental practice appears to reduce impairment and improve motor function in acute, subacute, and chronic stroke (Liu, Chan, Lee, & Hui-Chan, 2004b; Page, 2000; Page, Levine, & Leonard, 2005; Page, Levine, Sisto, & Johnston, 2001b). Case studies have noted specific improvements in functional grip and grasp tasks (Page, Levine, Sisto, & Johnston, 2001a), gait speed and range of motion of knee (Dickstein, Dunsky, & Marcovitz, 2004), and a foot-sequencing task (Jackson, Doyon, Richards, & Malouin, 2004). Consistent with these data, studies also reported increased affected arm use (Page et al., 2005) and function (Liu, Chan, Lee, & Hui-Chan, 2004a). Mental practice is most effective when combined with overt physical practice of tasks (Bachman, 1990; Gentili, Papaxanthis, & Pozzo, 2006; Sidaway & Trzaska, 2005; Yaguez et al., 1998). In fact, a randomized, placebo-controlled trial by Page, Levine, & Leonard (2007) concluded that the addition of mental practice to conventional motor therapy significantly decreased impairment and increased movement in the more-affected arm. Recent systematic reviews have also asserted that mental practice as an additional therapy may provide benefits for recovery after stroke (Braun, Beurskens, Borm, Schack, & Wade, 2006; Zimmermann-Schlatter, Schuster, Puhan, Siekierka, & Steurer, 2008).

The presence of IMA with hemiparesis could conceivably limit the rehabilitation benefit of otherwise efficacious treatment interventions. We evaluated whether combined physical and mental practice would increase functional performance and self-perception of performance in a patient with hemiparesis and concomitant IMA after stroke. This study is of particular interest to occupational therapists, because patients after stroke may present with comorbid disorders that exacerbate interference with the ability to live independently and to engage in meaningful occupation.

Method

Patient Selection

Inclusion/exclusion criteria were based on prior research (Page, Levine, & Hill, 2007; Page, Levine, & Leonard, 2007; Page et al., 2005). Potential candidates were screened from the University of Kansas Medical Center's stroke registry using the following inclusion criteria: (1) age 18 yr and <75 yr; (2) single stroke experienced >6 mo before enrollment; (3) ability to actively flex at least 10° from neutral at the more-affected wrist and the metacarpophalangeal and interphalangeal joints of two digits; (4) presence of apraxia as indicated with <70% on a revised abbreviated version of the Florida Apraxia battery gesture-to-verbal command task (Hanna-Pladdy, Heilman, & Foundas, 2001; Hanna-Pladdy et al., 2003); (5) absence of dementia, as indicated by a score of 24 on the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975). Exclusion criteria were (1) history of >1 stroke; (2) excessive pain in the more-affected arm, as defined by a score of 4 on a 10-point visual analog scale; (3) history of concurrent, unstable medical condition; and (4) current participation in any rehabilitation or drug studies.

Case Description

The patient was a 44-yr-old White man who experienced a single stroke 7 mo before enrollment. His past medical history is significant for a patent foramen ovale. On admission to a local hospital, a computed tomography scan revealed an acute ischemic infarct in the

distribution of the distal left middle cerebral and left anterior cerebral artery. He received approximately 30 days of inpatient rehabilitation (3 hr/day, 5 days/wk), including concurrent speech, physical, and occupational therapy. He is a right-handed, native English speaker with 14 yr of formal education. At the time of initial assessment, the patient reported problems with writing, math, and more hemiparesis in the right arm than in the right leg.

Instruments

The Arm Motor Ability Test (AMAT; (Kopp et al., 1997)) is a 13-item test that measures deficits in ADLs. The AMAT is a valid, stable, and reliable scale, and it correlates positively with other stroke-specific functional scales (Kopp et al., 1997). It rates ADLs according to a Functional Ability Scale (FAS; 0 = does not attempt to use more-affected arm; 1 = more-affected arm does not participate functionally, however attempt is made to use more-affected arm; 2 = more-affected arm is used for minor readjustments or as a helper/stabilizer in bilateral tasks; 3 = movement is influenced by synergy, performed very slowly, or with effort; 4 = movement is close to normal, but slightly slower; may lack precision and fluidity; 5 = movement appears normal or comparable to less-affected arm). AMAT tasks include ADLs such as use of a knife and fork, eating with a spoon, combing hair, and tying shoelaces. Time to complete each task is recorded to the nearest tenth of a second. Although FAS scores and time-to-complete tasks were obtained for each task, summed scores were used in our analysis.

The Canadian Occupational Performance Measure (COPM; (Carswell et al., 2004)) is a semistructured interview used to identify occupational performance problems. It is confirmed as being useful in helping to guide treatment. The COPM has been reported to be a valid, reliable, clinically useful, and responsive outcome measure for occupational therapists and researchers (Carswell et al., 2004). The assessment records the client's responses to questions in three main categories: self-care, productivity, and leisure. The client is then asked to rate the importance of each item on a scale ranging from 1 to 10 (1 = not important at all; 10 = extremely important). Once the top five activities are determined, each is rated according to perceived

performance (1 = not able to do it; 10 = able to do it extremely well) and satisfaction with performance (1 = not satisfied at all; 10 = completely satisfied). Performance and satisfaction scores are summed and divided by the number of problems identified (5), and this total score is used in the analysis. This subjective measure detects and tracks changes in the client's own perception of performance and satisfaction.

Similar to protocols in previous investigations, an abbreviated version of the Florida Apraxia battery gesture-to-verbal command task was used to assess the severity of IMA (Hanna-Pladdy et al., 2001, 2003). The patient used only the ipsilesional upper extremity during testing, so that motor impairment did not influence apraxia performance. The patient was asked to pantomime or gesture a set of 10 transitive tasks (e.g., "show me how to use a hammer to drive a nail into a wall"). Two trained judges scored responses on a severity scale ranging from 0 to 6 (0 = no response, unrecognizable, 1 to 2 = severely degraded, 3 = moderately degraded, 4 to 5 = mild impairment, 6 = perfect). The number of errors was considered in determining severity of IMA; lower scores indicated greater severity. Percentages were derived by subtracting the number of errors from the total possible, then dividing by the total possible.

Procedures

After obtaining informed consent, approved by the Institutional Review Board of the University of Kansas Medical Center, a research team member administered the AMAT and COPM (PRE). Postassessments occurred immediately after intervention (POST1) and again 4 wk after intervention ended (POST2). POST2 determined whether treatment benefit persisted in the absence of intervention. Intervention consisted of physical and mental practice of two specific tasks: reaching for and grasping a cup and turning pages in a book. Of the mental practice tasks previously studied (Page, Levine, & Hill, 2007; Page et al., 2005; Page et al., 2001a), these tasks were chosen because they are common activities, do not require use of the dominant hand, and involve different types of movements. The intervention took place 3 times

per week in 60-min sessions for 6 consecutive wk. The patient practiced (1) reaching and grasping a cup for the first 3 wk and (2) turning pages in a book for the remaining 3 wk.

Physical Practice

The first 30 min of each session involved physical practice of the task. The patient practiced tasks with his more-affected arm using actual objects (i.e., cups and books). During this time, we graded the task to appropriately challenge the patient (e.g., began by reaching for an empty cup, later moved to a cup half-full of water, and finally used a full cup). Interventions included obtaining and moving a cup to and from surfaces at various heights, transferring liquids from container to cup, and practicing larger activities encompassing the target task (e.g., preparing and drinking a cup of tea). Whole-task practice and part-task practice were incorporated into treatment. Part-task practice consisted of decomposing the target task into a sequence of smaller steps and focusing practice on the smaller steps that the patient found difficult. Rest periods were included as needed or as requested by the patient, particularly before beginning the mental practice.

Mental Practice

The second 30 min of each session consisted of mental practice corresponding to physical practice (i.e., mental practice of reaching for and grasping a cup after physical practice of the same task). Guided mental practice using audiotape for instructions was used, because this approach has been used in previous studies for people with stroke who exhibit hemiparesis or hemiplegia (Page, Levine, & Hill, 2007; Page, Levine, & Leonard, 2007; Page et al., 2005; Page et al., 2001a; Page et al., 2001b). Mental practice occurred in a quiet room; the patient was seated and listened to a 30-min mental practice audiotape. The initial 5-min segment of the tape encouraged a progressive relaxation of muscles as the patient imagined experiencing a relaxing environment (e.g., a warm beach). The next 20-min segment consisted of actual mental practice of the specific task practiced that day in therapy (i.e., mental practice of reaching for a cup after physically practicing reaching for a cup). The mental practice audiotape emphasized

both visual and kinesthetic information while guiding the patient through all steps necessary to perform the actual movement. The final 5-min segment allowed the patient to reorient to the surrounding environment. The patient was encouraged to listen to the mental practice audiotape in its entirety without disruption. The therapy session for that day concluded when the audiotape ended.

Results

During the course of the intervention, the patient complained of minor fatigue, increased frustration with more challenging tasks, and boredom. Regardless, the patient attended all treatment sessions, was agreeable to treatment suggestions, and reported actively engaging in each mental practice session. Comparison of AMAT and COPM scores before and after intervention was used to determine change in functional performance and self-perception of performance.

Before intervention, the patient exhibited decreased efficiency in performing ADLs, as evidenced by AMAT scores (Table 1). Scores from the COPM reflected lower perceived performance and satisfaction than the patient's performance on the AMAT indicated. The patient reported diminished performance in tasks such as clipping his nails, managing finances, and woodworking, along with difficulty with driving and with doing laundry (Table 2). In addition, low satisfaction scores with his current performance were recorded for all tasks identified in the COPM. The patient presented with moderate-to-severe IMA, which was determined by a gesture-to-verbal command score of 31 of 60 (51.67%).

After intervention, the patient demonstrated improvements in functional performance as measured by the AMAT, specifically with tasks involving reaching and bringing items toward the body such as the knife-and-fork task, eating a sandwich, eating with a spoon, drinking from a mug, combing hair, using the telephone, and wiping up spilled water. Composite AMAT data are presented in Table 1. The composite FAS component score of the AMAT before intervention was 79, compared with 95 at POST1.

The composite time taken to complete all AMAT tasks decreased. The patient required 302.9 s to complete all tasks before the intervention and 211.7 s after the intervention. Scores obtained 4 wk after completion of the intervention (POST2) are also notable, because the FAS score improved to 102 and the time required to complete all tasks decreased to 183.1 s. Self-perception of performance (COPM) scores reflected outcomes similar to those on the AMAT. The patient reported improved ability in clipping nails, managing finances, and participating in woodworking activities at POST1 (Table 2). Satisfaction scores associated with the performance of these tasks also increased. The changes continued to be evident at POST2, with slightly improved scores in some areas; however, the driving and laundry goals identified by the patient showed no change from PRE to POST1 or POST2.

Gesture-to-verbal command scores indicated the continued presence of IMA at all assessment time points. The percentages derived from scores were 51% at PRE to 60% at POST1 and 63.3% at POST2.

Discussion

The primary purpose of this single-case report was to examine change in functional performance of ADLs and self-perception of performance in someone with concurrent hemiparesis and IMA after stroke. After physical with mental practice, the patient showed increases in measures of functional performance and self-perception of performance, despite persistent IMA. We assessed apraxia severity by evaluating change in scores on the gesture-to-verbal command test, and the patient exhibited persistent IMA with scores clinically unchanged from PRE to POST1 and POST2. The observed changes in the AMAT revealed improvements in functional ability scores associated with decreased time needed to complete tasks at POST1 (Table 1). This patient demonstrated an improved ability to bring objects from lower surfaces to higher ones (i.e., tasks involving primarily elbow flexion with some shoulder flexion), perhaps because one of the training tasks involved practicing bringing a cup toward the mouth. Improved

fine motor abilities were also noted, as evaluated by AMAT tasks involving picking objects up from a table's surface.

Although an increase in FAS scores of the AMAT was observed, the patient exhibited decreased FAS scores in some tasks at POST1. A composite decrease in time was observed, even though the patient took longer to complete certain tasks. These findings are important, given the relationship between FAS and time, two components of the AMAT. The most desirable outcome in the present setting is to obtain a higher FAS score with decreased time (an inverse relationship). The possibility of a direct relationship (i.e., increased FAS with increased time or decreased FAS with decreased time), however, must be considered. In this study, the patient demonstrated a direct relationship of FAS and time on multiple occasions. As additional effort was exerted to achieve a higher FAS score, the time required to complete the task increased. This relationship was observed in 7 of 11 total tasks and may underlie some changes observed in FAS scores and time.

Examining the subcomponents of AMAT tasks did not reveal a consistent pattern or type of task that displayed this relationship. Moreover, most bilateral tasks exhibited this relationship, suggesting that perhaps bilateral integration during two-handed motor tasks plays a role in both quality and timing of such tasks. Despite variability among individual AMAT items, composite AMAT scores do identify an inverse relationship (an increase in FAS score associated with a decrease in time), supporting a therapeutic benefit for this intervention as described by these outcome measures.

COPM scores also improved from PRE to POST1. The patient reported a perceived increased ability to perform some activities, whereas others remained unchanged. Of the five activities listed in Table 2, three showed positive change in scores on both performance and satisfaction, because the patient was able to readily engage in those activities. The patient reported inadequate balance to carry laundry up and down a flight of stairs and, thus, chose not to participate in this activity. In addition, the patient required physician's approval to resume

driving; in this case, permission was not granted until a later date. Accordingly, COPM scores accurately reflected the patient's circumstances. The laundry and driving tasks, however, were not appropriate problems for gauging improvements from the intervention. Other changes in scores from the COPM are positive because the patient reported increased confidence and ability to perform the activities. Although increased self-perception of and satisfaction with performance are important, such perceptions should ideally be substantiated by a comparable increase in functional performance. The scores from the AMAT and COPM indicate that the patient experienced an increase in both functional performance and self-perception of performance.

Scores obtained at POST2 from the AMAT and COPM were compared with scores from POST1 to assess sustained changes in functional performance and self-perception of performance. The patient did not partake in any form of rehabilitation during the 4 wk between POST1 and POST2, including the treatment intervention described in this study. In the absence of the treatment intervention, the patient demonstrated improvements in scores obtained 4 wk after completion of the intervention phase of the study, suggesting that the patient continued to improve on the primary outcome measures.

The changes noted on AMAT scores are clinically relevant. Improvements revealed that the patient was more able to perform tasks at POST1 and POST2 than at PRE. In addition, the patient demonstrated increased efficiency with the tasks, as indicated by higher FAS scores associated with decreased time. Although the patient did not demonstrate clinically important changes between assessment time points on the COPM (designated as two or more points), a steady increase in scores is evident across time.

The effect of IMA on rehabilitation has been neglected, despite the fact that 30%–50% of patients with left hemisphere stroke display persistent IMA (De Renzi, Motti, & Nichelli, 1980; Donkervoort, Dekker, van den Ende, Stehmann-Saris, & Deelman, 2000; Kertesz & Ferro, 1984). In the current study, the patient exhibited persistent skilled movement deficits (i.e., IMA)

at all assessment points yet was able to demonstrate improvements in the AMAT and COPM. This finding accords with previous work suggesting that patients with IMA are able to benefit from traditional rehabilitation, although their improvement may not be comparable to that of patients without IMA (Unsal-Delialioglu, Kurt, Kaya, Culha, & Ozel, 2008). The results in Unsal-Delialioglu et al. (2008) should be carefully considered, however, because the study failed to define and control for type of rehabilitation intervention. The current study overcomes this limitation by using a specific rehabilitation intervention (i.e., physical with mental practice) to study whether a person can improve on functional measures after stroke despite persistent IMA.

Taken together, these findings are relevant, because therapists and clinical researchers must remember that IMA is indeed a persistent disorder after stroke. More important, the presence of IMA in addition to hemiparesis may reduce effectiveness of rehabilitation interventions deemed successful in people with hemiparesis alone. This patient's extent of apraxia did not hinder his ability to make clinically significant improvements on measures of functional performance and self-perception of performance after treatment consisting of physical with mental practice of tasks.

Limitations and Future Research

Our preliminary data support the concept that a patient may derive benefit from treatment of hemiparesis even if IMA persists. It is unclear, however, to what degree IMA influences rehabilitation potential and whether the patient in this study would have demonstrated greater gains without comorbid IMA. Further research is warranted to explore the potential efficacy of using mental practice (efficacious motor rehabilitation techniques) in light of comorbid IMA or other disorders that may directly affect functional motor performance.

Although the patient's improvements were marked, a single-case report prohibits inferences from results obtained for an individual. In addition, with this design, we cannot be certain that the patient would have made greater functional gains in the absence of IMA. A training effect could account for the improvements observed, limiting a clear attribution to the

intervention applied here. Future studies should ensure adequate ability to perform mental practice using appropriate measures. The same investigator performed all treatment and assessments, which contributes to potential bias of results. As suggested by Sunderland and Shinner (2007), IMA may be a hidden barrier to rehabilitation; therefore, future studies should include larger sample sizes with proper control groups (e.g., patients with either hemiparesis or IMA) to further examine the effects of IMA on rehabilitation benefit. Despite these shortcomings, the findings of this study represent an initial step toward considering treatment of patients with stroke presenting with multiple disorders that may affect their potential to benefit from rehabilitation efforts.

Table 1. AMAT Composite Scores Before and After Intervention

Component	PRE	POST1	POST2
Functional Ability Scale	79	95	102
Time to complete tasks, s	302.9	211.7	183.1

Note. PRE = before assessment; POST1 = immediately after intervention; POST2 = 4 wk after intervention ended; AMAT = Arm Motor Ability Test

Table 2. COPM Scores Before and After Intervention

Occupational Performance Problem	PRE		POST1		POST2	
	COPM-P	COPM-S	COPM-P	COPM-S	COPM-P	COPM-S
Clipping nails	1	1	5	5	7	7
Driving	1	1	1	1	1	1
Managing finances	4	1	5	2	6	2
Woodworking	4	1	5	1	7	2
Laundry	1	2	1	2	1	2
COPM-P	2.5		3.4		4.4	
COPM-S	1.2		2.2		2.8	

Note. PRE = before assessment; POST1 = immediately after intervention; POST2 = 4 wk after intervention ended; COPM-P = Canadian Occupational Performance Measure-Performance subscale; COPM-S = Canadian Occupational Performance Measure-Satisfaction subscale.

Rehabilitation Outcome Following Acute Stroke: Considering Ideomotor Apraxia

Abstract

Background: Stroke-induced hemiparesis commands much of the attention in rehabilitation, with little consideration offered to other stroke-related neurologic consequences that may influence movement performance. Ideomotor apraxia is one such sequela that involves learned skilled movements that has important implications for daily life functioning.

Objective: To investigate the presence of ideomotor apraxia and inpatient stroke rehabilitation outcome.

Methods: This pilot study compared two groups: subjects with and without ideomotor apraxia. All subjects were admitted to an inpatient rehabilitation unit and received standard of care. Clinical outcome measures were the Functional Independence Measure and the Fugl-Meyer Assessment, both administered upon admission and again at discharge.

Results: Fifteen subjects who sustained a left hemisphere stroke were included in this study, ten of whom had ideomotor apraxia. Subjects with ideomotor apraxia exhibited improvement from admission to discharge on both clinical outcome measures. Data analysis revealed significant differences between groups at admission with independence in activities of daily living, but groups did not differ with amount of change in clinical outcome measures. While not significant between groups, motor impairment scores and length of stay warrant additional studies.

Conclusions: Ideomotor apraxia is present after stroke, although assessment of apraxia is not routine. Presence of apraxia can have implications for the degree of ADL independence of patients after stroke. Rehabilitation professionals can anticipate less independence in patients with ideomotor apraxia upon admission. Additionally, these patients may experience reduced ADL independence even at discharge, at a level comparable to that of patients without ideomotor apraxia when they are admitted to the inpatient rehabilitation unit. Ideomotor apraxia as a factor in stroke rehabilitation and recovery deserves further attention.

Introduction

Stroke remains a leading cause of death and disability in the United States, affecting approximately 795,000 people yearly (Roger et al., 2012). Stroke sequelae span multiple domains, including motor, cognitive, and sensory subsystems that all may compromise performance of activities of daily living (ADLs) and quality of life (Duncan et al., 1997). Hence, stroke contributes significantly to long-term disability (CDC, 2001; Delaney & Potter, 1993), and addressing stroke sequelae effectively continues to be a concern for the field of rehabilitation as well as patients and caregivers.

Upper extremity hemiparesis is a common impairment following stroke with reports of nearly 70% of patients with some degree of paresis upon hospital admission (Nakayama, Jorgensen, Raaschou, & Olsen, 1994). Hemiparesis contributes to a vicious cycle of disuse after stroke, leading to central nervous system changes that may further decrease voluntary motor behavior (Gracies, 2005a). Expectedly, it is a frequent target of traditional rehabilitation efforts for these reasons (Gresham et al., 1995); little consideration, however, exists for other stroke sequelae that also may influence the nature or quality of overall movement performance (Goldenberg, Daumuller, & Hagmann, 2001; Goldenberg & Hagmann, 1998; Smania et al., 2000).

Ideomotor apraxia (IMA) is a stroke sequela that can have important implications for daily life functioning. IMA is a disorder of learned skilled movements not attributable to other common stroke deficits, such as primary motor impairments, sensory impairments, or language comprehension difficulties (De Renzi, 1989; De Renzi et al., 1980; Heilman, Maher, Greenwald, & Rothi, 1997). Hugo Liepmann's original concept of ideomotor apraxia was that patients with IMA retain an accurate 'movement formula' (i.e., spatio-temporal image of the action), but have difficulty with retrieval and translation of movement representations into motor innervations necessary for action (Goldenberg, 2003). Consequently, patients display specific spatial and temporal movement errors that interfere with efficient manipulation of objects (Foundas et al.,

1995; Hanna-Pladdy et al., 2003; McDonald, Tate, & Rigby, 1994; Poeck, 1986). More common after left hemisphere damage, ideomotor apraxia is often associated with lesions involving the left inferior parietal lobule (Buxbaum, 2001; Buxbaum, Johnson-Frey, & Bartlett-Williams, 2005; Haaland, Harrington, & Knight, 2000; Heilman, Rothi, & Valenstein, 1982). The parietal cortex appears to be critical to the praxis system, particularly in overlearned skilled motor behavior (Koski, Iacoboni, & Mazziotta, 2002). There are additional reports of IMA in patients with damage to the left middle frontal gyrus or parts of superior parietal lobe (Haaland et al., 2000; Heilman et al., 1982).

Estimates of the incidence of ideomotor apraxia after left hemisphere stroke range from 30% (Donkervoort, Dekker, & Deelman, 2006; Donkervoort et al., 2000) to 50% (Barbieri & De Renzi, 1988; Basso, Capitani, Della Sala, Laiacina, & Spinnler, 1987; Kaya, Unsal-Delialioglu, Kurt, Altinok, & Ozel, 2006). A lack of consensus exists regarding resolution of IMA, as some believe that IMA resolves spontaneously (Basso et al., 1987; Poeck, 1986), while more recent studies indicate the contrary (Donkervoort et al., 2006; Foundas, Raymer, Maher, Rothi, & Heilman, 1993; Poeck, 1986). Because IMA deficits are most noticeable in a testing environment, and particularly so when pantomiming use of objects (Goodglass & Kaplan, 1963), researchers and clinicians alike dismiss the impact of IMA on everyday life (De Renzi et al., 1980; Geschwind, 1965a, 1965b). While patient performance improves with actual objects and tools, kinematic analyses reveal that performance remains degraded (Poizner, Mack, Verfaellie, Rothi, & Heilman, 1990).

Recent evidence suggests that IMA does indeed influence function, with reports that greater IMA severity correlates with reduced independence in daily living skills (such as mealtime or dressing activities, and brushing teeth) (Bjørneby & Reinvang, 1985; Donkervoort et al., 2000; Hanna-Pladdy et al., 2003; Sundet et al., 1988; Walker, Sunderland, Sharma, & Walker, 2004) and reduced improvement in ADL functioning (Donkervoort et al., 2006). Despite accumulating evidence that the presence of IMA has a negative influence on daily functioning

(Foundas et al., 1995; Goldenberg & Hagmann, 1998; Hanna-Pladdy et al., 2003; Sunderland & Shinner, 2007) and more authors suggesting that rehabilitation programs consider the presence of apraxia in patients after stroke (Smania et al., 2000; van Heugten, Dekker, Deelman, Stehmann-Saris, & Kinebanian, 2000; van Heugten et al., 1998), the potential impact of IMA on stroke rehabilitation receives limited attention in many clinical settings.

Persons with ideomotor apraxia after stroke appear to benefit from traditional rehabilitation approaches (Donkervoort et al., 2006). Unsal-Delialioglu and colleagues (Unsal-Delialioglu et al., 2008) compared independence in ADLs, cognitive functions, and language in 26 subjects with IMA and 21 without IMA. The investigators found improvements in both subject groups at discharge, but they reported that the discharge scores of subjects with IMA failed to reach the scores at admission for subjects without IMA. Results confirm the suggestion by Kaya et al. (2006) that apraxia may present in persons with stroke demonstrating low Functional Independence Measure (FIM™) scores. In a single case report, Wu and colleagues (Wu, Radel, & Hanna-Pladdy, 2011) described one subject seven months post-stroke who participated in a physical and mental practice regimen involving two tasks: reaching for and grasping a cup and turning pages in a book. After six consecutive weeks of intervention (one hour three times per week), this subject exhibited improved performance on the Arm Motor Ability Test (Kopp et al., 1997) and self-perception of performance on the Canadian Occupational Performance Measure (Carswell et al., 2004) despite persistent IMA.

The purpose of the present pilot study was to explore rehabilitation outcome of patients during inpatient rehabilitation stay. Specifically, to investigate ADL independence and primary motor impairment of patients with ideomotor apraxia after first time left hemisphere stroke. While similar to the study conducted by Unsal-Delialioglu (2008) in examining functional outcomes, we assessed primary motor impairment, and our subjects were days rather than months post-onset of their stroke.

Methods

Study Subjects

Occupational therapists screened subjects via chart review, for this study at two urban hospitals using the following inclusion criteria: (1) age ≥ 18 years and ≤ 85 years, (2) first-time left hemisphere stroke confirmed by CT/MRI, and (3) admission to an inpatient rehabilitation facility. Exclusion criteria used to rule out potential underlying motor impairment that would confound a diagnosis of apraxia were: 1) prior history of other CNS disease, 2) bilateral CVA, 3) dementia, and 4) major head trauma. Prior to enrollment in the current study, all subjects provided informed consent. The study protocols and informed consent process were approved by the institutional review boards for the participating institutions prior to initiation of the study.

Between August 2011 and October 2012, research occupational therapists at two study sites screened a total of 50 patients diagnosed with stroke. We excluded 24 patients with right hemisphere stroke, five patients with history of bilateral stroke, two patients with history of brain tumor, and one patient refused to provide informed consent. Additionally, three subjects performed $< 70\%$ on the pantomime-to-photograph matching subtest and were not included in our final analyses.

Using inclusion/exclusion criteria 15 subjects were included in the final analyses and we identified 10 of 15 (66.67%) subjects with ideomotor apraxia using the FAB gesture-to-verbal command subtest. Groups at admission did not differ significantly on age or stroke period as indicated by separate Mann-Whitney U tests (age, $U = 15$, $z = -1.592$, $p = 0.129$; stroke period, $U = 18$, $z = -0.860$, $p = 0.440$). Subject characteristics are summarized in Table 1.

Study Design

This descriptive comparison study examined two groups: subjects with IMA and subjects without IMA. Apraxia testing occurred at admission and clinical outcome measures occurred at admission and discharge for all study subjects.

Clinical Outcome Measures

The Functional Independence Measure (FIM™; (Keith, Granger, Hamilton, & Sherwin, 1987) assesses independence with 18 ADLs in such areas as self-care, transfer, locomotion, communication, and social cognition. The FIM™ demonstrates excellent reliability and validity (Chau, Daler, Andre, & Patris, 1994; Dodds, Martin, Stolov, & Deyo, 1993; Hobart et al., 2001; Hsueh, Lin, Jeng, & Hsieh, 2002; Keith et al., 1987), and all evaluators in this study were certified by the Uniform Data System. Items are rated on a 7-point ordinal scale indicating level of assistance required (1 = *total assistance*; 2 = *maximum assistance*; 3 = *moderate assistance*; 4 = *minimal contact assistance*; 5 = *supervision or setup*; 6 = *modified independence*; 7 = *complete independence*). A score of 0 was assigned only if the activity did not occur (applicable to admission score only). Maximum total score was 126, with higher scores signifying greater ADL independence.

The Fugl-Meyer Assessment (FMA; (Fugl-Meyer, Jaasko, Leyman, Olsson, & Steglind, 1975) is a performance-based index recommended highly for clinical and research evaluation of motor impairment after stroke (Gladstone, Danells, & Black, 2002). The FMA demonstrates excellent test-retest reliability, interrater reliability, and construct validity (DeWeerdts & Harrison, 1985; Duncan, Propst, & Nelson, 1983; Fugl-Meyer, 1980; Gladstone et al., 2002; Sanford, Moreland, Swanson, Stratford, & Gowland, 1993; Wood-Dauphinee, Williams, & Shapiro, 1990). For the present study, we administered only the upper extremity motor subsection, which assessed voluntary movement, coordination, and reflex action of the subject's right shoulder, elbow, forearm, wrist, and hand. Performance on tasks was scored on a 3-point ordinal scale (0 = *cannot perform*; 1 = *performs partially*; 2 = *performs fully*), and the total score (maximum score = 66) was used in the analysis; higher scores indicate less motor impairment.

Apraxia testing

Similar to protocols used in previous investigations (Hanna-Pladdy et al., 2001, 2003; Rothi, Raymer, & Heilman, 1997; Wu et al., 2011), an abbreviated version of the Florida Apraxia

Battery (FAB) gesture-to-verbal command subtest was used to assess IMA (Rothi et al., 1992). Subjects used only the ipsilesional (left) upper extremity during testing so that primary motor impairment did not influence apraxia testing. Subjects were asked to pantomime a set of ten transitive (tool-use) tasks, and they were encouraged to demonstrate as if actually holding the tool. Two trained judges, not involved in administering the test, scored videotaped responses of each task. Each task could receive a maximum score of six (total max raw score = 60), and errors resulted in deductions of one point except for an uncorrected body part as tool error (-3) and no response or unrecognizable (-6). Number and type of errors determine IMA and errors originated from four main categories: content (perseverative, related, nonrelated); spatial (amplitude, internal and external configuration, body part as tool, movement); timing (sequencing, timing, occurrence); and other (no response, unrecognizable) (see Appendix H for detailed scoring (Rothi, Mack, Verfaellie, Brown, & Heilman, 1988; Rothi et al., 1997)). We used a predetermined cut-off score of 50%, based on previous reports (Rothi et al., 1997; Rothi et al., 1992) to categorized subjects with IMA ($\leq 50\%$) from those without IMA ($>50\%$). We did not include apraxia severity in our primary analyses.

A modified version of the pantomime-to-photograph matching subtest derived from the Florida Apraxia Battery-Extended and Revised Sydney (FABERS; (Power, Code, Croot, Sheard, & Gonzalez Rothi, 2010) was administered after the gesture-to-verbal command subtest to rule out comprehension deficits. We chose to use the same set of ten transitive pantomimes used in the gesture-to-verbal command subtest described above. Evaluators performed the pantomimes and asked subjects to point to the correct photograph of the tool. Responses were recorded as 0 = incorrect or 1 = correct. Subjects scoring 70% or higher were included in the final analyses.

Occupational therapists with at least three years of inpatient rehabilitation experience administered all assessments. Regular meetings and frequent review of testing procedures helped to ensure consistency among administrators. FIM™ and FMA data were collected within at least three days of admission to inpatient rehabilitation and again within three days before

discharge. Apraxia testing was administered at admission and videorecorded for later scoring. All therapists knew of the study's purpose, but they were unaware of apraxia categorization (IMA vs. no IMA) so as to avoid potential attention bias and possible influencing of daily rehabilitation interventions.

Inpatient Rehabilitation

The data collection sites were large urban hospitals with organized inpatient unit stroke care similar to that described by the Stroke Unit Trialists' Collaboration (Govan, Weir, & Langhorne, 2008). Board-certified physical medicine and rehabilitation physicians directed all patient care including coordinating a multidisciplinary team comprised of medicine, nursing, social work, occupational, physical, and speech therapies. Patients admitted to an inpatient rehabilitation facility receive at minimum three hours a day of a combination of occupational, physical, and speech-language therapy five of seven days per week. Study subjects differed only from other patients with respect to completing periodic assessments described above, otherwise receiving standard of care. Rehabilitation therapists established intervention plans individualized according to patient presentation and included ADL retraining, therapeutic activities/exercises, neuromuscular reeducation, mobility/gait training, speech-language, and cognitive retraining. Team meetings occurred weekly to review patient progress, to establish a prognosis, and to plan for discharge.

Statistical Analyses

All statistical analyses were performed using IBM SPSS Statistics v. 20.0*. Level of significance for all statistical analyses was set *a priori* as $\alpha = 0.05$. Subject demographic information was summarized using descriptive statistics, including means, standard deviations, and frequencies as percentages.

Initially, scatterplots and histogram distributions assessed the preliminary data to identify trends and potential violations of the assumption of normality. Non-parametric statistics were

* SPSS, Armonk, NY: IBM Corp.

chosen for use due to small sample size and lack of normality in data from clinical outcome measures. Mann-Whitney U tests compared clinical outcome measures at admission, change scores, and length of stay between groups. Additional post hoc analyses were conducted on subsections of the FIM™. Wilcoxon signed-rank tests compared within-group differences on clinical outcome measures to establish whether subjects with IMA demonstrated improvement after rehabilitation.

Results

The inter-rater reliability for the raters on five gesture-to-verbal command subtest scores was Kappa = 0.809 with $p < 0.001$ indicating substantial agreement between raters (Landis & Koch, 1977). Subjects with IMA improved from admission to discharge on clinical outcome measures (Table 2). Wilcoxon signed-rank tests indicated statistically significant improvement in ADL independence ($z = -2.805$, $p = 0.005$) and in right upper extremity motor impairment ($z = -2.207$, $p = 0.027$). Mean FIM™ scores of subjects with IMA improved from 33.50 ± 19.67 at admission to 67.10 ± 21.90 at discharge. Mean FMA scores of subjects with IMA also improved from 14.10 ± 18.48 at admission to 23.40 ± 22.55 at discharge.

Table 3 displays comparisons between groups for clinical outcome measures and length of stay. Mann-Whitney U tests were used to evaluate scores between subjects with and without IMA on admission FIM™ and FMA scores, the amount of change on the FIM™ and FMA from admission to discharge, and length of stay. We found significant between-group mean admission FIM™ scores ($U = 6$, $z = -2.329$, $p = 0.019$). Subjects with IMA exhibited lower mean admission FIM™ scores of 33.50 ± 19.67 compared to subjects without IMA scoring 62.80 ± 13.95 . On admission, subjects with IMA scored significantly lower than subjects without IMA on the FIM™ cognitive subtotal score ($U = 2.5$, $z = -2.776$, $p = 0.003$), mean 9.5 ± 6.13 vs. mean 24 ± 5.05 . On admission, subjects with and without IMA did not differ in terms of their FIM™ motor subtotal score ($U = 12$, $z = -1.595$, $p = 0.129$), mean 24 ± 15.62 vs. 38.8 ± 17.2 . Between-

group FMA comparisons did not differ significantly at admission ($U = 14$, $z = -1.353$, $p = 0.206$). The mean admission FMA score of subjects with IMA was 14.10 ± 18.48 compared to 32.80 ± 28.89 for subjects without IMA.

Comparing the amount of change in clinical outcome measures between groups resulted in no statistical differences on either the FIM™ ($U = 22.5$, $z = -0.308$, $p = 0.768$) or the FMA ($U = 21.5$, $z = -0.437$, $p = 0.679$). Mean changes for subjects with IMA on the FIM™ (33.60 ± 16.99) and the FMA (9.30 ± 13.99) were similar to mean changes for subjects without IMA on the FIM™ (33.00 ± 9.38) and the FMA (12.20 ± 16.80). Although there was no between-group difference in mean FIM™ change, mean discharge FIM™ scores between groups remained different, statistically. We observed the mean discharge FIM™ score of subjects with IMA (67.10 ± 21.90) to be similar to the mean admission FIM™ score of subjects without IMA (62.80 ± 13.95) ($U = 20.5$, $z = -0.552$; $p = 0.581$). There was also no statistically significant difference in mean length of stay between subjects with IMA (24.40 ± 14.26) and subjects without IMA (18.40 ± 8.59) ($U = 18.5$, $z = -0.675$, $p = 0.513$).

In addition, we also reviewed discharge plans for study subjects. Of ten subjects with IMA, five (50%) were discharged to home, four (40%) to a skilled nursing unit, and one (10%) returned to the acute care setting due to medical complications. Nearly all subjects without IMA were discharged to home (4 of 5; 80%), and only one (20%) was discharged to a skilled nursing unit. These differences appear quite pronounced but may also be associated with discharge FIM™ score, rather than simply presence of IMA, since the mean discharge FIM™ score of subjects with IMA were lower (67.10 ± 21.90) compared to the mean discharge FIM™ score of subjects without IMA (95.80 ± 10.38) ($U = 7$, $z = -2.208$, $p = 0.028$).

Discussion

The present pilot study considered the presence of ideomotor apraxia when comparing inpatient rehabilitation outcomes for a group of subjects following initial left hemisphere stroke. Subjects with IMA exhibited greater ADL independence at the end of their inpatient rehabilitation

compared to their admission ADL independence, with mean FIM™ improvement of 33.60 ± 16.99 . This finding is not surprising, since the intensity of rehabilitation services provided in acute inpatient rehabilitation results in more favorable functional outcomes (Ozdemir, Birtane, Tabatabaei, Kokino, & Ekuklu, 2001) and consequently, more patients are likely to be alive, independent, and living at home after one year (Govan et al., 2008). Also, as upper extremity hemiparesis is a commonly-treated condition and a frequent target of traditional stroke rehabilitation efforts (Gresham et al., 1995), subjects with IMA displayed less motor impairment at discharge compared to admission, with a mean FMA change score of 9.30 ± 13.99 .

To address other study objectives, we categorized subjects into two groups (with and without IMA) with two-thirds of our sample identified with ideomotor apraxia. This is higher compared to other studies reporting that approximately half of patients display IMA after left hemisphere stroke (Barbieri & De Renzi, 1988; Basso et al., 1987; Kaya et al., 2006) and likely is attributable to our small sample size. Analyzing between-group data yielded mixed results supporting differences between groups only for admission FIM™. Specifically, we observed subjects with IMA admitted to inpatient rehabilitation exhibiting less ADL independence compared to subjects without IMA, scoring approximately 30 points less on average on the FIM™, an amount considered clinically significant (Beninato et al., 2006). Subjects with IMA still exhibited nearly the same amount of difference in ADL independence at discharge compared to subjects without IMA. The additional analysis of FIM™ subsections revealing lower mean cognitive subtotal score between groups confirms the suggestion that subjects with IMA present with more impairments in other domains (Buxbaum et al., 2008).

Interestingly, the observed mean discharge FIM™ score of subjects with IMA was 67.10 ± 21.90 , which was similar to mean admission FIM™ score of subjects without IMA, 62.80 ± 13.95). Although subjects with IMA in the present study improved while in the inpatient rehabilitation unit, this similarity seems to suggest that they are discharged displaying a level of ADL independence similar to those subjects without IMA when they enter inpatient

rehabilitation. This finding resonates with a recent study reporting discharge FIM™ scores of patients with IMA failing to reach admission FIM™ score of patients without IMA (Unsal-Delialioglu et al., 2008). Moreover, Kaya et al. (2006) suggests that apraxia may be present in patients demonstrating low FIM™ scores, a result we observed in the present study and similarly in a study by the same group (Unsal-Delialioglu et al., 2008). While Unsal-Delialioglu and colleagues (2008) studied subjects within approximately 90 days of inpatient rehabilitation admission, the present study included subjects within approximately 8 days of stroke; results of both studies appear congruent and indicate a disparity in ADL independence between subjects with and without IMA. Studies of patients six months post-onset of stroke revealed similar findings; patients with IMA required more assistance with ADLs (Sundet et al., 1988). We believe the results from the present study lend additional support to there being differences in ADL independence in individuals with IMA after stroke.

Variability in our sample appears quite high for both clinical outcome measures, which should be taken into account when interpreting the results. We examined an alternative grouping of subjects based on gesture-to-verbal-command subtest scores using the following categories: 0 to 0.35 as severe, 0.36 to 0.54 as moderate, and 0.55 to 1.0 as mild (no study subject scored 1.0). Categorizing subjects using this scheme was not helpful in explaining the high variability in scores for either clinical outcome measure. In addition to analyzing motor and cognitive subtotal scores on the FIM™, we also further divided items on the FIM™ into the following categories: self-care, sphincter control, transfers, locomotion, communication, and social cognition. Upon close visual examination of these FIM™ subsection scores, we did not find any particular subsection to contribute more heavily to the overall observed FIM™ change. Despite variability, subjects with IMA in our study demonstrated mean FIM™ improvement greater than established criteria of minimally clinically important difference (MCID) (FIM™ total score of 22 points (Beninato et al., 2006)) and we also observed this MCID between groups for mean admission FIM™ scores (33.50 + 19.67 vs. 62.80 + 13.95).

Motor impairment findings appear to follow a similar pattern as FIM™ scores. Admission motor impairment findings between groups were not statistically significant, likely due to the small sample size of the present study and lack of statistical power to detect differences (computed achieved power $(1 - \beta) = 0.343$) (GPower 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007)). However, mean admission FMA score of subjects with IMA appeared lower than the mean admission FMA score of subjects without IMA, which is supported when considering the MCID (FMA upper extremity portion of 10-point difference) (Shelton, Volpe, & Reding, 2001), observed between groups means, 14.10 + 18.48 vs. mean 32.80 + 28.89. Additionally, while mean FMA change score of subjects with IMA does not quite reach the established MCID, it does meet minimal detectable change (5.2 for FMA upper extremity portion) (Wagner, Rhodes, & Patten, 2008) which represents true FMA change (accounting for error) from admission to discharge. Despite the small sample size and variability, it appears that our results are in keeping with previous studies demonstrating improved ADL independence (Unsal-Delialioğlu et al., 2008) and increased more-affected upper extremity function (Wu et al., 2011) despite IMA; however, further investigation is necessary.

No differences between subjects with and without IMA in terms of amounts of change in either clinical outcome measure (discharge score – admission score) were apparent in our sample. Subjects with IMA demonstrated equivalent amounts of improvement in ADL independence and motor impairment compared to subjects without IMA. In contrast, previous studies have reported less improvement in ADL functioning with more severe apraxia, suggesting apraxia's adverse influence on ADL recovery (Donkervoort et al., 2006). Perhaps the similarities we observed in the amount of change in FIM™ and FMA scores reflect that the scoring method used in the present study to classify subjects with and without IMA did not take into account IMA severity, which limits interpretation.

Length of stay was also not statistically different between groups, but subjects with IMA stayed 24.40 + 13.48 days compared to subjects without IMA 18.40 + 8.59. This is potentially an

important finding particularly when considering we observed no differences in change scores on clinical outcome measures between groups. Thus, subjects with IMA may require a longer stay in the inpatient rehabilitation unit to achieve an equal amount of improvement. Additional studies should further explore length of stay as an important factor in discharge planning for subjects with IMA.

Related to tracking length of stay, we also reviewed documented discharge plans. A recent retrospective study of a large national database revealed admission FIM™ score to be a strong predictor of discharge placement; specifically, patients with admission FIM™ scores below 60 are nearly six times more likely unable to return home following inpatient rehabilitation stay (Pohl, Billinger, Lentz, & Gajewski, 2012). Our small study sample corresponds similarly with only 50% of subjects with IMA discharged home – a sample demonstrating a mean admission FIM™ score of 33.50 ± 19.67 . Comparatively, a higher percentage (80%) of subjects without IMA discharged to home exhibited a mean admission FIM™ score of $62.80 + 13.95$. Discharge FIM™ data are also aligned with suggestions from Pohl (2012) as subjects without IMA demonstrated greater ADL independence (mean = $95.80 + 10.38$), justifying return to home. Moreover, the admission FIM™ score is closely linked to the discharge FIM™ score (Alexander, 1994; Lin, Hsieh, Lo, Hsiao, & Huang, 2003; Ween, Alexander, D'Esposito, & Roberts, 1996). Although likely a function of FIM™ scores as several authors indicate (Alexander, 1994; Pohl et al., 2012; Ween et al., 1996), presence of IMA also seems to be associated with discharge outcome. Additional studies are necessary to explore this relation further.

Clinical Relevance

Findings of this study have considerable clinical relevance. Occupational therapists should recognize ideomotor apraxia as a disorder commonly present after stroke. Patients with IMA may display lower ADL independence at admission and, even with intense rehabilitation, may not reach a level of ADL independence comparable to the admission status of patients

without IMA. Occupational therapists should also routinely screen for ideomotor apraxia instead of assigning a diagnosis of apraxia as an explanation for poor ADL performance when no other evident causal factor exists (Bolduc & Lawrence, 2011). We videorecorded performance on gesture-to-verbal command tasks, which is considered the gold standard in assessing the presence of apraxia (Rothi et al., 1997); however, reliable and consistent videorecording of patients' performance is impractical in a clinical setting. Additionally, ensuring accurate scoring can be a time-intensive endeavor that conflicts with productivity requirements demanded of clinicians. Therefore, clinicians may want to consider using a newly-developed test for apraxia requiring less time and effort but still yielding valid and reliable results at bedside (Vanbellinggen et al., 2011).

Limitations

These findings must be interpreted with caution, as our sample size was relatively small ($n = 15$) with unequal groups. Furthermore, our data demonstrate considerable variability in clinical outcome measures. We expect to overcome these limitations by enrolling additional subjects. While all study subjects received standard of care treatment in the present study, it is possible that treatment intervention varied since therapists base treatment plans on patient presentation. Future studies would benefit by examining interventions (i.e., type and duration) between groups. Factors other than the presence of IMA could also be accounting for the between-group difference in FIM™ admission scores.. Including additional assessments and patient characteristics (e.g., co-morbid medical conditions, relevant past medical history, etc.) will certainly enhance our understanding of the relation between IMA and rehabilitation outcome after stroke.

Also, it was challenging to use a pre-determined cutoff score to categorize subjects with and without ideomotor apraxia, particularly when subject performance was near the cutoff threshold. The scoring method we used in the present study did not take into account apraxia severity. The test for upper limb apraxia (TULIA) (Vanbellinggen et al., 2010) and the associated

apraxia screen of TULIA (AST) (Vanbellingen et al., 2011) are viable measures able to assign a severity rating, but they were unavailable at the time of initial data collection and considerable information can still be lost when categorizing a continuous variable (apraxia score).

Conclusion

The findings of this pilot study reiterate the importance of considering ideomotor apraxia and its particular relevance to rehabilitation outcome of patients after stroke. Subjects with IMA in the present study exhibited lower admission ADL independence than subjects without IMA. While subjects with and without IMA demonstrated a comparable amount of change in ADL independence during rehabilitation, subjects with IMA display at discharge appear to display similar ADL independence at discharge compared to subjects without IMA upon admission. Preliminary results from this pilot study are encouraging and warrant additional studies to investigate further rehabilitation outcome and ideomotor apraxia after acute stroke.

Table 1. Subject Demographic and Stroke Characteristics

Subject	Age (yrs)	Sex	APR score	Stroke type	Stroke period (days)	Lesion site
No IMA group						
1	56	F	0.58	Ischemic	6	Po
2	60	F	0.70	Ischemic	9	IC
3	43	M	0.93	Ischemic	6	F-T, BG
4	42	F	0.87	Unknown	5	MCA
5	59	F	0.78	Ischemic	1	MCA
Means (SD)	52 (8.80)				5.4 (2.88)	
IMA group						
1	64	M	0.47	Ischemic	8	Po
2	68	F	0.47	Ischemic	8	BG
3	79	M	0.35	Ischemic	9	MCA
4	63	M	0.45	Ischemic	2	PCA
5	70	M	0	Ischemic	20	IC
6	63	M	0	Hemorrhagic	7	MCA
7	50	M	0	Ischemic	5	F-P
8	66	M	0.50	Ischemic	12	Po
9	61	M	0.45	Ischemic	14	MCA
10	76	M	0.27	Ischemic	12	F
Means (SD)	66 (8.11)				9.7 (5.06)	

Note. APR score = score from gesture-to-verbal command test derived using the formula: number correct/number possible; cutoff score ≤ 0.50 ; stroke period = time from stroke to admission to inpatient rehabilitation unit

Po = pons; IC = internal capsule; BG = basal ganglia; MCA = middle cerebral artery; PCA = posterior cerebral artery; F = frontal; P = parietal; T = temporal; O = occipital

Table 2. Within-Group Comparisons for Subjects with IMA for FIM™ and FMA Scores

Variable	Admission	Discharge	p [†]
FIM™	33.50 ± 19.67	67.10 ± 21.90	0.005*
FMA	14.10 ± 18.48	23.40 ± 22.55	0.027*

Note. Values are mean ± standard deviation; FIM™ – Functional Independence Measure; FMA – Fugl Meyer Assessment (upper extremity portion only; max = 66)

* Denotes statistical significance $p < 0.05$

† p values from Wilcoxon's signed-rank test

Table 3. Between-Group Comparisons for FIM™, FMA scores and LOS

Variable	IMA (n = 10)	No IMA (n = 5)	p [†]
FIM™			
Admission	33.50 ± 19.67	62.80 ± 13.95	0.019*
Discharge	67.10 ± 21.90	95.80 ± 10.38	
Δ	33.60 ± 16.99	33.00 ± 9.38	0.768
FMA			
Admission	14.10 ± 18.48	32.80 ± 28.89	0.206
Discharge	23.40 ± 22.55	45.00 ± 23.17	
Δ	9.30 ± 13.99	12.20 ± 16.80	0.679
LOS in days	24.40 ± 13.48	18.40 ± 8.59	0.440

Note. Values are mean ± standard deviation; FIM™ – Functional Independence Measure; FMA – Fugl Meyer Assessment (upper extremity portion only; max = 66); LOS – length of stay

* Denotes statistical significance $p < 0.05$

[†] p values from Mann-Whitney U Tests

Concluding Remarks

These studies extend prior knowledge and address the paucity of research examining ideomotor apraxia and function. Specifically, they represent additional investigation of ideomotor apraxia as the disorder relates to rehabilitation outcome after stroke. The findings demonstrate presence of IMA associated with less independence in activities of daily living. These findings are important for recognizing the significant implications for stroke rehabilitation that may improve daily functioning in individuals after stroke.

Rarely do occupational therapists assess for ideomotor apraxia in current practice, even though apraxic disorders demonstrate considerable influence on independent daily functioning (Buxbaum et al., 2008; Hanna-Pladdy et al., 2003; Sunderland & Shinner, 2007). Rather, a diagnosis of apraxia results when no other explanation for the functional limitations exists (Bolduc & Lawrence, 2011). These studies represent initial steps in considering ideomotor apraxia after stroke by integrating assessment of IMA during the various stages of stroke. We videorecorded apraxia performance, which is considered to be the gold standard for accurate scoring at a later time (Rothi et al., 1997). However, reliable and consistent reviewing of apraxia performance and ensuring accurate scoring can be a time-intensive endeavor in a clinical setting. Thus, clinicians should consider using a screening tool at bedside that offers valid and reliable assessment of ideomotor apraxia (Vanbellingen et al., 2011).

Knowledge concerning ideomotor apraxia suffers greatly from the absence of a standardized means of assessment, contributing to relatively little progress in our understanding of this disorder. This partly is due to a lack of consensus regarding what constitutes ideomotor apraxia and to a poor understanding of this disorder. Our apraxia testing protocol utilized a pre-determined cutoff score to classify subjects with or without IMA. This method is especially problematic when subject performance was near the cutoff threshold, which does not allow for interpretation of varying levels of apraxia severity. The complexity of apraxia testing involves

assessment of various processing routes to elicit gestures (Dovern, Fink, & Weiss, 2012), with subject performance most severely degraded when asked to pantomime (Goodglass & Kaplan, 1963) with greater difficulty pantomiming transitive movement compared to intransitive and meaningless gestures (Leiguarda & Marsden, 2000). The apraxia testing used in our studies did not assess performance of intransitive (i.e. salute, hitchhike), meaningless gestures, or use of real objects, as suggested by a recent review of diagnosis and treatment of upper limb apraxia (Dovern et al., 2012). The test for upper limb apraxia (TULIA) (Vanbellingen et al., 2010) and the associated apraxia screen of TULIA (AST) (Vanbellingen et al., 2011) are viable measures recommended by Dovern and colleagues (2012) that overcome some of the noted limitations, but they were unavailable at the time of initial data collection.

There is a need to test for ideomotor apraxia particularly during the acute stage of stroke in order to identify patients with IMA early. It is crucial that thorough consideration be given to the array of factors influencing performance when assessing patients after stroke. Our second study is similar to a previous study by Unsal-Delialioglu and colleagues (2008) of patients with and without IMA after three months of initial infarct. The present study included subjects within one week of stroke and also studied motor impairment as an outcome measure following stroke rehabilitation.

Our second study showed that, on average, subjects with IMA were discharged from inpatient rehabilitation at a similar level of independence in ADLs as subjects without IMA when they entered the inpatient rehabilitation. Therefore, early identification of patients with IMA could at least allow for early planning of caregiver training and discharge to occur in anticipation of lower ADL independence at discharge. Our study sample exhibited significant variability on clinical outcome measures at admission and discharge, limiting more definite conclusions regarding IMA and differences found between groups.

Contrary to the belief that IMA resolves spontaneously are more recent studies reporting IMA to be a persistent disorder (Donkervoort et al., 2006; Foundas et al., 1993; Manuel et al.,

2012; Poeck, 1986). Indeed, we confirmed the presence of IMA with our single subject in the initial study upon enrollment (seven months after stroke), through the six-week intervention, and four weeks after study completion. We also suspect the sample in our second study continued to experience persistent IMA even after discharge from inpatient rehabilitation and verified presence of apraxia in a small sample of our subjects. Since the literature on rehabilitation for IMA is limited, we suggest that patients with IMA should perhaps remain longer in rehabilitation to achieve greater ADL independence for discharge to home. This may help to alleviate the burden of care experienced by caregivers.

Since IMA manifests bilaterally (Goldenberg, 2009; Leiguarda, 2001), addressing only the more-affected upper extremity with paresis related to ADLs is inadequate. Many daily activities involve use of both upper extremities to perform efficiently (e.g., dressing, bathing, carrying objects, etc). While paresis is a prevalent impairment and a frequent target of traditional rehabilitation efforts (Gresham et al., 1995), numerous reports suggest significant continued paresis despite the patients receiving therapeutic interventions targeted at paresis specifically (Gowland, deBruin, Basmajian, Plews, & Burcea, 1992; Gresham et al., 1975; Mayo et al., 1999). Patients demonstrating minimal residual paresis are likely able to perform and accomplish tasks with relative greater ease, particularly bilateral tasks. Patients with extensive residual paresis after stroke, reflective of subjects with IMA in the present study, therefore must often rely on the less-affected upper extremity to perform daily activities. Since Liepmann in 1905, studies continue to demonstrate the dominance of the left hemisphere in praxis function (Basso, Luzzatti, & Spinnler, 1980; De Renzi, Faglioni, & Sorgato, 1982; De Renzi et al., 1980; Kertesz & Ferro, 1984), including imaging studies (Haaland, 2006; Haaland et al., 2000). Left dorsal premotor and parietal areas are activated in the selection of movement characteristics necessary for skilled performance of either hand (Haaland, Elsinger, Mayer, Durgerian, & Rao, 2004). Accordingly, IMA deficits are apparent in the ipsilateral arm, a finding confirmed by the apraxia testing procedure we implemented in our studies. Combined with unresolved paresis in

the contralateral arm, patients with IMA therefore may experience additional difficulty with performing valued activities (Goldenberg & Hagmann, 1998; Walker et al., 2004), which contributes to decreased independence and potential greater disability.

Related to IMA being persistent is that IMA deficits also translate into difficulty with performance in a natural environment. A natural environment assumes use of actual tools and objects, yet patient performance remains degraded (Poizner et al., 1990). Proper object use requires accurate spatial and temporal representations of movement characteristics, and IMA errors represent difficulty with retrieval of these motor engrams (Rothi et al., 1997). The consequences of IMA intersect with real-life performance, and people with IMA appear clumsy and less-adept with handling objects, which can negatively influence performance and promote further disability. While self-care activities (ADLs) are commonly the focus of inpatient rehabilitation, practice of these tasks does not adequately prepare the patient to function within his/her natural environment. Patients discharged home will undoubtedly experience difficulty and additional challenges as they perform activities not practiced in rehabilitation, especially involving tools or objects.

Understanding the influence of ideomotor apraxia on a patient's potential for achieving independence necessitates design of effective rehabilitation interventions. Although the second study demonstrated that subjects with IMA also derived benefit from traditional rehabilitation that was on an order comparable to subjects without IMA, application of best practice principles suggests this status quo simply is not sufficient. Rehabilitation professionals should consider interventions and approaches to support patients with persistent IMA so they reach levels of function comparable to patients without IMA. Furthermore, there is a pressing need for treatment paradigms to address IMA.

Mental practice is a promising therapeutic intervention strategy that has demonstrated increased affected arm use and function for patients in the acute, sub-acute, and chronic stages of stroke (Liu et al., 2004b; Page, 2000; Page et al., 2005; Page et al., 2001b). Our initial single-

subject study applied a combined physical and mental practice training program for a patient demonstrating concurrent paresis and IMA (Wu et al., 2011). While it was not the intent to treat IMA, this subject exhibited improved more-affected upper extremity performance and self-perception of performance that persisted even four weeks after treatment ended. Mental practice is most effective when combined with overt physical practice of the same tasks (Bachman, 1990; Gentili et al., 2006; Sidaway & Trzaska, 2005; Yaguez et al., 1998). A study by Decety and colleagues (1996) reveals similar brain areas activated during imagined movement as during actual movement. More recent neuroimaging studies also demonstrate similar findings of neural structures subserving both actual and imagined movements (Lacourse, Turner, Randolph-Orr, Schandler, & Cohen, 2004; Lafleur et al., 2002; Mellet, Petit, Mazoyer, Denis, & Tzourio, 1998). While studies demonstrate individuals with lesions to left parietal cortex displaying difficulty with motor imagery, particularly with timing (Buxbaum et al., 2005; Sirigu et al., 1996), studies to date have not examined mental practice of more complex movements in well-designed randomized trials. Taken together, mental practice therefore could conceivably represent a unique technique to address IMA deficits with the added benefit of also remediating paresis. Although rehabilitation of IMA is in its infancy, the design of innovative treatment paradigms to address the complex disorder will ultimately affect the future of stroke rehabilitation.

This work has added new information to the existing literature related to ideomotor apraxia after stroke and the relation of IMA to rehabilitation outcome after stroke. Moreover, it represents a potential shift in stroke rehabilitation by supporting consideration of IMA during assessments after stroke and during the resulting rehabilitation interventions. Although this work has provided a foundation and increased our understanding of ideomotor apraxia in acute stroke, it is clear that future studies are necessary to elucidate further the implications for patient care.

Appendix A: Comprehensive Literature Review I

From Thought to Action: Neural Structures Underlying the Brain's Ability to Plan and Execute Goal-directed Movements

This work was approved June, 2010.

Introduction

Movement is a fundamental ability that allows us to interact with our environment in a meaningful manner. Successful interaction, though, entails that various parts of the central nervous system function in synchrony. Particularly remarkable is the apparent ease with which the brain coordinates movements in ever-changing, context-specific situations. Even more astonishing is the diverse range of movements the brain is capable of programming and carrying out. Effortless movements we perform routinely mask the impressive and intricate design of the human brain. It is important to recognize not only what neural structures are involved, but also to understand the complex neural interactions that facilitate goal-directed movement. This paper will address how motor plans are developed and refined and how multimodal sensory information contributes to goal-directed movements. Identifying and describing neural mechanisms of motor control will lead to enhanced comprehension of the brain's ability to plan and execute goal-directed movements. This perspective will provide a better foundation for being able to observe and understand neurological movement disorders as they occur in people interacting in everyday life.

The neural structures responsible for motor programming and execution have been traditionally classified as being cortical or subcortical, with cortical structures taking on the roles of planning and executing of motor plans. Subcortical structures have generally been assumed to inform, influence, and even correct movement indirectly. A brief review, in light of new evidence, will be provided in order to further elucidate specific structures and functions of the primary motor cortex (M1), premotor cortex (PMC), supplementary motor complex (SMC), posterior parietal cortex (PPC), prefrontal cortex (PFC), basal ganglia (BG), and cerebellum as they relate to goal-directed movement.

Cortical structures

Our understanding of the human brain would not be possible without at least an acknowledgment of studies undertaken with non-human primates, specifically macaque

monkeys. This population allows for manipulation of various parts of the brain otherwise unethical in humans. Lesion studies are particularly informative because of the ability to isolate damage to a discrete area of the brain. This method then allows for relatively accurate comparison of lesions compared to intact brains free of neurological damage. While useful, extrapolating results from non-human primate studies to be applied to humans can be challenging.

Studies in man instead rely on damage already caused. Stroke models are valuable because neuroimaging, such as MRI, can map and quantify the resulting lesions. Lesion analysis provides useful information and helps to expand our understanding of brain structure and function (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Alexander et al., 2010; Fellows & Farah, 2007; Goodale & Milner, 1992; Karnath, Fruhmann Berger, Kuker, & Rorden, 2004). Correlating information between the species is a common approach to studying the brain, though the direct application to humans can often be difficult. Thus, studies employing various neuroimaging techniques and psychophysical and behavioral experiments have emerged to supplement deficiencies. The diversity of studies ultimately contributes to the creation of a more complete representation of brain function and motor control. This review will reference primarily studies conducted in humans, while using non-human primate studies where needed.

The primary motor cortex (M1) remains the most widely and extensively studied cortical region (Cheney, 1985). The traditional view is that motor cortex cells are somatotopically organized across and around the precentral gyrus, an area commonly referred to as Brodmann's area 4 (Penfield & Rasmussen, 1950; Woolsey, 1958; Woolsey et al., 1952). Several early studies have confirmed this, most notably studies involving electrical stimulation and lesion studies. Early work in humans by Wilder Penfield demonstrated that direct electrical stimulation of certain brain areas elicited individual motor responses. He was then able to create cortical maps of the sensory and motor areas of brain using this innovative technique. The

amount of cortical area corresponding to each body area is not determined by the size of the body part as the face, lips, and hands occupy larger cortical areas than the shoulder, back, and legs. This disproportionate representation suggests that the motor cortex is more involved and specialized for distal rather than proximal movements. Another important feature of M1 is that cells are largely contralateral in their action, meaning that activation of one motor hemisphere results in movement of the opposing side of the body (Penfield & Rasmussen, 1950).

Recent evidence, though, suggest that there is an overlapping of M1 functional regions (Colebatch, Deiber, Passingham, Friston, & Frackowiak, 1991). Sanes and Donoghue (1997) argue that representation of the arm in M1 is highly distributed and without somatotopy. Data from several lines of research have demonstrated variability in the cortical representation of motor and sensory areas. Studies using an intracortical stimulation technique have reported a mosaic pattern of muscle representation in monkeys (Donoghue, Leibovic, & Sanes, 1992; Gould, Cusick, Pons, & Kaas, 1986; Kwan, Mackay, Murphy, & Wong, 1978). Non-invasive imaging techniques have also confirmed the lack of complete somatotopy in humans (Colebatch et al., 1991; Grafton, Mazziotta, Woods, & Phelps, 1992; Kim et al., 1993; Rao et al., 1993). These studies support the hypothesis of mosaicism of motor cortical regions (Branco et al., 2003; Sanes, Donoghue, Thangaraj, Edelman, & Warach, 1995), which is contradictory to the classic notion of a precisely organized M1 as originally proposed by Penfield.

Neurons from multiple cortical contributions including M1, supplementary motor area (SMA), dorsal and ventral premotor cortex, and somatosensory cortex, converge and cross the midline to form the lateral corticospinal tract (Canedo, 1997; Davidoff, 1990; York, 1987). However, approximately 10 percent of fibers remain uncrossed and this incomplete decussation of corticospinal forms the anterior corticospinal tract. The corticospinal tract is vital to the generation of voluntary movements and demonstrates innervation with proximal and distal musculature of the upper extremity. A recent review (Jang, 2009) concludes that preservation of the corticospinal tract is mandatory for recovery following stroke.

M1 serves as the connection to lower motor neurons via the spinal cord and its defining function is to generate neural signals that control voluntary movement. Asanuma (1989) proposes that M1 sends commands to muscles while Goldring and Ratcheson (1972) term M1 as a 'final common path determiner of movement'. A distinctive role of M1 is to handle the coding and programming involved in the execution of the movement rather than the initial planning or timing of the movement. Other higher association areas assume this function. Indeed, studies in macaque monkey demonstrate that M1 is connected to fewer cortical structures than premotor areas (Matelli & Luppino, 1997). Other studies propose, instead, that M1 plays a greater role in the generation of complex versus simple finger movements (Gerloff, Corwell, Chen, Hallett, & Cohen, 1998).

The particular manner in which the primary motor cortex codes a specific motor plan depends on information received from many nonprimary motor and somatosensory areas. Parameters of individual movements and basic movement sequences are specified by M1. It encodes for both the force and direction of voluntary movements (Kandel, Schwartz, & Jessell, 2000). The output command encoded by the M1 includes what muscles to contract (and relax), the force of contraction, the extent of movement, and the speed and duration of movement. Evarts (1968) found in macaques that the firing rate of neurons in M1 corresponds to the output force of the innervated muscle. Different subpopulation of neurons in M1 demonstrate varying activation levels in anticipation of voluntary movement, dependent upon the direction of movement (e.g. flexion or extension) (Georgopoulos, Kalaska, Caminiti, & Massey, 1982). In fact, lesions to M1 typically result in a varying degrees of impairments related to force, muscle tone, and decreased ability to generate independent movements of the fingers (Porter & Lemon, 1993).

Of significance to M1 function is its role in corollary discharge to the. As M1 sends motor commands destined for spinal neurons, it also concurrently transmits an identical copy of the motor program to the cerebellum (Allen & Tsukahara, 1974), known as efference copy. This

serves to inform the cerebellum of the intended movement for comparison with actual performance. Further details about efference copy will be discussed in a later section to follow.

Another critical cortical area is the premotor cortex (PMC), an area that receives and processes information from various cortical regions in order to select movements appropriate to a given context. The premotor cortices (also identified as Brodmann's area 6) are extensively interconnected with higher association and sensory areas, and influence directly activity of M1 and of lower motor neurons in both the brainstem and spinal cord (Dum & Strick, 1991). Studies have demonstrated the dominance of the premotor cortex in the selection of movements (Deiber et al., 1991; Kalaska & Crammond, 1995; Thoenissen, Zilles, & Toni, 2002). PMC is involved in the preparation for and sensory guidance of movement (di Pellegrino & Wise, 1993; Gerloff et al., 1998; Kurata & Wise, 1988; Wise, 1985) and in organizing motor sequences (Halsband, Ito, Tanji, & Freund, 1993; Mushiake, Inase, & Tanji, 1991; Sadato, Campbell, Ibanez, Deiber, & Hallett, 1996). PMC is physiologically divided into dorsal premotor (PMd) containing representation of proximal arm muscles and ventral premotor cortex (PMv) representing distal hand muscles (Godschalk, Mitz, van Duin, & van der Burg, 1995; Sessle & Wiesendanger, 1982; Weinrich & Wise, 1982). While each partition has distinct functions related to the overall selection of particular movements, they are strongly interconnected (see review by (Chouinard & Paus, 2006).

The unique contribution of the dorsal premotor cortex (PMd) is its influence on movement, achieved by considering sensory information, such as external cues. The dorsal premotor cortex receives somatosensory and visual information from the medial intraparietal area of the superior parietal lobe in order to direct arm movements (Matelli & Luppino, 2000). Projections from this area of the brain to the primary motor and prefrontal cortex indicate how to respond to given external cues that prompt for a precise movement pattern. Chouinard et al. (2005) demonstrated that subjects are impaired at using arbitrary color cues to scale forces when transcranial magnetic stimulation was applied over the dorsal premotor cortex.

Additionally, studies in monkeys show an increase in activation of PMd neurons upon presentation of visuospatial cues to move in a particular direction (Mushiake et al., 1991). Collectively, this suggests the involvement of dorsal premotor cortex in directing movements according to external sensory information, particularly the processing of visual information.

The ventral premotor cortex (PMv) also is involved in processing visual information, but specializes in transforming visual representations to actions, particularly when concerned with hand movements. Connections with the anterior intraparietal area (AIP) in macaque monkey forms an important frontoparietal circuit (Rizzolatti et al., 1988) that aids in encoding the geometrical shape of objects into appropriate muscles of the hand. In addition, PMv also appears to assume some aspects of cognitive functions of movement in addition to executing object-related hand movements. Interestingly one particular class of neurons in this area, termed mirror neurons (Rizzolatti & Luppino, 2001), appear to fire upon making particular movements and when observing the same movements being performed. Gallese and colleagues (1996) demonstrated these neurons to be most active during grasping and manipulation of objects. These neurons in ventral premotor cortex are hypothesized to underlie our ability to understand actions and suggest an ability to represent movements.

Another discrete area of cortex related to motor control is the supplementary motor area (SMA). It is comprised of two discrete areas within the medial aspect of the frontal lobe in Brodmann's area 6: pre-supplementary (pre-SMA or rostral SMA) and supplementary motor area (SMA or caudal SMA). Pre-SMA has prominent projections to the prefrontal cortex (Luppino, Matelli, Camarda, & Rizzolatti, 1993) while SMA makes substantial direct connections to the corticospinal neurons (Dum & Strick, 1991). While both pre-SMA and SMA share similar responsibilities in motor planning, the areas appear to differ with respect to function. Pre-SMA codes new motor sequences and SMA is involved in retrieving movement sequences from memory, especially those repetitive in nature. These areas also appear to be concerned with the temporal organization of a motor sequence (Halsband et al., 1993; Laplane, Talairach,

Meininger, Bancaud, & Orgogozo, 1977). Pre-SMA provides a template for the temporal ordering of motor sequences and SMA functions to integrate temporal coding with the required movement sequence. In this schema, the pre-SMA assumes a preparatory role. The integrative function of the SMA, along with its reciprocal connections with M1, suggests SMA to be directly associated with motor output (Rizzolatti, Luppino, & Matelli, 1996).

SMA is responsible for the assembly of motor programs has a preferential role in selecting and initiating movements that are specified internally rather than by external cues. Passingham and others demonstrate a difficulty in making internally generated movements in monkeys with lesions to SMA (Passingham, 1989). Not surprisingly, this phenomenon is also observable in Parkinson's disease as there is a paucity of self-initiated movement owing to Parkinson's disease altering input to the SMA (Marsden, 1989). SMA appears to contribute significantly to the initial preparation of movement (Barrett, Shibasaki, & Neshige, 1986; Deecke & Kornhuber, 1978; Deecke, Lang, Heller, Hufnagl, & Kornhuber, 1987; Deiber, Ibanez, Sadato, & Hallett, 1996; Ikeda, Luders, Burgess, & Shibasaki, 1992, 1993; Ikeda et al., 1995; Kornhuber & Deecke, 1965; Rektor, Fève, Buser, Bathien, & Lamarche, 1994; Toro, Matsumoto, Deutschl, Roth, & Hallett, 1993). The function of SMA in the internal planning of movement sequences was also documented by an early regional cerebral blood flow (rCBF) study involving several experiments. Roland et al. (1980) demonstrated an increase in rCBF in the area of SMA as subjects performed a motor task mentally, in the absence of overt physical movement. In fact, these areas appear to be activated even before actual onset of movement (Deecke & Kornhuber, 1978). SMA also appears to share responsibilities with the coordination of bimanual movements. It receives major input from the putamen of the basal ganglia and both appear to be part of a distributed network underlying bimanual coordination of movements (Weisendanger, 1993).

Posterior parietal cortex (PPC) encompasses Brodmann's areas 5, 7, 39, and 40 and has traditionally been regarded as those areas associated with sensorimotor integration

supporting motor control and movement. These areas of the parietal cortex serve to prepare and direct movements (Grafton et al., 1992; Kalaska & Crammond, 1995; Sadato et al., 1996). Distinct areas within the parietal cortex are concerned with visuospatial attention or attention as it relates to the control of limb movements (Andersen & Buneo, 2002; Rushworth, Paus, & Sipila, 2001). Parietal area 5 demonstrates larger contributions to the planning of movements in association with somatosensory information, particularly spatial processing. Parietal area 7 is involved in aspects of visually-guided arm movements. These areas project directly to the primary motor cortex and provide information concerning body position and visual stimulus.

Prefrontal cortex (PFC) is involved with the selection of appropriate motor sequences (Coull, Frith, Frackowiak, & Grasby, 1996; Frith, Friston, Liddle, & Frackowiak, 1991; Stephan et al., 1995). It is identified as Brodmann's areas 9, 10, and 11 and housed in the most frontal part of the frontal lobes. The prefrontal cortex directs movement indirectly through its prominent projections to the other cortical motor areas, the basal ganglia, and the cerebellum. Specifically, the dorsolateral prefrontal cortex (DLPFC) has been demonstrated to be related to the generation or internally specified responses (i.e. willed actions) (Frith et al., 1991; Petersen, Fox, Posner, Mintun, & Raichle, 1988). It is responsible for the motivation and intention to move as it receives input from the pre-SMA, which demonstrates greater activation when subjects perform free-choice movements (Nachev, Wydell, O'Neill, Husain, & Kennard, 2007). Abundant support exists for DLPFC being active when making decisions (Deiber et al., 1991; Frith et al., 1991; Jueptner, Jenkins, Brooks, Frackowiak, & Passingham, 1996). The contrary is true once the performance of the task becomes learned, suggesting PFC's role in initiation of new movement rather than overlearned repetitive movements.

Initiation of movement requires the formation of a plan, a responsibility undertaken by the interplay of cortical structures reviewed. The desire to make a voluntary movement can arise internally and is specified by input from the prefrontal cortex. Unconscious or automatic motor movements do not necessarily involve input from PFC, as the brainstem and spinal cord

mediate these actions. Intention to move prompts action by the higher association areas of motor control including the premotor cortices and supplementary motor area. These areas contribute to the development of a motor plan appropriate for the given situation, determined in part by the role of the posterior parietal cortex, along with contribution from the prefrontal cortex. The PPC prepares for movement by integrating pertinent visual and spatial information (Grafton et al., 1992; Sadato et al., 1996) to be used by the premotor and supplementary motor areas in assembling motor programs. Activity in PMC and SMA differ depending upon how the movement is initiated and guided with PMC more active during visually-guided movement and SMA more active when the movement was recalled from memory and internally-guided (Mushiake et al., 1991). Resulting motor programs are transmitted to M1, and directly to spinal neurons, which specifies the timing and force of specific muscles necessary to accomplish the given movement. The subcortical structures are of interest in the following section as they allow for coordination and refinement of movements.

Subcortical structures

A substantial contribution to human movement comes from a collective group of subcortical nuclei referred to as the basal ganglia (BG). The basal ganglia can be separated into two functional categories: input structures and output structures. The corpus striatum includes caudate and putamen nuclei and serves as the primary input of the basal ganglia. It receives vast projections from nearly all cortical areas, namely multimodal sensory information from association cortices of the frontal and parietal lobes. The main output structures of the basal ganglia are the internal segment of globus pallidus and substantia nigra pars reticulata (SNr). These structures project to various motor areas of the brain including supplementary motor area and premotor cortex via the ventral anterior and ventral lateral thalamic nuclei (Deiber et al., 1991; Frith et al., 1991; Grillner, Hellgren, Menard, Saitoh, & Wikstrom, 2005; Groenewegen, 2003; Jueptner et al., 1996).

This set of structures forms one of two subcortical loops that share some responsibility for initiation and inhibition of movement. The gaiting function of the basal ganglia (i.e. the disinhibition of intended motor plans and inhibition of competing ones) incorporates information from the motor, sensory, and association cortices (Mink, 1996). With this information, the basal ganglia are able to coordinate the timing and sequence of motor acts. It has a role in the execution of overlearned automatic movements (Jueptner & Weiller, 1998; Marsden, 1982). The basal ganglia also assume functions related to bimanual coordination (Kraft et al., 2007). One mechanism is that the influence of basal ganglia in the neural control of bimanual coordination is through its projections to SMA (also implicated in bimanual coordination) via the putamen (Castiello & Bennett, 1997). Additionally, basal ganglia share a role in nonmotor aspects of behavior related to cognition and mood. The pallidum and substantia nigra pars reticulata are part of the dorsolateral prefrontal cortex implicated in executive functions including organization of behavior. The anterior cingulate circuit formed by the anterior cingulate gyrus and ventral striatum, with prominent projections from the limbic areas, appears to be involved in motivated behavior (Kandel et al., 2000).

The cerebellum is another subcortical structure that optimizes voluntary movement through a feedback mechanism. It receives inputs directly from the spinal cord and from the cerebral cortex, mainly primary and secondary sensory areas of the parietal lobes as well as primary and premotor areas of the frontal lobes. Just as it receives input from these areas, the cerebellum projects back to those areas and thus forms a loop, with information about the timing, direction, and force of a particular movement. In addition to connections, Thach (1992) concludes that cerebellar nuclei house representations of body maps responsible for coordinating movements involving multiple parts of the body. Furthermore, that the cerebellum coordinates movements by combining simpler movements into more complex movements (for a review on cerebellum and the coordination of movement, refer to (Thach, Goodkin, & Keating, 1992). Thus, it has been implicated heavily in the correction and adjustment of ongoing

movements, due, in part, to the function of M1 providing a carbon copy of the motor program. This efference copy sent to the cerebellum suggests a possible mechanism for the cerebellum as a comparator of movements with the ability to adapt and modify movements in progress via projections back to the motor cortex (Allen & Tsukahara, 1974; Evarts & Thach, 1969; Thach et al., 1992).

The contributions from these two subcortical structures to the control of goal-directed movements are important, but do not necessarily assume primary responsibility for the planning or execution. The basal ganglia serve to inform the activity of M1 and higher association areas, but do not directly cause motor output. Proper functioning of the basal ganglia appears to be crucial to normal motor control and movement; particularly revealing are studies of patients with Parkinson's disease or Huntington's disease. In these diseases, function of the basal ganglia is obviously disturbed and results in specific disorders either in initiation or in inhibition of movement. The cerebellum's influence on goal-directed movement is by monitoring output by M1 and other higher structures in the motor hierarchy. One explanation of this role originates from the fact that cerebellum receives considerable afferent sensory contributions. The cerebellum uses this information to compare the intended movement with actual movement in order to adjust and refine the movement appropriately. Indeed, damage to cerebellum produces recognizable deficits in the smoothness of movement, such as in ataxia.

Goal-directed movement

Significant to the discussion of goal-directed movement are motor control theories, as they provide a useful framework for understanding the control of movement. Researchers have long studied various theories of control of actions and behaviors. In the early 1900s, the works of Sir Charles Sherrington lead to the idea of reflexes as the foundation for complex movements. He suggested that complex behaviors are the result of individual reflexes chained together in succession (Sherrington, 1947). Reflex theory though, cannot explain movements occurring in the absence of sensory stimuli and voluntary movements. Alternatively, one of the

most recognized motor control theories is the hierarchical theory proposed by Hughlings Jackson. He argued that motor control is organized hierarchically with higher association areas exerting influence upon lower levels of control (Förster, 1936). Recent concepts of motor control (Hikosaka, 1998; Kandel et al., 2000) have acknowledged that each level does possess the ability to influence the generation of movement, as reflexes do not necessarily regard higher levels of control when initiated. While neither theory can adequately account for the organization of motor control, integrating components from each theory offers a more complete view of how movement is controlled.

The neural components underlying the brain's capacity to develop and execute motor plans involve the interaction, both hierarchical and parallel, of multiple brain areas and structures. Although each with unique contributions, it is with the concerted effort of these structures that enables humans to function efficiently in daily life. For the purpose of this review, goal-directed movements will refer to voluntary movements of the arms that are both meaningful and involve interaction with the environment. This section will highlight the neural basis of reaching and grasping, movements that facilitate our ability to engage in tasks in a meaningful and effective manner.

The brain develops motor programs for movement by undertaking various levels of information processing necessary that ultimately converge at M1, resulting in a signal to be executed at the level of spinal cord neurons (Asanuma, 1989; Goldring & Ratcheson, 1972). A distributed neural network comprised of cortical and subcortical structures forms the control system governing goal-directed movement. Kandel (2000) distinguishes three categories of movements: reflexes, rhythmic motor patterns, and voluntary movements. Similarly, Hikosaka (1998) proposed three levels for the control of actions: 1) innate movements or actions, 2) learned movements acquired by practice, and 3) new movements not yet automatic requiring attention and effort. In both models, the levels of control of actions are determined by different neural structures that regulate movement.

Reflexes (or innate actions) are the simplest of motor behaviors and are governed at the level of the brain stem and spinal cord. These motor behaviors are not regarded as under voluntary control and are elicited by the presentation of a sensory stimulus as in the knee jerk. The second level consists of learned or rhythmic movements such as walking that combine features of the lowest (reflex) and highest (voluntary) level of control. The cerebral cortex initiates repetitive, rhythmic movements but these movements then persist with continued input from the brainstem and spinal cord. The highest level of control is voluntary movements that are characterized by two features: purposeful or goal-directed and movements that are largely learned (Kandel et al., 2000). Motor learning is the underlying process that enables the formation of innate movements into motor programs (i.e. learned movements). Before becoming learned though, movements require attention and practice. New movements involve multiple sensory and feedback systems that closely monitor performance. According to this classification, additional systems determine the level of control of actions with higher levels involving more attention and effort than lower levels.

This review will use reaching and grasping as a means of examining the neural structures and mechanisms underlying goal-directed movements. Research suggests that reaching and grasping is dependent upon both task and stimulus variables (Jeannerod, 1984) with reaching depending primarily on target distance and grasping relying on object size. Two anatomically distinct circuits are proposed to control reaching and grasping: a dorsomedial circuit responsible for the reaching component consisting of the anterior portion of the occipitoparietal sulcus and PMd; a dorsolateral circuit controlling the grasp and consist of anterior intraparietal area (AIP) and PMv (Galletti, Kutz, Gamberini, Breveglieri, & Fattori, 2003; Tanne-Gariepy, Rouiller, & Boussaoud, 2002). Indeed, Flanagan et al. (2003) supports that reaching mechanisms differ from those of grip.

Reaching

An often essential precursor to grasping objects is transporting the hand to the necessary location. Reaching serves to bring the hand to specific positions in space and results from synergistic activation of muscles acting on shoulder and elbow joints. The combined degrees of freedom existing at each of these joints result in a considerable potential range of complex movements. Despite variety, studies in man have demonstrated that reaching movements share similar features of straight hand paths and consistent patterns of muscle activation (Morasso, 1981; Soechting & Lacquaniti, 1981).

While M1 deploys command signals that activate individual muscles, the dorsal premotor cortex is specialized in planning reaching movement sequences. Activating neurons in dorsal premotor cortex evokes coordinated muscle contractions, namely proximal arm muscles for reaching (Godschalk et al., 1995; Sessle & Wiesendanger, 1982; Weinrich & Wise, 1982). Studies in monkeys show that PMd neurons fire in correlation with reaching parameters such as direction and amplitude (Kalaska, Scott, Cisek, & Sergio, 1997). Graziano (2001) posits that control of reaching is hand-centered, noting that neurons in the premotor cortex share in coding for movements of the arm and hand. Compared with cells in M1, neurons in PMd demonstrated less sensitivity to different arm postures, which is consistent with PMd's role in the planning of reaching rather than the execution (Scott, Sergio, & Kalaska, 1997). Hollerbach (1982) proposed this planning to occur at the object level, which translates to joint movements and eventually muscle activations necessary to reach the object of interest. The hierarchical plan identifies muscle activations as the last step in planning of a motor program. This supports the concept that the brain develops motor programs according to patterns of movements, rather than coding for individual muscles or joints and then combining these individual codes to accomplish a task.

Visually-guided reaching has been extensively studied, as this sensory modality [vision] is a vital component to movement. Paillard (1982) offers an explanation regarding three aspects of visual information used in reaching: 1) visual localization of the target in space, 2) the relative

position of the hand and target, and 3) the motion of the arm across visual fields. Before onset of the reach, the visual system has already engaged the eyes to orient in the direction of the object of interest with the head following the eyes. The eyes move more quickly than either the head or hand and are able to focus on the target even before the head stops (Jeannerod, 1990). Upon reaching, the eyes have already arrived at the target and are then able update the arm movement as necessary (Prablanc & Martin, 1992).

The continuous updating of visual space is necessary to efficient movement of the arms. Discrete areas within the parietal areas are thought to contribute to eye movements. Studies demonstrate patterned discharge of parietal neurons in association with the direction of visual attention (Colby & Goldberg, 1999), particularly with right parietal regions (Vallar, 2001). In addition to parietal areas is the premotor cortex, which consolidates visual information for the planning of arm movements. Experiments by Fujii et al. (1998) found areas of the ventral premotor cortex to be activated in association with neurons underlying saccadic eye movements and movements of the arm and neck. This agrees with previous work implicating parietal cortex and PMv in visuomotor transformation, specifically ventral premotor cortex's role in the selection of movements based on visual information (Rizzolatti et al., 1988).

Goodale and colleagues (1992) review two visual pathways, originally proposed by Miskin and Ungerleider (1982) that help to explain the unique contributions of neural structures involved in visually-guided reaching. The dorsal stream, formed by connections from the visual to the parietal cortex, provides important action-related information about the reaching movements such as object position and orientation. This pathway relays information about what is being reached for while the other pathway (ventral stream) provides details about the object in space. Ventral stream projections exist between the visual and temporal cortex and aids in the ability to process the specific orientation and dimension of objects pertinent to movement. Recent investigations have targeted the controversial two streams hypothesis with evidence that this dichotomy in visual processing does not exist (Franz, Gegenfurtner, Bulthoff, & Fahle, 2000;

Franz, Scharnowski, & Gegenfurtner, 2005). A review also questions this hypothesis and suggests that it is “difficult if not impossible to test” (Cardoso-Leite & Gorea, 2010).

The importance of sensory contributions, particularly the visual system, to goal-directed reaching is well-documented. Studies have demonstrated reaching accuracy to be greater with vision directly before movement than without (Prablanc, Echallier, Komilis, & Jeannerod, 1979). In fact, accurate reaching performance depends not only on vision before, but also throughout the reaching movement (Desmurget, Rossetti, Prablanc, Stelmach, & Jeannerod, 1995; Prablanc, Echallier, Jeannerod, & Komilis, 1979). This continuous visual monitoring of reaching has been suggested to be due to the need to determine hand position relative to the object. Contributions of somatosensory information are important to effective reaching, but do not substitute for vision. Animal studies of monkeys who underwent deafferentation of one limb were eventually able to perform adequate reaching, despite the lack of somatosensory input (Taub & Berman, 1968). In a study of normal and deafferented subjects, the authors arrived at two conclusions: proprioception is necessary to accurately program movement trajectory and visual monitoring of the arm can partially substitute for deficient proprioceptive information (Ghez, Gordon, Ghilardi, Christakos, & Cooper, 1990).

The planning of goal-directed reaching involves transforming the spatial location of an object into muscle activity required to bring the hand to the object (Jeannerod, 1990; Kalaska & Crammond, 1992). This involves transformation of visual three-dimensional space. The mechanism linking perception to action is difficult to identify since it involves transformation of perceptual space into movement (Rizzolatti, Fogassi, & Gallese, 1997). The posterior parietal cortex is the cortical area widely recognized to integrate sensory information necessary to the optimal performance of reaching. Both intrinsic and extrinsic information contribute to the development of motor plans for reaching (Sabes, 2000). Graziano (2001) summarized that reaching includes proprioceptive input from the arm and a continuous view of both the hand and target. Reaching requires integration of mainly visual and spatial information, which are derived

from both internal representations and external stimuli. The posterior parietal cortex appears to maintain an internal representation of the body as a necessary precursor to movement (Wolpert, Goodbody, & Husain, 1998) by continually updating where our limbs are in space. Additionally, it is responsible for transforming visuospatial information from the environment into signals that aid in directing reaching movements of the arm (Gold & Shadlen, 2001). Thus, the posterior parietal cortex receives inputs from dorsal premotor cortex, forming frontoparietal circuits that control goal-directed reaching.

Grasping

The hand is regarded as the tool with which we manipulate objects with grasping as an evolved skill specialized in humans and primates. Napier's early work (1956) distinguished human grasping movements as either power or precision grip. Power grip involves transmission of force from the thumb and fingers toward the palm and object. Precision grip requires forces to be directed between the pads of the thumb and index finger. Both are used for different purposes dependent upon the intended activity (Jueptner et al., 1996; Napier, 1956). Precision grip is a defining characteristic of dexterous hands because it allows for object manipulation within or relative to the hand (Shumway-Cook & Woollacott, 2007). Discussed previously was that reaching served to bring the hand to specific locations in space or toward an object. In combination with reaching, the ability to grasp objects that enables us to interact meaningfully with objects in our environment.

The work of Jeannerod has contributed considerably to our understanding of grasping (Jeannerod, 1981). Preshaping of the hand, specifically the fingers, occurs during the transport phase of the hand toward an object (i.e. reaching). Grasp begins with opening of the grip with straightening of the fingers, followed by a progressive closure of the grip to match the object size. Grip aperture correlates highly with the size of the object and is largest well before coming in contact with the object (Gentilucci et al., 1991; Jeannerod, 1984). On approach toward objects, the hand begins to reflect the shape of the object to be grasped. This was

demonstrated in monkeys where a perfect match with object geometry was achieved just prior to contact with the object (Santello, Flanders, & Soechting, 2002; Santello & Soechting, 1998) and is based on visual properties of objects (Cattaneo et al., 2005; Jeannerod, Arbib, Rizzolatti, & Sakata, 1995; Santello & Soechting, 1998; Wang & Stelmach, 1998)

Effective grasping entails that the brain undertake multiple transformations of the properties of objects into appropriate motor commands (Jeannerod et al., 1995), unlike transforming abstract space into commands necessary for reaching. The brain predicatively generates finger forces necessary to grasp objects based on physical properties of the object (Gordon, Westling, Cole, & Johansson, 1993; Jenmalm, Dahlstedt, & Johansson, 2000; Jenmalm & Johansson, 1997; Johansson & Westling, 1988; Salimi, Hollender, Frazier, & Gordon, 2000; Witney, Vetter, & Wolpert, 2001). Jeannerod (1984) identifies two types of properties that influence grasp formation: intrinsic properties such as object size and shape and extrinsic properties such as object orientation and distance from the body. Somatosensory input more necessary when contacting objects as it informs us about the objects characteristics and we are then able to adjust appropriately given the weight, size, and orientation. In fact, the grasping phase of reach-to-grasp tasks is not affected much in the absence of vision (Jeannerod, 1990).

Grasping requires coordinated distal movements of the wrist and fingers. The integrity of M1 is essential to the execution of grasping movements because of its control of the hand and fingers. Wrist, hand, and finger representation comprises a substantial portion of M1. It is well-known that lesions to the M1 produce difficulty producing fractionated finger movements (Porter & Lemon, 1993), although synergistic movement of all fingers may be preserved. Different grasping patterns activate areas of M1 at varying levels. Muir and Lemon (1983) demonstrate a special role of M1 neurons that discharge during precision grip but not during power grip. Simply being able to produce fractionated finger movements is not sufficient as grasping also requires finely turned fingertip forces (Castiello, 2005; Johansson & Westling, 1984). Premotor areas and

anterior intraparietal sulcus (AIP) appear to be more involved in the visuomotor transformations of object and space necessary for grasp. Neurons in both areas code for grasping actions specific to the type of object. These areas show discrete activation during grasp tasks in both monkeys (Rizzolatti et al., 1988) and in humans performing precision grip (Binkofski et al., 1998; Culham et al., 2003; Frey, Vinton, Norlund, & Grafton, 2005). Important functional distinctions exist between these two areas as AIP is more concerned with the visual representation of the object's properties than premotor cortex (Murata, Gallese, Luppino, Kaseda, & Sakata, 2000). An fMRI study studying grasp in humans identified activation in the dorsal stream, including AIP, and suggests that this pathway is involved in object processing required for grasping (Culham et al., 2003).

An important discovery by Rizzolatti (1988) revealed that grasping neurons in PMv are selective for the type of grasp: precision, finger prehension, and whole-hand prehension. The implication of this finding is that objects can be grasped in many different ways. Fagg and Arbib (1998) propose a model in which AIP provides multiple descriptions of the object while the PMv selects the most appropriate movement, which is in accord with previous evidence (Kalaska & Crammond, 1995; Thoenissen et al., 2002). Being highly interconnected with PMv, it is not surprising that dorsal premotor cortex also appears to share some responsibility in grasping. Raos and others (2004) have proposed that PMd is involved in the accuracy of grasping movements while PMv conveys information about the selection of type of grip to dorsal premotor cortex. PMd is then able to mediate grasping actions, through connections with M1, and continuously update the configuration and orientation of the hand in route towards the object (Raos, Umiltà, Gallese, & Fogassi, 2004).

Subcortical contributions to movement

The basal ganglia and cerebellum are two structures important to movement and form subcortical loops with higher cortical centers. These subcortical structures are not primary to motor function, but serve to modulate eventual motor output. It is evident that lesions in these

areas do not produce paralysis, but rather difficulty with producing smooth, coordinated movements. The unique contribution of the subcortical structures concerns the timing and coordination of movements.

Since many motor programs may often result in the same movement pattern, a control mechanism for selection must exist. Basal ganglia's influence on movement occurs via projections to multiple cortical areas while receiving input from sensory association areas (Alexander & Crutcher, 1990). It appears to select appropriate motor programs (Mink, 1996), with the striatum as the most likely candidate involved in the selection of movement (Grillner et al., 2005; Jueptner & Weiller, 1998). The output structures of the basal ganglia, or pallidum, project to higher motor centers (i.e. SMA, PMC, and PFC) and keep them under tonic inhibition. The striatum is responsible for the gating function as it acts to release or block the action of the pallidum, thereby allowing for initiation of movement (Grillner et al., 2005; Hikosaka, Takikawa, & Kawagoe, 2000). Suggested previously was that disorders of the basal ganglia result in problems with initiation or inhibition of movement. Parkinson's disease presents with poverty or slowness in initiating movement (i.e. akinesia, bradykinesia, or hypokinesia) assumed to result from diminished dopamine activity in the striatum. Conversely, enhanced dopamine activity in the striatum leads to involuntary movements (i.e. hyperkinesia and dyskinesia) apparent in Huntington's disease (DeLong, 1990; Grillner et al., 2005; Groenewegen, 2003).

Feedforward control of movement

Predictive or feedforward control of movements is important to efficient reaching and grasping. In a review on the organization of voluntary movement, Ghez and colleagues (1991) conclude that the brain needs to reference an internal model of the limb when motor planning. Internal models enable the central nervous system to develop a motor plan predictively based on previous experience. Feedforward control relies on internal models of movement based on previous experience and can anticipate the results of a given movement (Flanagan & Wing, 1993, 1997; Kawato, 1999; Wolpert, Ghahramani, & Jordan, 1995). Thus this control system is

able to exert online influence on movements in progress (Desmurget & Grafton, 2000) and adapt motor commands based on relevant task demands (Flanagan & Wing, 1997; Ghez, Hening, & Gordon, 1991; Johansson & Cole, 1992; Lacquaniti, 1992; Miall & Wolpert, 1996). Individuals first use an inverse model to develop a motor plan that is copied to the forward model. The forward model of the projected arm movement is generated and also anticipates the expected sensory consequences to be used in comparison to the actual sensory consequences (Wolpert & Ghahramani, 2000; Wolpert et al., 1995). The internal model is adapted and updated when the information from the above comparison results in differences (Kawato & Wolpert, 1998).

Reaching trajectories demonstrate straight hands paths with similar bell-shaped velocity profiles and activation of synergistic muscles (Abend, Bizzi, & Morasso, 1982; Flanders, 1991; Karst & Hasan, 1991; Lacquaniti, 1989; Lacquaniti, Soechting, & Terzuolo, 1986; Morasso, 1981; Soechting & Lacquaniti, 1981). Since unobstructed reaching under normal conditions demonstrate these features, direction of movement appears to be planned in advance before movement onset (Ghez et al., 1990). Recent studies attribute this, in part, to proprioceptive input that 1) provides initial information on limb position and 2) updates internal models of the limb (Flanders, 1991). Ghez et al. (1990) examined the role of proprioceptive information in movement planning and suggested that feedforward mechanisms were responsible for improvements in reach with and without vision. The authors suggest an indirect role for vision and proprioception in updating the internal model of the limb used to plan movements.

Basal ganglia functions also extend to aspects related to predictive planning of force grip (Prodoehl, Corcos, & Vaillancourt, 2009). Specifically anterior basal ganglia nuclei demonstrate activation with the initial planning of grip force (Pope, Wing, Praamstra, & Miall, 2005; Vaillancourt, Yu, Mayka, & Corcos, 2007) while posterior nuclei are involved in the scaling of grip force output, such as rate (Vaillancourt, Mayka, Thulborn, & Corcos, 2004) and amplitude (Spraker, Yu, Corcos, & Vaillancourt, 2007).

Johansson, Westling and colleagues conducted several studies examining how subjects coordinate finger forces necessary for precision grip (Forssberg, Eliasson, Kinoshita, Johansson, & Westling, 1991; Johansson & Westling, 1990). Subjects used grip forces (opposition of forefinger and thumb flexion) and load forces (achieved by elbow flexion), in order to lift boxes varying in size and weight. Somatosensory information (i.e. object weight and resistance) was not available until lift onset, thus the authors concluded that the initial coordinated forces necessary for effective grasp and lifting of the boxes were generated in a predictive/feedforward manner (Forssberg et al., 1991; Gordon, Forssberg, Johansson, & Westling, 1991a, 1991b; Johansson & Westling, 1990). Interestingly, Gordon et al (1991;1993) suggests that visual information also contributes to the predictive determination of grip and load forces. Subjects in this experiment demonstrated scaling grip and load forces based on the size of the boxes (i.e. visual information) rather than weight. Consequently, this 'size-weight' illusion resulted in subjects lifting larger boxes more rapidly despite that the smaller boxes were the same weight. This supports the concept that humans initially process visual information to retrieve an internal model that can appropriately predict and anticipate upcoming force requirements (Johansson, 1998).

Feedback control

The connections to and from the cerebellum suggest a role in sensory processing of movement-related actions. Weiller (1996) used passive range of motion to separate efferent and afferent contribution to movement. The study demonstrated that the cerebellum appears to be just as active in both active and passive range of motion, thus suggesting its role in monitoring movements. Higher sensory association areas, particularly the PPC (Desmurget et al., 1999; Desmurget & Grafton, 2000) update the cerebellum with information about the location of the object, and arm, in visual space. Proprioceptive feedback from the arm movement aids in optimizing movements in process (Ito, 1984; Stein & Glickstein, 1992; Thach et al., 1992) and without intact proprioception, individuals experience difficulty with compensating for inherent

inertial properties of the arm (Ghez et al., 1990). Bastian and colleagues (1999; 2001) studied cerebellar activity and examined the ability to adjust to various loads with a catching task. This series of studies suggests a role for the cerebellum in adaptation to changing task conditions through trial and error practice.

Movement error is closely related to sensory contributions to the central nervous system with sensory information aiding in adaptation during movement execution. Relative to movement, an inherent delay of processing of sensory information exists. Thus, feedback control of movement has been suggested to be inappropriate due to the constant change in arm trajectory during reaching movements (Gerdes & Happee, 1994; Hollerbach, 1982). To resolve this, sensory feedback is hypothesized to be most influential in the correction of movements towards the end of movement trajectory rather than initially (Meyer, Abrams, Kornblum, Wright, & Smith, 1988; Milner, 1992; Plamondon & Alimi, 1997) and the endpoint error contributes to adaptation of movement (Magescas, Urquizar, & Prablanc, 2009).

Much like the basal ganglia, the cerebellum is not directly responsible for the planning or execution of motor plans but rather in monitoring and adjusting movements. It regulates movement indirectly by exerting its influence upon the premotor cortices and M1 via the thalamus. The cerebellum assesses differences between actual performance and intended movement through corollary discharge from M1. Reaching movements demonstrate endpoint variability that is directly proportional to the speed of movement (Fitts, 1954; Fitts & Peterson, 1964; Marteniuk, MacKenzie, Jeannerod, Athenes, & Dugas, 1987), that is, movements performed more quickly suffer at the expense of accuracy at the endpoint. Efference copy of the neural command, along with afferent signals from the movement are utilized in order to optimize muscles to correct for variations in movement (Flament, Hore, & Vilis, 1984). Studies therefore suggest that changes in velocity profiles can be indicative that movements are under the influence of feedback control (Flament et al., 1984), with the cerebellum carrying out this function (Allen & Tsukahara, 1974; Ito, 1984).

Originally proposed as a motor processing structure (Blomfield & Marr, 1970; Eccles, 1973; Glickstein, 1992), recent investigators such as Jueptner and others (1997) suggest that the cerebellum is driven entirely by sensory systems and may act as a 'comparator' or 'detector' (Eccles, Sabah, Schmidt, & Taborikova, 1972; Horne & Butler, 1995). It is indistinguishable in human studies though, the functional relevance of sensory processing carried out by the cerebellum (Jueptner & Weiller, 1998). The exclusive role of the cerebellum in sensory processing (Gao et al., 1996) has been challenged and evidence demonstrates that motor processing occurs in the cerebellum in the absence of sensory input (Weeks, Gerloff, Honda, Dalakas, & Hallett, 1999).

The cerebellum detects movement errors and makes adjustments to match the intended movement through input from the visual and proprioceptive systems. Jueptner (1998) found that the cerebellum was highly activated when subjects performed a line-tracing task. Additionally subjects were also asked to generate new lines. This design allows subjects to freely draw lines in any direction; hence no errors were possible (Jueptner & Weiller, 1998). In generating new lines where subjects could freely choose how to draw a line, almost no cerebellar activation was present. The results of this rCBF experiment suggest cerebellum's role in optimizing movements by using sensory information to detect and correct movement errors. Holmes (1939) first noticed signs and symptoms associated with cerebellar disorders as patients experienced ataxia: the difficulty coordinating voluntary movements. The distinct features of ataxia include errors in the range, force, rate, and regularity of movements (Kandel et al., 2000). Evidence of errors in movements further lends support to the cerebellum acting as a comparator and regulator of movements.

Motor Learning

Related to the current discussion of motor control is motor learning, a process of acquiring the knowledge and/or ability to perform movements. Much of present current review centers on the performance of movements, emphasizing movements of higher levels of control

(i.e. reaching and grasping rather than innate actions such as locomotion). Motor learning similarly engages higher levels of cortical control, also subcortical structures. It is a process by which we acquire movements and motor learning undoubtedly has important implications for improving movements over time with practice. This section will serve to briefly highlight the contributions of the basal ganglia and cerebellum to motor learning.

Motor learning can involve two different aspects: learning of procedures and learning of movements (Hikosaka, 1998). The basal ganglia and cerebellum are important in improving and learning movements. The striatum, parts of the pallidum, and several areas of the cerebellum demonstrate increased rCBF activity, and studies employing PET, when learning a new task (Doyon, 1997; Halsband & Lange, 2006; Jueptner et al., 1997; van Mier, Tempel, Perlmutter, Raichle, & Petersen, 1998), associated with improvement of performance or motor learning. These structures cooperate with higher association areas, both motor and sensory, and communicate with PMd in the selection of movements based on given sensory information (Kandel et al., 2000; Krakauer & Ghez, 2000). Basal ganglia and cerebellum are distinct in their roles associated with learning due to their unique connections with cortical areas.

Hikosaka (1998) proposes that the connections between the basal ganglia and cerebral cortex subserve procedural learning, particularly the striatum (Kandel et al., 2000). Evidence reveals that basal ganglia (and cerebellum) are involved when subjects improve performance of movements (Jueptner & Weiller, 1998). Theories propose various functions the basal ganglia serve in motor learning and amongst the most prominent is that the basal ganglia are involved in the formation and storage of memory programs. Hikosaka (1994) hypothesizes that the basal ganglia are involved in the initial formation of a template for motor behaviors. This theory suggests that procedural learning results from interactions between the basal ganglia and cerebral cortex. The proposed mechanism is that the basal ganglia temporarily retain a trace memory of the behavior. Over time with repeated rehearsal of the motor behavior, a template is formed from which the cerebral cortex learns and creates the procedural memory.

Doya (1999;2000) suggests that the basal ganglia and cerebellum are specialized for the type of learning. Under this theoretical model, the basal ganglia are involved in reinforcement learning, based on the processing of a reward signal encoded in the dopamine system in the substantia nigra (Houk & Wise, 1995; Montague, Dayan, & Sejnowski, 1996). The cerebellum is suggested to be responsible for supervised learning, through the coding of potential error signals (Doya, 1999, 2000) that may be useful in improving movement performance.

Cerebellum's role in motor learning can be defined as the learning of movements (Hikosaka, 1998) and adaptation of movement (Thach et al., 1992). Receiving much of its projections from sensory systems, the cerebellum is concerned with the accuracy of movements (Hikosaka, 1998). Experiments involving subjects wearing prisms and throwing darts or balls at a target have been used to examine the adaptive function of the cerebellum (Baizer & Glickstein, 1974; Weiner, Hallett, & Funkenstein, 1983). The prisms alter the location of the target and therefore the initial throws will be inaccurate. With repeated practice, the arm is able to coordinate with the visual system and throws will become increasingly more precise and eventually on target. The adaptive feature demonstrated in the previous experiment can be attributed to interactions between the cerebellum and cerebral cortex. Thus, the cerebellum provides a means for movement to be executed quickly and accurately through an adaptive process of learning. Baizer (1974) first demonstrated the inability of macaques to adapt reaching movements, which was then later confirmed in humans with cerebellar disease (Baizer & Glickstein, 1974; Weiner et al., 1983). The subjects continually committed movement errors due to the lack of proper cerebellar function. Thach (1992) also indicates that muscimol injections to the cerebellum prolong adaptation time and even abolishes the ability for several days.

Conclusions

This review has focused on the specific neural structures underlying the ability to plan and execute goal-directed movements. First, the cortical and subcortical structures were briefly

described to provide a foundation for understanding how each structure contributes to movement. Reaching and grasping objects was used as the primary example in order to illustrate the processes the brain undertakes. This movement sequence was selected because it is a goal-directed action that requires conscious effort, rather than repetitive, rhythmic motor behavior such walking.

Upon review, the higher order cortical structures the premotor cortices (PMd and PMv) and supplementary area (SMA) appear to assume functions related to the planning of movements. Each cortical area uniquely takes into account various factors as plans are formulated. PMd considers external sensory information while PMv appears to be most involved in visuomotor transformations as it is highly connected with the anterior intraparietal area. SMA contributes to the planning of movements by selecting and initiating internally-guided movements. Plans are not formulated without input though, and the basal ganglia have a primary role. The basal ganglia select an appropriate motor plan to implement from an array of possible plans. The gating function of the basal ganglia therefore disinhibits the appropriate motor plan while inhibiting competing ones.

The somatosensory system is critical for accurate executing of goal-direct movements. Proprioception provides initial information as well as updates concerning limb position and is important to accurate movement trajectory. In its absence though, vision can partially substitute and enable individuals to monitor the arm in order to produce more accurate and efficient reaching and grasping movements. The eyes locate the object in 3D space and provide information on distance and location as well as the inherent properties of the object of interest. Input from the posterior parietal cortex provides PMd/PMv/SMA with information about visual space and object-related features necessary for the planning of reaching and grasping. Preshaping of the hand for grasping occurs during the transport phase (reaching) in anticipation of the object's shape and size. Posterior parietal cortex shares responsibility for converting visual information into motor behavior. It processes visual information to assist in directing

reaching movements of the arm and forming hand postures for grasping. The posterior parietal cortex is also involved in maintaining an internal representation of the body, specifically where the limbs are in visual space.

Forming subcortical loops, the basal ganglia and cerebellum exert indirect influence upon cortical structures. These structures are primarily concerned with smoothness and coordination of movements as evident by their connections from sensory association areas. Output structures of basal ganglia are connected with premotor areas and regulate the selection of appropriate movements by inhibiting competing movements. This supports, in part, basal ganglia's role in the quality of movements. The cerebellum is more implicated in refining and adjusting movements. As previously mentioned, the cerebellum takes on a 'comparator' role in assessing difference between intended and actual movements. The calculated difference is deemed as error, which can be corrected by the cerebellum.

Important implications can be derived from the material presented in this review. First, fundamental knowledge of neural structures involved in goal-directed movements will facilitate understanding of clinical presentation of movement disorders. Second, the clinician or scientist will be able to be more comprehensive in their approach to evaluating neurologically-based movement disorders. Last, this review will aid in developing evidence-based, efficacious treatment interventions while considering concomitant causes of movement disorders.

Appendix B: Comprehensive Literature Review II

Impairments of the Central Nervous System That Impose Constraints on Functional, Goal-directed Movement

This work was approved October, 2010.

Introduction

Movement arises from the interaction of various systems of the central nervous system. Understanding the unique contribution of these systems and processes is instrumental in the identification and qualification of disorders in motor control due to neurological pathology. Since problems with motor control can exist at different levels of cortical and subcortical control, consequently clinical manifestation will vary as well. The present review focuses specifically on the clarification of the numerous impairments within the central nervous system resulting in constraints on functional, goal-directed movement. This paper will address primary disturbances in motor control including differentiating between positive and negative signs/symptoms following upper motor neuron lesions and a discussion of proposed mechanisms. Next, secondary or adaptive features arising from primary impairments will be discussed.

Overview of the levels governing voluntary movement

Central command of movement can be organized into various levels of control including higher, middle, and lower levels (Prochazka, Clarac, Loeb, Rothwell, & Wolpaw, 2000). The higher level of control is responsible mainly for contributing the kinematic profile of movement and motivation to move (Gracies, 2005a). It determines movement parameters including spatial location and temporal features to what is referred to as mental representation (Hanakawa et al., 2003; Kalaska et al., 1997; Sirigu et al., 1996). Movement occurring at this level can be further subdivided into externally guided and internally driven movements and different neural networks are thought to assume these functions. Cortical areas directing externally-guided movements (i.e. movements triggered by sensory information) involve the posterior parietal and lateral premotor areas (Hanakawa et al., 2003; Kalaska, Cisek, & Gosselin-Kessiby, 2003; Kalaska et al., 1997; Sirigu et al., 2004; Sirigu et al., 1996) while the inferior parietal and prefrontal areas mediate internally-driven movements (i.e. automatic movements/motor memory) (Buxbaum, Sirigu, Schwartz, & Klatzky, 2003; Goldman-Rakic, Bates, & Chafee, 1992). The intention or volition to move involves the anterior cingulate circuits, shown consistently to be active in simple

reaction tasks (Mulert, Gallinat, Dorn, Herrmann, & Winterer, 2003; Winterer, Adams, Jones, & Knutson, 2002). Magnetic resonance imaging (MRI) lesions in these areas produce deficits such as apraxia and slow motor performance (Pistarini, Majani, Callegari, & Viola, 1991; Rothi & Heilman, 1984; Watanabe et al., 2002).

The middle level of control programs the motor plan, specifying precise movement parameters. This level prepares for movement by encoding the duration and timing of muscle contractions necessary to carry out the mental representation of movement (Gracies, 2005a). Researchers suggest involvement of the supplementary motor area (SMA) during this encoding process, as it appears active during various stages of movement preparation (Cunnington, Windischberger, Deecke, & Moser, 2003; Lee, Chang, & Roh, 1999; Roland, Larsen, Lassen, & Skinhoj, 1980). Also, SMA forms reciprocal connections with the basal ganglia (BG) (Jurgens, 1984) of which the subthalamic nucleus shares in the role of movement preparation (Paradiso, Saint-Cyr, Lozano, Lang, & Chen, 2003). The cerebellum, in addition to SMA, is found to be involved in coordinating the timing pattern involved in movements (Mayville, Jantzen, Fuchs, Steinberg, & Kelso, 2002), thus suggesting its participation in this middle level of control (Gracies, 2005a; Watanabe et al., 2002). Injury or disease within these two levels of control (i.e. higher and middle) does not, by itself, produce paresis (Buxbaum et al., 2003; Corcos, Chen, Quinn, McAuley, & Rothwell, 1996; Fukaya et al., 2003; Mai, Bolsinger, Avarello, Diener, & Dichgans, 1988; Wiese et al., 2004).

The lower level of control's role in voluntary movement is executing movement plans, with the primary motor cortex (M1), internal capsule, and corticospinal tract assuming this function (Hanakawa et al., 2003; Roland, Skinhoj, Lassen, & Larsen, 1980). Disturbances at this level result in many primary impairments evident after central neurological injury including paresis, loss of dexterity, hyperreflexia/spasticity (Gracies, 2005a, 2005b). The following sections serve to detail individual impairments with a discussion of their pathophysiology.

Motor units

A brief review of normal force production is useful in understanding the various mechanisms underlying paresis. Sherrington first introduced the term motor units as consisting of the motoneuron and the muscle fibers it innervates. Activating motor units that innervate skeletal muscle fibers produces muscle force. Muscle force depends on not only the number of motor units but also the type of units activated (Henneman & Mendell, 1981). Motor units are classified according to type based on resistance to fatigue and twitch tension. Fast-contracting, fast-fatiguing motor units (FF) are capable of generating high twitch tension while fast-contracting, fatigue resistant (FR) and slow-contracting, fatigue resistant (S) motor units produce low-twitch tension (Burke, 1981). Although described for the cat and rat, sufficient evidence exists to suggest that human motor units are similar (Floeter, 2010).

Motor units demonstrate an orderly recruitment pattern, which affects muscle force production. Low-force motor units (S) are recruited first and, as task demands increase (i.e. force requirements increase), higher-force producing motor units (FR to FF) are recruited. As force demands decrease, motor units display the reverse pattern. Easily fatigable motor units are the first to stop firing and the slow, fatigue resistant motor units are the last to stop firing (Bourbonnais & Vanden Noven, 1989). The different types of motor units and recruitment pattern enable smooth gradation of force in either direction, increasing or decreasing. This ordered recruitment also offers a metabolic advantage since type S motor units possess favorable attributes for sustaining active force without easily fatiguing as is needed in maintaining posture (Floeter, 2010).

Firing rate of motor units also adjusts muscle force. When a motoneuron fires, the muscle fibers it innervates activate to produce a single-twitch contraction. A summation of twitch contractions over time reflects as higher force output of innervated muscles. An increase in the firing rates of active motor units effectively increases resultant muscle force (Burke, 1981; Henneman & Mendell, 1981). As with ordered recruitment, firing rates of motoneurons respond to force requirements of tasks, continuing to increase to meet the demand until the motor unit

achieves maximal force output. Although limited in output, increasing firing rates of motor units will speed the development of contraction. This shortens the time necessary to reach maximum output since individual twitch contractions summate more rapidly (Rothwell, 1987).

Upper motor neuron lesions

In classic upper motor neuron (UMN) syndrome, primary impairments result directly from injury or lesion to cortical and subcortical structures. Hughlings Jackson differentiated impairments as negative or positive features (Föerster, 1936; Jackson, 1958; Walshe, 1961). Negative features are the loss of normal motor behavior such as paresis, slowness in movement, and loss of dexterity (Burke, 1988; Landau, 1988). Positive features are characterized as being abnormal or exaggerations of behavior including increased proprioception and reflexes (spasticity) (Landau, 1980). In recent years authors classify an additional set of symptoms, termed adaptive features (Carr & Shepherd, 1998) or secondary effects. These features do not arise from the lesion, but rather develop from primary impairments (Schenkman, 1992). This reflects the typical sequence that signs manifest following upper motor neuron injury and it is likely that these features contribute to degraded functional movement after central neurological injury.

Paresis

Many regard negative features after brain injury, such as paresis, as more disabling impairments compared to positive features (Landau & Sahrman, 2002; Newham & Hsiao, 2001). Paresis is defined as decreased voluntary motor unit recruitment (Gracies, 2005a) and reflects difficulty in recruiting sufficient motor units to produce movement. It is an acute consequence of UMN lesion involving damage to descending voluntary motor command. The pyramidal tract is the executive pathway for voluntary movement (Phillips & Porter, 1977) and injury to these pathways (i.e. loss of descending control) results in loss of movement.

Following UMN lesion, inability to generate and sustain appropriate force results in weakness expressed (Bourbonnais & Vanden Noven, 1989). This phenomenon arises from

mechanisms including decreases in motor unit activation and number of motor units, changes in motor unit properties, type and firing rate, and alterations in motor unit recruitment order. Additionally, inappropriate cocontractions may contribute to expressed muscle weakness. These mechanisms are reviewed.

Decreased central voluntary activation (decreased number of motor units)

Failure of central voluntary activation reflects a decrease in the absolute number of active motor units (McComas, 1994; McComas, Sica, Upton, & Aguilera, 1973; Yang, Stein, Jhamandas, & Gordon, 1990). In fact, a study examining patients 2 to 6 months after unilateral stroke reports a reduction of approximately one half of functioning motor units (McComas et al., 1973). Another study demonstrates the mean level of maximal voluntary activation of biceps brachii to be 66 percent and 89 percent for the paretic in comparison to the nonparetic side respectively (Riley & Bilodeau, 2002). These results suggest that motoneurons undergo trans-synaptic changes following degeneration of the corticospinal tract (Dietz, Ketelsen, Berger, & Quintern, 1986; McComas et al., 1973). Additionally, there is greater difficulty recruiting high-threshold motor units, which reduces the amount of overall force (Dietz et al., 1986; Zijdwind & Thomas, 2003). A reduction in central activation of motor units has direct implications for movement since force output relies partly on number of motor units.

Changes in properties of motor unit and type

Evidence suggests that central neurological damage alters the properties of motor units. Fiber measurements taken from muscles after neurological injury show atrophy in fast-contracting fibers (those belonging to type FR or FF motor units) (Brooke & Engel, 1969; Dietz et al., 1986; Edstrom, Grimby, & Hannerz, 1973; Scelsi, Lotta, Lommi, Poggi, & Marchetti, 1984) and hypertrophy in slow-contracting fibers of type S motor units (Edstrom, 1970). The consequence of such changes contributes to diminished capacity of motor units to produce necessary force. Besides changes in properties, research suggests changes in motor unit type following neurological injury. Various authors report prolonged contraction times in paretic

muscles following stroke (McComas et al., 1973; Visser, Oosterhoff, Hermens, Boon, & Zilvold, 1985), especially fast-contracting motor units (Young & Mayer, 1982). Young and Mayer (1982) describe a class of motor units, not existing in normal muscles, with unique characteristics: slow-contracting and fatigable. Thus, muscles with a higher proportion of such motor units will fatigue more easily and be unable to sustain muscle force appropriately.

Changes in motor unit recruitment order

Conflicting evidence exists for whether central nervous system damage disrupts motor unit recruitment order. Authors even suggest alterations in motor unit recruitment ordering can contribute to weakness (Carr & Shepherd, 1998). Early studies document changes in recruitment order of tibialis anterior once fatigued (Grimby, Hannerz, & Ranlund, 1974), but this finding is not confirmed by later studies (Rosenfalck & Andreassen, 1980). In a more recent study of thenar muscles, researchers implement varying levels of stimulation to test fatigability. Researchers conclude that the normal order of recruitment from fatigue-resistant to fatigable units appears to be preserved in patients with paresis (Godfrey, Butler, Griffin, & Thomas, 2002). More evidence, using advanced recording technology, will be useful to determine whether motor unit recruitment order occurs after brain damage.

Changes in motor unit firing rate

Decreases in the firing rate of active motor units will effectively decrease the amount of force production. Research suggests that lowered firing rates of active motor units yields an overall decreased amount of tension (Rack & Westbury, 1969). In order to compensate for reduced firing rates, additional motor units are necessary in order to produce adequate levels of force or achieve the intended movement. Indeed, patients with hemiparesis following stroke exhibit increased electromyographic (EMG) activity per unit force in elbow flexors of the affected side than the unaffected (Tang & Rymer, 1981). Decreased motor unit firing rates are also reported in intrinsic hand muscles (Freund, Dietz, Wita, & Kapp, 1973) and tibialis anterior (Rosenfalck & Andreassen, 1980). One study though, did not find firing rates of gastrocnemius

to be different between the affected and unaffected sides of patients with hemiparesis (Dietz et al., 1986). Authors generally agree that decreased firing rates would ultimately contribute to muscle weakness (Rosenfalck & Andreassen, 1980; Tang & Rymer, 1981) and that this may contribute to greater sense of effort since patients would need to increase central voluntary drive.

Inappropriate and ungraded cocontraction

Abnormal patterns of muscle activation may contribute to the manifestation of muscle weakness in patients (McLellan, 1977; McLellan, Hassan, & Hodgson, 1985). This involves difficulty managing the temporal relationship between agonist and antagonist muscle pairs (Bourbonnais & Vanden Noven, 1989). Individuals without neurological disease demonstrate coactivation of agonist/antagonist muscles across a joint during normal postural (Keshner, Allum, & Pfaltz, 1987) and voluntary movements (Smith, 1981). Patients following stroke also demonstrate cocontraction in gait (Conrad, Benecke, & Meick, 1985; Dietz, Quintern, & Berger, 1981; Knutsson & Richards, 1979) and in other voluntary movements (Angel, 1975). These findings could reflect a lack of skill, such that patients may involuntarily cocontract muscles to adapt to poor strength or control of limbs.

Cocontraction of antagonist muscles interferes with movement and potentially limits force generation when activated inappropriately (Bourbonnais & Vanden Noven, 1989). In fact, researchers found this to be the case when comparing active and passive movements in patients with spastic paresis. Their results indicate that restraint from antagonist is greater in voluntary movements compared to passive movements and more common with higher than lower velocity movements (Knutsson & Martensson, 1980; McLellan, 1977). The authors posit that inappropriate cocontraction results from misguided descending control during voluntary movements (Knutsson & Martensson, 1980). Despite these results, abnormal cocontraction and ‘antagonist restraint’ are merely hypothesized to underlie observed weakness in patients. Further details concerning cocontraction will be discussed in a later section.

Slowness in muscle activation

Another negative feature often present after UMN lesion is slowness of motor unit activation. This refers to the inability to generate force quickly enough to carry out the intended movement at an appropriate speed (Carr & Shepherd, 1998). Patients after stroke demonstrate a slowness in movement in walking (Giuliani, 1990) and in sit to stand (Ada & Westwood, 1992). Authors suggest that slow and fast movements appear to suffer from the slowness of initiating movements (Knutsson & Martensson, 1980). It appears though, the capacity to generate force is more impaired in higher velocity movements. Patients seem to express greater difficulty developing sufficient force to move at high velocities (Bohannon & Smith, 1987). An EMG study reports delayed EMG activity before fast movements due to prolonged contraction time for maximum tension to accrue (Tsuji & Nakamura, 1987). The authors suggest this is in part attributable to the loss of fast corticospinal descending neurons.

Muscle overactivity

Muscle overactivity emerges in the subacute and chronic stages following disruption of descending motor systems and refers to “increased involuntary motor unit recruitment” (Gracies, 2005b). Muscle overactivity reflects difficulty in arresting active motor units and is observable during movement and rest. Spastic overactivity includes spasticity, spastic dystonia, and spastic cocontraction, all which are stretch-sensitive (i.e. affected by recruitment of stretch receptors) and may lead to changes in motor and spinal neuron excitability (Gracies, 2005b).

Reconfiguration of central nervous system

After damage to the descending motor pathway, the central nervous system undergoes changes that contribute to spastic overactivity. Axonal sprouting serves as a mechanism of neural compensation and occurs at spinal levels (Weidner, Ner, Salimi, & Tuszynski, 2001). The result of such changes is the emergence of excessive abnormal reflexes. Neural changes also take place at higher levels, which involves undamaged corticospinal neurons forming synapses with motor neurons (Farmer, Harrison, Ingram, & Stephens, 1991). The prevailing hypothesis

suggests that these adaptive neural changes contribute to the development of muscle overactivity (Chapman & Wiesendanger, 1982; Gracies, 2005b).

Spasticity

While paresis is considered a more disabling impairment after UMN lesion (Landau & Sahrman, 2002; Newham & Hsiao, 2001), spasticity occupies more of the neuroscience and rehabilitation literature to date. Spasticity is a positive sign that occurs after damage to descending motor systems. Clinicians and scientists use 'spasticity' to describe a wide range of sequelae associated with brain lesions including hyperactive stretch reflexes, abnormal limb posturing, excessive cocontraction of antagonists, clonus, and resistance offered to passive movement (Carr & Shepherd, 1998; Shumway-Cook & Woollacott, 2007). Carr and Shepherd (1998) even suggest that clinicians use the term 'in a generic sense', encompassing all phenomena following UMN lesion and this lack of consensus fosters miscommunication amongst professionals. The now widely accepted definition of spasticity is "a motor disorder characterized by a velocity-dependent increase in stretch reflexes (muscle tone) with exaggerated tendon jerks resulting from hyperexcitability of the stretch reflex as one component of the upper motor neuron syndrome (Lance, 1980).

Spasticity is triggered specifically by the phasic component of the stretch reflex, which responds to quick abrupt stretch of muscle. Abnormal muscle activity therefore reflects alterations in the stretch reflex mechanism. Some individuals attribute that changes in threshold and/or gain of the stretch reflex lead to increased stretch-sensitivity. These studies demonstrate consistently the various changes in the stretch reflex threshold or gain in spastic muscles (Katz & Rymer, 1989; Latash, Gelfand, Li, & Zatsiorsky, 1998; Powers, Campbell, & Rymer, 1989; Thilmann, Fellows, & Garms, 1991).

Studies compare joint torque for elbow extension in normal subjects and patients with spastic hemiparesis. Patients with spastic elbow flexors demonstrate increased EMG activity at a velocity of 112 degrees/sec compared to normal subjects who did not exhibit significant

stretch response at the same velocity. Results indicate a linear relationship between EMG magnitude of spastic muscles and stretch velocity, as similar to previous reports (Ashby & Burke, 1971; Burke, Gillies, & Lance, 1970, 1971). The two groups did not differ; however, with respect to stretch reflex gain. Given these findings, researchers postulate that decreased stretch reflex threshold, and not increase in gain, accounts for increased EMG of muscles in response to stretch (Katz & Rymer, 1989; Powers et al., 1989).

Researchers also use EMG activity as a means to measure degree of reflex response to limb displacement. Thilmann and colleagues (1991) reports EMG response of biceps brachii muscle to passive elbow extension at varying displacement velocities from 35 to 300 degrees/sec. The 12 normal healthy subjects consistently exhibit reflex responses only at velocities above 175 degrees/sec. Patients with spastic hemiparesis; however, demonstrate early reflex response, at velocities as low as 110 degrees/sec and late EMG activity persisting at velocities as low as 35 degrees/sec. These results demonstrate that EMG activity is highly correlated with displacement velocity and duration of imposed stretch. The authors suggest that imposed stretch in patients with spastic hemiparesis is related to a pathological increase in stretch reflex gain (Thilmann, Fellows, & Garms, 1991).

Spastic dystonia

In spastic dystonia, muscles are unable to rest and are overactive proportionally to the stretch imposed on the muscle. This type of spastic overactivity is triggered primarily by the tonic component of the stretch reflex. Denny-Brown (1996) identifies spastic and dystonic features to be present simultaneously in muscle groups. Muscles exhibiting spastic dystonia respond to the degree and duration of tonic stretch imposed on those muscles (Denny-Brown, 1996). Studies demonstrate persistent tonic muscle contraction in both decerebrate animals (Pollock & Davis, 1930) and monkeys with brain damage (Denny-Brown, 1996). Motor units of paretic muscles are characterized with decreased derecruitment compared to recruitment thresholds (Zijdewind & Thomas, 2003) and thus, fail to cease firing even with feedback.

Spastic cocontraction

Spastic cocontraction is the inappropriate motor unit recruitment of antagonist muscles during voluntary command of agonist and occurs in the absence of phasic stretch (Gracies, 2005b). Cocontraction (i.e. concurrent activation of agonist and antagonist) itself is not inherently pathological as it occurs in normal movement (Aagaard et al., 2000; Smith, 1981) and decreases as skills increase with practice (Enoka, 1997). With the exception of relatively few studies, general consensus exists regarding evidence of abnormal cocontraction in patients with spastic paresis (Dewald, Pope, Given, Buchanan, & Rymer, 1995; el-Abd, Ibrahim, & Dietz, 1993; Gracies, Wilson, Gandevia, & Burke, 1997; Hammond et al., 1988; Knutsson & Martensson, 1980; Knutsson & Richards, 1979; Levin, Selles, Verheul, & Meijer, 2000; McLellan, 1977; Wing, Lough, Turton, Fraser, & Jenner, 1990).

Cocontraction is abnormal in patients with spastic paresis because it is excessive. Spastic cocontraction thus is inappropriate activation of antagonist muscles when attempting to selectively activate agonist for movement. Traditionally, abnormal cocontraction is considered a limiting factor in the execution of voluntary movement following neurological injury since it contributes to muscle weakness (Bobath, 1978; Knutsson, Martensson, & Gransberg, 1997; Knutsson & Richards, 1979). The mechanism underlying this assumption is that excessive activation of antagonist would prevent sufficient generation of agonist force, a concept termed 'antagonist restraint' (Bobath, 1978) or 'spastic restraint' (Knutsson & Richards, 1979). Inappropriate, concurrent activation of antagonist is therefore proposed to limit or prevent active limiting of the agonist.

While there is tradition in considering muscle overactivity to be a limiting factor in voluntary movement, results from studies to date do not support this idea. Many researchers still consider this topic controversial (Ada, Vattanasilp, O'Dwyer, & Crosbie, 1998; Landau, 1974; O'Dwyer, Ada, & Neilson, 1996; Sahrman & Norton, 1977). In fact, recent evidence contradicts previous findings, suggesting that spastic overactivity does not contribute significantly to

constraints in movement after CNS damage. Studies repeatedly fail to establish a strong causal relationship between antagonist activity and muscle weakness (Bohannon, 1991; Gowland et al., 1992; Newham & Hsiao, 2001; O'Dwyer et al., 1996). In a recent study of 95 patients, researchers report almost an even number of patients with and without spasticity that exhibited severe motor impairments. The authors conclude a low overall correlation between spasticity and functional limitation in patients 3 months after first time stroke (Sommerfeld, Eek, Svensson, Holmqvist, & von Arbin, 2004). The accumulating evidence against the 'antagonist restraint' hypothesis demonstrates diminished or insufficient agonist activation as the primary contributor to movement impairment (Adams, Gandevia, & Skuse, 1990; Bohannon & Andrews, 1990; Dietz et al., 1981; Gowland et al., 1992; McLellan & Maclellan, 1973; Miller & Light, 1997; Patten, Lexell, & Brown, 2004; Sahrman & Norton, 1977; Tang & Rymer, 1981).

Pathophysiology of spastic overactivity

The types of spastic overactivity Gracies (2005) identifies are defined by their triggering factor, phasic muscle stretch, tonic muscle stretch, or volitional command. The proposed pathophysiology of spastic overactivity is similar in that increased reflex stretch-sensitivity leads to changes in muscle response and activity. Proposed pathophysiological mechanisms of spastic overactivity are reviewed below.

Alpha-motor neuron excitability

Direct human evidence for alpha-motor neuron hyperexcitability after CNS damage does not exist. Early studies involving decerebrate animals demonstrate persistent tonic contractions in the absence of stretch reflex (Pollock & Davis, 1930). Researchers suggest that the loss of descending input, along with changes in spinal motor neurons and collateral sprouting of excitatory afferents (Wong, Atkinson, & Weaver, 2000), underlie alpha-motor neuron hyperexcitability leading to abnormal increases in stretch reflex.

Human studies on CNS damage rely upon methods that, at best, infer changes indirectly in alpha-motor neurons including increased Hmax/Mmax ratios (Angel, 1975) and changes in

motor neuron firing patterns (Edstrom et al., 1973). Recent research is advancing though, and researchers believe that changes in recruitment gain in motor neuron pools could contribute to spastic overactivity (Kernell & Hultborn, 1990). Hyperexcitability of alpha-motor neuron pools is suggested to be due to loss of descending inhibition, denervation supersensitivity, shortening of dendrites, and collateral sprouting (Mayer, Esquenazi, & Childers, 1997; Noth, 1991), yet Gracies (2005) argues that this does not represent direct evidence.

Presynaptic inhibition and homosynaptic depression

Decreased presynaptic inhibition on Ia afferent fibers is proposed to contribute to spastic overactivity. Presynaptic inhibition is a mechanism that prevents neurotransmitters from synapsing presynaptically, thus not generating excitatory postsynaptic potentials (EPSPs). Tendon vibration elicits discharge of Ia fibers (Burke, Hagbarth, Lofstedt, & Wallin, 1976) and depresses the H-reflex (De Gail, Lance, & Neilson, 1966). Patients with spastic paresis demonstrate an inability to inhibit the H-reflex (Burke & Ashby, 1972; Iles & Roberts, 1986; Somerville & Ashby, 1978) as compared to normal healthy subjects. This finding, termed homosynaptic depression (Hultborn et al., 1996), may amplify responses to tonic stretch. Presynaptic inhibition of Ia afferent fibers is also observed to be decreased in patients with spastic paresis (Aymard et al., 2000; Faist, Mazevet, Dietz, & Pierrot-Deseilligny, 1994; Nielsen, Petersen, & Crone, 1995). Without appropriate presynaptic inhibition, facilitatory input from stretch receptors could potentially be increased, thus enhancing muscle contractions in response to both phasic and tonic stretch (Gracies, 2005b).

Pathophysiology of spastic cocontraction

The aforementioned pathophysiological mechanisms may certainly contribute to the development of spastic cocontraction. Spastic cocontraction is likely due to abnormal patterns of descending drive (Dewald et al., 1995; Farmer et al., 1991; Gracies et al., 1997). Dewald and colleagues (1995) studied patients with hemiparesis performing a series of isometric contractions and identified multiple coactivation relationships across all subjects. An interesting

finding is that patients with spastic paresis demonstrate novel coactivation patterns, to which is attributed to a reduction in possible muscle combinations. The authors hypothesize this to represent loss of descending pathways and compensation from remaining brainstem pathways (Dewald et al., 1995). Additional mechanisms pertaining specifically to spastic cocontraction are considered.

Recurrent inhibition

The concept of inhibition is relevant especially to the discussion of muscle overactivity, particularly in the case of spastic cocontraction. Descending voluntary drive arises from activation of alpha-motor neurons, which are regulated postsynaptically by recurrent inhibition (Gracies, 2005b). Recurrent inhibition is a mechanism where activation of postsynaptic neurons excites motor axon collaterals that activate interneurons that, in turn, inhibit the original postsynaptic neurons. This interneuron is the Renshaw cell, which is influenced by supraspinal pathways that can either increase or decrease recurrent inhibition (Baldissera, Hultborn, & Illert, 1981). If CNS pathology inhibits Renshaw cell activity, response to tonic stretch could increase since alpha-motor neurons would be less opposed by recurrent inhibition (Gracies, 2005b). Researchers investigating this mechanism in humans demonstrate that recurrent inhibition is actually increased at rest in patients with spastic paresis (Katz & Pierrot-Deseilligny, 1982, 1999). Implications of increased Renshaw inhibition is important in possibly contributing to decreased reciprocal Ia inhibition (Hultborn, Jankowska, & Lindstrom, 1971a, 1971b, 1971c).

Ia reciprocal inhibition

Descartes and Sherrington both described reciprocal innervation as the principle governing control of agonist and antagonist muscle pairs. This allows muscle pairs across a joint to produce smooth movement when contraction of the agonist is directly proportional to relaxation of the antagonist. This mechanism of reciprocal inhibition is disynaptic and regulated via Ia afferents, in particular the Ia inhibitory interneuron (Laporte & Lloyd, 1952). It is likely that Ia inhibitory interneuron function is disrupted following damage to voluntary descending

pathways, including the corticospinal tract (Day, Rothwell, & Marsden, 1983; Iles, 1986; Iles & Pisini, 1992; Tanaka, 1974). According to Gracies (2005), this disruption may result in two distinct manifestations; dependent upon whether an increase or decrease in Ia reciprocal inhibition exists. The decrease in Ia reciprocal inhibition arises as a likely mechanism for spastic cocontraction since antagonist muscles act with less opposition. Indeed, evidence during voluntary contraction of agonist in patients with spastic paresis demonstrates absence of both normal increases in Ia reciprocal inhibition and increases in presynaptic inhibition on Ia afferents, both directed towards the antagonist (Morita, Crone, Christenhuis, Petersen, & Nielsen, 2001). Additionally these two mechanisms appear to only be observed in patients with spastic paresis, not normal healthy individuals (Gracies, 2005b).

Adaptive secondary impairments

CNS pathology involving damage to descending executive pathways gives rise to primary impairments, which lead to the development of secondary impairments that also influences functional movement. Negative features are more associated with disuse as is evident in the nature and pathology (i.e. decreased central voluntary activation, changes in motor unit firing rate, etc.). Limb disuse is the lack of central voluntary command exerted on the limb, while immobilization involves the peripheral consideration about a joint. Both are observable and often co-occur in patients with damage to executive pathways (Gracies, 2005a). Acute effects of immobilization is proposed to contribute to peripheral changes documented in muscles and joints while central effects are realized later, leading to changes in the central nervous system. The peripheral and central effects and consequences of such immobilization and disuse following neurological injury are discussed.

Peripheral effects of immobilization

Muscle contracture

Paresis, as reviewed, results in immobilization of muscles affected by the central injury. The consequences of such is that it causes peripheral changes including muscle unloading, an

initial mechanism of muscle contracture (Gracies, 2005a). Studies demonstrate the various changes in muscle that occur including atrophy, loss of sarcomeres, and accumulation of connective tissue and fat (Tardieu, Tardieu, Colbeau-Justin, Huet de la Tour, & Lespargot, 1979; Williams & Goldspink, 1984).

Muscle atrophy

Atrophy is the wasting or loss of muscle mass and can occur because of paresis. Muscle atrophy, though, does not necessarily account for reduced central muscle activation (i.e. paresis) (Hafer-Macko, Ryan, Ivey, & Macko, 2008). In subjects with no known central neurological injury causing paresis, atrophy results from prolonged limb immobilization. Researchers document changes in muscles such as decreased fiber diameter, reduced cross-sectional area and volume (Veldhuizen, Verstappen, Vroemen, Kuipers, & Greep, 1993; White, Davies, & Brooksby, 1984; Yue, Bilodeau, Hardy, & Enoka, 1997). Following four weeks of immobilization, quadriceps cross-sectional area are diminished 21% with muscle biopsies revealing a 16% decrease in muscle fiber diameter (Veldhuizen et al., 1993). Another study reports biceps brachii cross-sectional area diminished approximately 11% after the same period of immobilization (Yue et al., 1997). A recent review in the sports literature reveals many of the same changes related to muscle atrophy after immobilization and disuse and suggests that these processes may lead to a vicious cycle of musculoskeletal degeneration (Appell, 1990). A recent study using a cross sectional design compares the lean mass of the paretic and nonaffected legs, thighs, and arms in 60 patients more than 6 months after stroke. Structural changes are documented in skeletal muscles with leg, thigh, and arm lean mass lower 4%, 3%, and 7%, respectively in the paretic side and a 20% lower mid-thigh muscle cross-sectional area (both $p < 0.001$) (Ryan, Dobrovolny, Smith, Silver, & Macko, 2002). Another research group involving 35 patients after stroke and also document reduced lean muscle mass on the paretic compared to the nonparetic side (Celik, Ones, & Ince, 2008). Correlation analysis reveals that lean muscle mass loss increased with time since stroke. Reduced muscle mass is also

observed in patients 6 weeks after incomplete spinal cord injury (Gorgey & Dudley, 2007).

Taken together, researchers suggest that muscle atrophy does occur after upper motor neuron lesion and that it may contribute to functional disability. Decreased muscle volume of mid-thigh in patients after stroke correlates positively with Barthel Index, a measure of functional performance in activities in daily living (Metoki, Sato, Satoh, Okumura, & Iwamoto, 2003).

Loss of sarcomeres

Immobilization causes adaptive changes in the number and length of sarcomeres dependent upon prolonged position, lengthened or shortened. Studies in animals reveal addition of sarcomeres in lengthened muscle positions and sarcomeres lost when muscles are immobilized in a shortened position (Tabary, Tabary, Tardieu, Tardieu, & Goldspink, 1972). Sarcomeres are shortened when muscles are immobilized in a shortened position, thus muscles are unable to develop maximal tension. Reducing the number of sarcomeres, in conjunction with increasing sarcomere length, appears to overcome this by returning sarcomere length to optimum (Williams & Goldspink, 1978). Conversely, when muscles are immobilized in a lengthened position, sarcomere numbers increase associated with a decrease in sarcomere length (Tabary et al., 1972). Thus, authors seem to suggest that adaptations appear to be associated with imposed length of immobilization rather than immobilization itself. More important is the finding that sarcomere number and length are recovered or restored once immobilization is discontinued (Booth & Seider, 1979; Williams & Goldspink, 1973). The implications of adaptive changes in sarcomeres is important to understand, and particularly relevant, since damage to descending motor pathways contribute to immobilization and disuse (Appell, 1990).

Changes in connective tissue

While spastic overactivity is a neural mechanism underlying difficulty with functional movement, mechanical changes in tissues may also contribute. Animals demonstrate significant changes in intramuscular tissue followed by a period of immobilization, possibly contributing to

decreased extensibility (Jarvinen, Jozsa, Kannus, Jarvinen, & Jarvinen, 2002). Akeson (1973) describes the response of animal connective tissue to immobilization and documents that changes in connective tissue are due in part to water loss and collagen deposition. In fact, researchers find an increase in the overall ratio of collagen to muscle-fiber tissue (Tabary et al., 1972; Williams & Goldspink, 1978, 1984; Witzmann, Kim, & Fitts, 1982).

Similar results exist in humans such that researchers attribute resistance to passive movements to spastic overactivity and changes in mechanical properties of muscle, tendon, and connective tissue associated with immobilization and disuse (Berger, Horstmann, & Dietz, 1984; Carey & Burghardt, 1993; Dietz et al., 1981; Hufschmidt & Mauritz, 1985; Thilmann, Fellows, & Ross, 1991). Separate studies document decreased ankle movements, during walking, that cannot be accounted for by abnormal or overactive reflex response in patients with spastic paresis (Berger, Quintern, & Dietz, 1982; Dietz & Berger, 1983; Dietz et al., 1981). In subsequent investigations, these researchers investigate the reflex behavior and muscle tension of the upper limbs of patients with spastic paresis, comparing paretic to nonparetic side. The results indicate elbow EMG activity to be reduced and suggest that it is not the cause of muscle stiffness. Instead that changes in connective tissue underlie the observed upper limb resistance (Dietz, Trippel, & Berger, 1991). Thilmann and colleagues (1991) also argue that altered properties of soft tissue, including connective tissue, contribute to joint stiffness.

Increased intramuscular fat

Along with changes observed within muscle fiber composition, evidence for increased fat content is scarce. A study involving patients in the chronic stage of stroke (more than 6 months post injury) show significant differences in fat content between paretic and nonparetic side (Ryan et al., 2002), a finding more marked in the paretic arm than leg. The increased low-density lean mid-thigh tissue in the paretic leg versus nonparetic is an indication of greater intramuscular fat relative to muscle area. Decreased mid-thigh muscle area and greater fat infiltration in muscle is associated with poorer lower extremity performance as measured by 6-

meter walks and repeated chair stands (Visser et al., 2002). In a separate study investigating body composition in patients after stroke, no significant differences in fat content is evident between the paretic and nonparetic side (Celik et al., 2008), although the study confirms loss of lean body mass and bone mineral density.

Central effects of disuse

Paresis manifesting after damage to descending motor pathways contributes to a vicious cycle; disuse leading to CNS changes that may further decrease central voluntary command (Gracies, 2005a). Recent evidence in human studies reveal CNS adaptations resulting from chronic patterns of physical activity (Kleim, Jones, & Schallert, 2003), a phenomenon researchers termed 'learned non-use' (Taub et al., 1994). During prolonged periods of immobilization and disuse, reduced active movement is believed to alter CNS activity, particularly decreased motor neuron recruitment capacity (McComas, Miller, & Gandevia, 1995). Central nervous system consequences of immobilization and disuse are reviewed.

Failure of activation

Following immobilization or disuse, the central nervous system undergoes various changes affecting voluntary activation. In addition to decreasing motor unit size and number, the maximal firing rate also decreases in all motor units (Gracies, 2005a). One study examines the motor unit properties such as recruitment and firing rate in the abductor pollicis and first dorsal interosseus muscles following six to eight weeks of immobilization. In both muscles during voluntary isometric contraction, decreases in maximal firing rate of motor units are documented, although this decrease appears more striking for motor units with lower thresholds (Duchateau & Hainaut, 1990). The authors suggest that reduced ability to activate motor units could account for the decrease in maximal firing rate (Fuglsang-Frederiksen & Scheel, 1978), implying that changes in motor unit behavior reflect neural adaptation to disuse (Duchateau & Hainaut, 1990). Taken together authors hypothesize that disuse reduces the capacity for voluntary activation (Duchateau & Hainaut, 1987; McComas, 1994).

Decreased maximal force

The ability the CNS to develop maximal voluntary force in muscles declines even after brief immobilization. Numerous studies demonstrate decreased maximal power after bed rest (Berg, Larsson, & Tesch, 1997; Ferretti et al., 2001; Suzuki et al., 1994) and muscle immobilization (Duchateau & Hainaut, 1987, 1991; Hortobagyi et al., 2000; Sale, McComas, MacDougall, & Upton, 1982; White et al., 1984; Yue et al., 1997). White (1984) studied maximal force of triceps surae after immobilization by casts for two consecutive weeks. The authors report that strength declined 11% after the first week and 24% after week two, suggesting that short-term immobilization results in diminished capacity of muscles to develop maximal force. Similar findings exist in muscles of the hand following periods of immobilization with reports of declines in maximal voluntary force of adductor pollicis by 55% after six weeks (Duchateau & Hainaut, 1987) and thenar muscles by 42% after five weeks (Sale et al., 1982). The reduction in maximal force appears to increase with duration of immobilization or disuse (Grogor'eva & Kozlovskaia, 1987) but not proportionate to observed decreases in cross-sectional muscle area (Suzuki et al., 1994). Self-imposed disuse after neurological injury can produce comparable results as weakness develops in the relatively unaffected limb acutely (Hultborn et al., 1971b) and in the chronic stage (Colebatch & Gandevia, 1989).

Secondary contributions to adaptive impairments

Paresis is an acute impairment following damage to descending motor control that results in decreased movement. Since it is an immediate effect of the primary lesion, immobilization and disuse are primary factors that contribute to the development of adaptive soft tissue contracture. The previous sections highlighted consequences of muscle contracture from immobilization and disuse, both peripheral and central. The time course for development of muscle overactivity occurs in the chronic, sometimes subacute, stage after neurological injury. Thus, muscle overactivity is thus proposed to be a secondary contributor to muscle contracture.

Muscle overactivity also facilitates the development of another vicious cycle involving reciprocal potentiation between contracture and spastic overactivity (Gracies, 2005b; O'Dwyer et al., 1996)

Reducing muscle overactivity is suggested to decrease adaptive tissue shortening or muscle contracture. Reverse experiments demonstrate this in animals and patients with spastic paresis. In these experiments, researchers study whether intramuscular botulinum toxin A would prevent the development of calf muscle contracture in spastic hereditary mice. The authors report that muscles of spastic mice injected with botulinum toxin A grew to within two percent compared to normal mice, a highly significant finding. These authors suggest that decreasing muscle overactivity potentially limits muscle shortening and atrophy (McLachlan, 1983).

Randomized trials also confirm similar results (Cosgrove & Graham, 1994), which are suggested to apply also to patients with spastic paresis. Indeed, recent findings in children with cerebral palsy report increase in length of lower extremity muscles after repeated botulinum toxin injections (Eames et al., 1999; Thompson, Baker, Cosgrove, Corry, & Graham, 1998).

Conclusions

This review serves to elucidate impairments observed following upper motor neuron lesion, particularly to executive descending motor pathways. The primary impairments are reviewed along with underlying mechanisms. Paresis is an immediate effect of UMN lesions and results primarily from decreased central activation of motor units. Motor unit properties including type, firing rate and recruitment order are associated with expressed muscle weakness in patients. The subacute and chronic stage following UMN lesion is often when patients manifest positive features, mainly muscle overactivity. The different types of muscle overactivity are reviewed, including specific pathophysiological mechanisms for spasticity overactivity and spastic cocontraction. Increased stretch reflex response and decreased inhibition are the prominent mechanisms for muscle overactivity after neurological damage.

With prolonged periods of immobilization and/or disuse induced by paresis, muscles are susceptible to adaptation, either shortening or lengthening depending upon position.

Immobilization and disuse brings about notable alterations in muscles and connective tissues, features that intensify with increasing duration. When allowed to persist, these individual impairments contribute to each other and thus form a detrimental cycle of paresis-disuse-paresis. Similar to the paresis-disuse-paresis cycle, a second vicious cycle of overactivity-contracture-overactivity is proposed to develop in parallel.

It is essential that these features arising from UMN lesion be clarified. Scientists and clinicians alike mistaken these signs and symptoms and this only facilitates miscommunication. The aim of the present review is to make clear the numerous features and impairments commonly observed following damage to descending motor control. These are important to distinguish and further consider since a genuine understanding of features influences research questions as well as clinical decisions. Without such clarity, decisions made may result in poor outcomes for patients, present and future.

Appendix C: Comprehensive Literature Review III

Background Concepts in Stroke Rehabilitation

This work was approved February, 2011.

Introduction

The present review aims to clarify important concepts and considerations in stroke rehabilitation. Of particular interest are movement difficulties that arise as a result of the initial neurological insult. The following review will present underlying concepts related to disease, health, and human functioning by reviewing briefly conceptual models of disability serving as a bridge to discuss the implications for stroke rehabilitation. Rehabilitation clinicians select interventions based on a variety of factors in an effort to optimize function and work towards collaborative goals established by the therapist and patient. It is imperative to understand fully functional movement limitations, including how and to what extent underlying impairments contribute. Without such clarity, selection of interventions may not achieve the most optimal outcomes, an important consideration in light of current health care reimbursement and restrictions on rehabilitation coverage. The present review will not discuss specific interventions in stroke rehabilitation, but will instead discuss evaluation and assessment as a vital component leading up to the intervention planning.

Conceptual models

Before discussing recovery after stroke, it is important to first establish basic definitions of concepts given that effective communication amongst professionals is fundamental to the rehabilitation process. Conceptual models of disability describe the various consequences of disease or injury and influence on the person. These models are useful and parallel well with clinical health care models comprised of evaluation, diagnosis, prognosis, and intervention. Conceptual models contribute to important concepts related to health and disability (Barnes & Mercer, 2003). Prominent models include the statistical model, medical model and, most pertinent to the present discussion, the behavioral or disablement model (Umphred, 2007). The medical model is one that attributes disability as a feature of the person resulting directly from an underlying disease or health condition. In this model then, interventions target the individual in an effort to 'fix' or 'correct' the person. The social model views disability, not as an

attribute of the person, but instead as a socially-created problem. The unaccommodating and rigid environment, physical and social, creates the disability and often demands a political response. Neither model alone is adequate; although each is valid to a degree. Disability is complex (Badley, 1995; Fougereyrollas et al., 1998; Verbrugge & Jette, 1994; WHO, 2001) and can result from numerous circumstances; entirely internal features of the person, entirely external considerations, and an interaction between features of the person and the overall context. The biopsychosocial model attempts to integrate aspects of both the medical and social models of disability (Engel, 1977). This model views disability as the consequence of the interaction of biological, individual, and social factors and is the basis of contemporary frameworks.

Nagi's model of disablement

The disablement model is a model that describes the interaction of separate phenomena important to rehabilitation. Conceptualized by Nagi in the 1960's, this model proposes four distinct phenomena, active pathology, impairment, functional limitation and disability (Nagi, 1964, 1965, 1991). This model defines active pathology as disease or injury causing disturbances at the molecular and cellular level and the body's associated response. An example is cerebrovascular accident or stroke and the corresponding coping mechanisms in response to the injury (i.e. resolution of edema and ischemic penumbra and reorganization of the central nervous system). Active pathology can result in impairments, which refers to a loss or abnormality in function at the body system level. Impairments such as cardiopulmonary deconditioning or muscle weakness can occur at the site of pathology or elsewhere in the body. Functional limitations denote certain restrictions in activity and/or performance of the person. These functional limitations can, but are not necessarily associated with impairments. Such functional limitations may include difficulty with managing various activities of daily living (ADLs) and disturbances in gait and mobility.

Nagi viewed disability as a “limitation in performing socially defined roles and tasks expected of an individual within a sociocultural and physical environment” (Nagi, 1991). Disability exists as a discrepancy between a person’s capacity to function and the demands of an environment, physical or social. The disablement model proposes that similar underlying pathologies can produce, but does not necessarily predict, different patterns and levels of disability (Kelly-Hayes et al., 1998). Nagi’s model of disablement assumes a linear progression of response to an injury, disease or underlying health condition. The unfortunate consequence of this assumption is that disability is static, instead of a dynamic complex process (Badley, 1995; Fougeyrollas et al., 1998; Verbrugge & Jette, 1994; WHO, 2001).

World Health Organization model

The World Health Organization (WHO) is responsible for developing a similar framework that describes concepts related to disease and health conditions. WHO’s work in 1980 led to the development of the International Classification of Impairments, Disabilities, and Handicaps (ICIDH) (WHO, 1980). Much like Nagi’s disablement model, the ICIDH framework identifies and defines impairments, disabilities, and handicaps as separate ideas. The original intent of the ICIDH was to organize information about disease consequences (Haber, 1990). Facing criticism over the years, WHO eventually released major revisions to their original classification of disability in 2001, the International Classification of Functioning, Disability, and Health (ICF) (WHO, 2001). The emphasis of the revised framework shifts away from the traditional medical/disablement model to an enablement model based on the biopsychosocial model, representing an integration of both the medical and social models. Rather than disability, the ICF focuses on health and human functioning that change in accordance with the dynamic interaction of underlying health conditions and various contextual factors. The ICF provides a useful forum for discussing how underlying impairments affect functional outcomes, a basic concept to rehabilitation clinicians.

The ICF framework (WHO, 2001) identifies that function exists at three distinct levels: body, person, and the person in their environment. Within these levels are three separate domains of body functions and structures, activities, and participation, which roughly correspond to the previous Nagi and ICDIH models. The ICF defines body functions as physiological functions of the body whereas body structures are the anatomical parts of the body, such as organs and limbs. ICF defines activities as the execution of a given task or action by the person and participation as involvement in a life situation. ICF denotes disability as a decrease of functioning at any particular level. The ICF framework advocates the use of qualifiers to determine the presence of disability within a particular domain. Impairments are problems existing at the body function and structure level, which can be temporary or permanent in nature. Activity limitations indicate difficulty carrying out tasks or activities while participation restrictions represent disability in the participation domain.

The ICF, although an improved version of the ICIDH, still receives criticism and is far from being a comprehensive product (Hemmingsson & Jonsson, 2005). Since its release, disability researchers push to develop more clear definitions and expand the theoretical ideas of the ICF. For example, researchers believe that the ICF framework lacks overall clarity (Imrie, 2004). Imrie even suggests that a simple lack of clarity can lead to conflicting interpretations by practitioners. Barnes (2000) identifies that disability rights communities may not widely accept the ICF classification system, citing that labeling and classifying people with disabilities leads to stigmatization. Perhaps the most apparent shortcoming of the ICF framework is its lack of consideration of the subjective experience of the person, an observation shared by several authors (Hemmingsson & Jonsson, 2005; Perenboom & Chorus, 2003; Ueda & Okawa, 2003; Wade & Halligan, 2003). This is particularly the case with regards to the participation domain, defined as “involvement in a life situation” (WHO, 2001). Authors question whether an outsider can gauge participation and suggest instead that the respondent is best suited (Perenboom & Chorus, 2003) arguing that mere observation of a person performing a task in a life situation is

not sufficient to qualify as “participation”. Thus, several studies question whether participation can be considered outside of the person’s subjective experience (Hemmingsson & Jonsson, 2005; Perenboom & Chorus, 2003). In addition to the absence of subjective input, authors find it challenging to define clearly the various qualifiers (Steiner et al., 2002), which influences determining presence of disability at any given level of function.

ICF and rehabilitation

Conceptual models describing various concepts related to disease and disability are useful in several regards. The field of rehabilitation, particularly effective stroke care, is characterized by a coordinated multidisciplinary team approach to patient care (“Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. Stroke Unit Trialists' Collaboration,” 1997; Langhorne & Pollock, 2002). Researchers and clinicians from various professions including physiology, neuroscience, medicine, and occupational and physical therapy find themselves involved in stroke rehabilitation. Much debate occurs within a profession and arguably, more may occur between professions concerning terminology, which engenders miscommunication. Patient care would benefit greatly as rehabilitation disciplines and patients alike could use common language with which to discuss disability and related outcomes. WHO contends that the ICF framework will serve as “an essential basis for the standardization of data concerning all aspects of human functioning and disability around the world” (WHO, 2001). Although inherent, universal language and terminology would also facilitate better understanding of the complex interaction of various factors involved in disability and health. The ICF framework and definitions is useful in rehabilitation care as it would aid clinicians in understanding how underlying impairments relate and contribute to functioning and disability (Steiner et al., 2002)

The field of rehabilitation emerges as the most likely candidate to make use of the models and corresponding views of disablement and health. Drawing from the public health literature, four separate health strategies exist: prevention, cure, rehabilitation, and support

(IOM, 1991), each with a distinct goal. The primary goal of rehabilitation is optimal functioning, achieved by applying integrative approaches to optimize an individual's capacity (Stucki, Cieza, & Melvin, 2007). The interdisciplinary management of an individual's functioning and health entails minimizing symptoms and the potential disability arising from an underlying health condition. Previous definitions of rehabilitation derive their meaning from a medical model and are criticized for a narrow perspective (Bickenbach, Chatterji, Badley, & Ustun, 1999). As reviewed, the medical model assumes an inherent need for the individual with a disability to achieve social integration (WHO, 1980). Along with revisions to the ICIDH, definitions of rehabilitation should therefore be more comprehensive and be based on human functioning and health (Bickenbach et al., 1999).

In light of the criticisms, authors now use the ICF as the basis for describing rehabilitation. Many regard the ICF as the most comprehensive model of functioning and disability, including the World Health Assembly with their approval in 2001 (Stucki, 2005). Rehabilitation is broadly defined as “a health strategy that...aims to enable people with health conditions experiencing or likely to experience disability to achieve and maintain optimal functioning in interaction with the environment” (Stucki et al., 2007). This definition implies that rehabilitation involves more than simply management of the individual; rather it encompasses consideration of facilitating an individual's capacity within the environment.

Overview of components of stroke rehabilitation

The aim of the present review is to elucidate background concepts important to the discussion of stroke rehabilitation. The information provided thus far serves as the foundation for understanding how health conditions and disease influence human functioning. The attention now shifts from a theoretical discussion to application to the field of stroke rehabilitation, an area of practice that continues to expand dramatically. The remainder of the review will be limited intentionally to discussing stroke rehabilitation, within the context of ICF. The review will not

specifically address interventions; instead evaluation of movement will be the primary focus as it is an essential component in stroke rehabilitation and pervasive throughout the process.

Stroke impact

Each year approximately 795,000 people in the United States have a stroke, with about 610,000 first time and 185,000 recurrent strokes. It is not surprising that stroke or cerebrovascular accident is the third leading cause of death in the United States, only behind heart disease and cancer. The estimated cost of stroke is on the rise from a reported \$62.7 billion in 2007 to \$68.9 billion in 2009 (Lloyd-Jones et al., 2009). This total includes both direct costs such as incurred within the health system (i.e. health care services, medication, rehabilitation) and also indirect costs such as missed days of work. The American Heart Association (2009) estimates that there are currently about 6.4 million stroke survivors and of these, many are left with severe impairments and disability. In addition to being a leading cause of death, stroke is a significant source of long-term disability (CDC, 2001; Delaney & Potter, 1993) and up to nearly 30% of patients are subsequently admitted to nursing homes (Brown et al., 1999; Gresham et al., 1995; Gresham et al., 1979; Wade & Hower, 1987; Wilson, Houle, & Keith, 1991). A more recent study involving five-year outcomes of 370 cases of first time stroke, authors report approximately one in three with remaining disability and one in seven requiring institutionalization (Hankey, Jamrozik, Broadhurst, Forbes, & Anderson, 2002). Taken together, the impact of stroke is a growing cause of concern for the field of rehabilitation.

Stroke rehabilitation

Stroke rehabilitation provides the necessary demands required for central nervous system reorganization, which leads to a decrement of impairment (Bach y Rita, 1981; Moore, 1986). Over the last several decades, much controversy exists concerning how best to manage stroke care within the inpatient hospital setting. This is attributable, in part, to the heterogeneity of the interventions and interaction with various aspects of care ("Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. Stroke Unit

Trialists' Collaboration," 1997). There seems to be no consensus regarding what constitutes effective stroke rehabilitation and why it is effective (Langhorne & Dennis, 1998). A systematic review reports on the effects of organized stroke unit care on death, dependency, and need for institutionalization. Work by the Stroke Unit Trialists' Collaboration suggests that organized inpatient (stroke unit) care is more effective when compared to conventional care. This group identifies several components to comprise effective stroke rehabilitation including 1) a coordinated, multidisciplinary team with weekly meetings; 2) early rehabilitation (i.e. within 1-2 weeks of event); 3) goal setting; 4) early assessment of impairments and function; 5) early discharge planning; 6) staff specialization in stroke or rehabilitation; 7) close interaction with nursing; 8) routine staff education and training; 9) information provided about stroke, recovery and services ("Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. Stroke Unit Trialists' Collaboration," 1997; Langhorne & Pollock, 2002; "Organised inpatient (stroke unit) care for stroke," 2007). The review of 31 separate trials containing outcome information on 6946 subjects suggests that patients who receive organized inpatient stroke unit care (characterized above) are more likely to be alive, independent, and living at home after one year ("Organised inpatient (stroke unit) care for stroke," 2007). Teasell and colleagues also concur and provide several useful reviews on various topics related to stroke rehabilitation (Teasell et al., 2009)

Evaluation in stroke rehabilitation

With the advent of this universal terminology (ICF definitions), it then becomes the responsibility of the field of rehabilitation to distinguish between these concepts. There is agreement that understanding the patient's functioning serves as the basis to the rehabilitation process (Rauch, Cieza, & Stucki, 2008). The ICF provides clinicians in practice and researchers with a framework for understanding various factors influencing patient outcomes. Often overshadowed by treatment, is the evaluation or diagnostic process a clinician undertakes before selecting interventions and includes the collection of information, application of criteria,

and decision-making (Nagi, 1964). This evaluation or assessment process is a fundamental step necessary to obtain and analyze data in order to identify patient problems (i.e. establish a diagnosis). Understanding all relevant factors will assist in determination of prognosis and appropriate goal-setting (Umphred, 2007; Wade, 2002), which leads to the selection of the most appropriate interventions.

The evaluation process demands that the clinician consider thoroughly the array of factors contributing to difficulty in functional movement. Instead of considering how impairments lead to functional limitations, clinicians commonly examine functional movement problems and then determine underlying impairments. Taking this approach, the process is more efficient and helps the clinician establish a broad prognosis to develop realistic short and long term goals for recovery. It is not enough, though, to only determine functional movement problems without an understanding of how impairments contribute. Since dysfunctional movement patterns and disability may arise from different impairments, nuances can influence patient care (McWhinney, 2001). Thus, it is imperative that clinicians and researchers utilize evaluation tools appropriately so that outcomes and conclusions are accurate. Salter and colleagues (2005) provide an excellent series of reviews examining the psychometric and administrative properties of outcome measures common in stroke rehabilitation at each ICF level. In summary, there appears to be good consensus about indicators of outcome measures at the body function and activity levels, while no consensus at the participation level. The authors advocate strongly that rehabilitation disciplines should consider carefully, “the nature and scope of outcome measurement” (Salter, Jutai, Teasell, Foley, & Bitensky, 2005; Salter, Jutai, et al., 2005a, 2005b).

Evaluation of activity limitations

According to the ICF framework, activity limitations present as the restriction or difficulty carrying out tasks and activities at the person level (WHO, 2001). Activity limitations do not take into account performance within a context (i.e. ICF: participation). Performance of functional

activities reveals difficulty or inability to execute motor patterns necessary for successful completion. Observation of functional performance (i.e. functional testing) helps a clinician to determine the cause of dysfunctional movement patterns. Evaluation tools that measure activity limitations examine a person's performance on activities of daily living as well as specific functional skills. Examples of scales and evaluation tools include the Functional Independence Measure (FIM) (Bottemiller, Bieber, Basford, & Harris, 2006; Hamilton, Laughlin, Fiedler, & Granger, 1994; Keith et al., 1987; Linacre, Heinemann, Wright, Granger, & Hamilton, 1994; Stineman et al., 1996), Barthel Index (Hsieh et al., 2007; Hsueh, Lee, & Hsieh, 2001), Arm Motor Ability Test (AMAT) (Chae, Labatia, & Yang, 2003; Kopp et al., 1997; Platz et al., 2005) and Wolf Motor Function Test (WMFT) (Wolf et al., 2001), all which assess functioning without much regard as to how tasks are completed. As such, these functional scales are not sensitive to detect specific impairments or motor patterns exhibited during performance. Implementing functional testing is more efficient in being able to determine the subsystems affecting the patient's inability or difficulty to perform activities.

While functional testing is both a useful and necessary, it is merely a part of the evaluation process. Functional testing provides information regarding the ability and status of patients being able to execute activities. Gauging recovery solely through these measures often implies that patients make large improvements. For example, the FIM scores the patient's ability to complete ADLs on an ordinal scale ranging from completely dependent to completely independent, with varying levels of assistance between (Bottemiller et al., 2006; Hamilton et al., 1994; Keith et al., 1987; Linacre et al., 1994; Stineman et al., 1996). A level of moderate assistance denotes patient performance of approximately 50% of the task. One point of improvement on this scale, minimal assistance, requires the patient to demonstrate 75% of the task, requiring roughly 25% assistance. The FIM, along with other functional testing measures, best approximates global functional performance rather than highlighting specific deficits and impairments.

Evaluation of impairments

Complementary to the evaluation of activity limitations is the evaluation of impairments, defined by the ICF framework as “problems in body function or structure such as a significant deviation or loss” (WHO, 2001). Impairments characterize an abnormality or loss to occur at the level of organ system or body structure/function level. The evaluation process first begins with the identification of activity limitations, using a range of measures to gauge functional performance (briefly reviewed above). With this information, clinicians can then focus in on subsystems involved in the movement patterns of concern. A closer examination of specific subsystems is then necessary to ascertain the particular impairments that may be contributing to the expressed functional performance deficits.

Impairment testing provides objective information regarding the status of the involved subsystems. Often in the case of neurological injury, impairments involve multiple body systems and fall broadly into two categories: impairments within the central nervous system and impairments outside the central nervous system (Umphred, 2007). Impairment in either category can influence and be the result of other impairments. Patients who exhibit body system impairments after central neurological injury can also display difficulty performing ADLs and functional tasks. Rehabilitation professionals working with patients need to establish the extent of impairment of each involved subsystem contributing to deficient motor behavior.

Impairments within central nervous system

The assessment of impairments within the level of the central nervous system encompasses determining the direct extent of the injury. At this level, impairments can exist in the motor, sensory, perceptual, and cognitive systems, which can influence motor patterns and movement. Within the neurological motor system are impairments that include difficulty with the timing or speed of movement, trajectory or pattern of movements, accuracy, and synergies either volitional or reflexive. Numerous scales exist to measure these phenomena, each qualifying the extent of a particular impairment. The Modified Ashworth Scale (Bohannon &

Smith, 1987) documents the degree of resistance to passive range of motion associated with spasticity. Another prominent motor scale after neurological injury is the Fugl-Meyer (FM) (Fugl-Meyer et al., 1975), a measure based upon Brunnstrom stages of neurological recovery (Brunnstrom, 1966). The Fugl-Meyer rates the degree of impairment in motor functioning, balance, and sensation in patients after stroke on a three-point ordinal scale. These measures judge primarily the impairments within the central nervous system. Again, neurological injury often involves other body systems including those outside of the central nervous system and it is important to consider these impairments.

Impairments outside central nervous system

Assessment of impairments outside the central nervous system is as vital to the evaluation process in determining the contribution of underlying impairments to movement performance. Impairments outside of the central nervous system are traditionally considered as peripheral, but these impairments still exist at the body function/structure level as defined by the ICF framework (WHO, 2001). Notable impairments at the peripheral level include decreased range of motion (ROM), diminished muscle strength or power, poor endurance, and involvement of other systems including cardiac and pulmonary function. Clinicians rely heavily upon musculoskeletal assessments of joint ROM and muscle strength and power, as these are elementary to movement. While these assessments are essential, it is more important to remain cognizant of the impairment's contribution to movement and consideration of task demands. Common ADLs (e.g. brushing teeth, dressing, bathing, etc) and daily tasks rarely require full anatomical/biomechanical ROM. Studies conducted on functional ROM report a range from 70° to 130° at the elbow joint for ADLs (Safae-Rad, Shwedyk, Quanbury, & Cooper, 1990; Vasen, Lacey, Keith, & Shaffer, 1995), which is less than full biomechanical ROM at the elbow (0° to

146°) (AAOS, 1965). A similar study on functional ROM at the wrist joint indicates that most ADLs can be accomplished with 70 percent of the maximal range of motion (Ryu, Cooney, Askew, An, & Chao, 1991). Taken together, labeling deficient ROM as impairment, therefore, is accurate, but its influence on subsequent disability depends on patient performance in the environment (WHO, 2001).

Connecting assessment to intervention

Evaluation or assessment of patients following CVA is an essential component of the rehabilitation process. This step serves to inform clinicians of a patient's movement difficulties and underlying impairments that may contribute. Clinicians utilize information from the assessment process to determine a patient's course of recovery after neurological injury. Understanding fully these concepts is essential to the development of an appropriate treatment plan and enables effective assessment of implemented treatment.

According to Nagi's model of disablement, disability represents a mismatch between a person's capacity to function and the demands of an environment, physical or social (Nagi, 1964, 1965, 1991). It is important to accurately establish the relationship (or lack thereof) between movement performance and underlying impairments (Umphred, 2007). Assessment of impairments following neurological injury often yields a list of functional problems and multiple impairments. Clinicians need to recognize how impairments relate to functional problems when deciding the appropriate treatment intervention, considering the extent and malleability of identified impairments. Impairments contributing greatest to movement difficulties are targets for interventions to result in measurable changes in functional performance (Ryerson & Levit, 1997).

Rehabilitation potential

The concept of rehabilitation potential arises inevitably when discussing stroke. Rehabilitation potential refers to 'an estimate of the individual's capability of cooperating with a rehabilitation program and making measured functional gains' (Rentz, 1991). Alternatively, Nagi

defines rehabilitation potential as involving a 'prognostic evaluation of the levels of functioning the individual is capable of reaching under certain circumstances (Nagi, 1964). Authors concur that rehabilitation potential remains a matter of clinical judgment (Cunningham, Horgan, & O'Neill, 2000; Umphred, 2007). In a recent pilot study, investigators attempt to determine the agreement between different members of a multidisciplinary rehabilitation team (physician, physical and occupational therapist, and nurse) by asking the question "Do you think this patient has good rehabilitation potential?". The authors conclude that clinical judgment results in poor agreement and is not reliable, owing to assessment differences and definition of rehabilitation potential. Instead standardized assessments should be considered in determining rehabilitation potential (Cunningham et al., 2000; Umphred, 2007).

Recovery versus compensation

Authors generally distinguish between two separate levels of recovery: neurological and functional (Langton Hower, 1990; Wade, Langton Hower, Skilbeck, & David, 1985). Neurological or intrinsic recovery refers specifically to remediation of neurological impairment. This type of recovery occurs as a result of brain repair or reorganization (Wade et al., 1985) attributed to multiple processes and mechanisms that are beyond the scope of the present review (Dombovy, 1991; Teasell et al., 2009) Functional or adaptive recovery represents improvement of independence or in the ability to perform tasks such as dressing or walking (Langton Hower, 1990; Wade et al., 1985). There is general consensus that functional recovery is more influenced and amenable to rehabilitation (Teasell et al., 2009).

Particularly relevant for this review is a common confusion between "motor recovery" and "motor compensation" following stroke. In a recent opinion paper, several authors attempt to clarify these terms as they apply to patients with central nervous system pathology (i.e. stroke) within the context of the ICF framework (Levin, Kleim, & Wolf, 2009). Related to terminology, genuine ambiguity exists in the term "functional recovery" as rehabilitation disciplines use this term without consensus as to whether recovery occurs at the body

function/structure or activity level (Dobkin, 2005; Levin et al., 2009; Wagner, Lang, Sahrman, Edwards, & Dromerick, 2007). The distinction is important on several levels throughout the rehabilitative process of evaluation, diagnosis, prognosis, and intervention. Levin and colleagues (2009) propose a schema applying definitions of recovery and compensation to the body function/structure and activity levels of the ICF framework. The definitions do not extend to the ICF participation level as “clear distinctions between processes of recovery and compensation are more difficult to identify” (Levin et al., 2009). Several authors also note that outcomes at the ICF participation level are difficult to attribute to specific rehabilitation interventions since many variables may account for the observed changes (Brenner, Curbow, & Legro, 1995; Roberts & Counsell, 1998).

ICF body function/structure level

At the body function/structure level, recovery and compensation is primarily concerned with motor performance. This therefore does not take into account the functional outcome of the movement, but rather considers the quality of the movement. Measurement of recovery at this level takes in account muscle tone, EMG output, movement kinematics, and range of motion (Levin et al., 2009). Recovery of body function/structure signifies restoration of “the ability to perform a movement in the same manner as it was performed before injury”. Recovery describes the reemergence of premorbid movement patterns. Thus, a more precise spatial and temporal movement profile or reduction in spastic overactive muscles demonstrates motor recovery at the level of body function/structure. Compensation at this ICF level refers to performance “of an old movement in a new manner”. The development or appearance of new or alternative movement patterns is characteristic of motor performance compensation. Examples of compensation of body function/structure after stroke would be elevating the shoulder excessively for the lack of active shoulder flexion in order to lift the arm (McCrea, Eng, & Hodgson, 2005; Zackowski, Dromerick, Sahrman, Thach, & Bastian, 2004).

ICF activity level

The ICF activity level refers to functional performance and movement outcome. Thus, recovery and compensation at this level are separate concepts, much like at the body function/structure level. Levin and colleagues (2009) define recovery at the activity level to encompass “successful task accomplishment using limbs typically used by nondisabled individuals”. An example of recovery at the ICF activity level is an individual with residual paresis who demonstrates successful upper body dressing, including buttoning a shirt using both hands. In contrast, compensation at the activity level occurs with “successful task accomplishment using alternate limbs”. Using the previous example then, an individual exhibits compensation at the activity level when buttoning a shirt using only one hand, instead of two. Rehabilitation disciplines should exercise caution when applying these definitions in patient care. These definitions contain underlying assumptions that may potentially influence decision-making, as in the wording ‘nondisabled’. This assumes a set standard for task completion, which compares patient performance against other individuals, rather than a premorbid state. Despite this though, the intent to define clearly terminology relevant to stroke rehabilitation is admirable, as it fosters improved communication between disciplines. The need for distinctions of recovery at various levels is particularly important since stroke rehabilitation is most effective when comprised of a coordinated, multidisciplinary team (“Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. Stroke Unit Trialists’ Collaboration,” 1997; “Organised inpatient (stroke unit) care for stroke,” 2007).

Conclusions

The present review provides information on background concepts of stroke rehabilitation. The models of disability are useful in understanding the complex relationship between factors contributing to the disability. A shift of focus from disability to the health and functioning of individuals is apparent throughout the years. The ICF helps to reframe views of disability by clearly defining concepts in accordance with current perspectives. Use of the ICF’s universal terminology in the rehabilitation process is essential. Stroke rehabilitation is most

effective when delivered by a multidisciplinary team; therefore communication between members is unavoidable. Clinicians need be accurate with communication, particularly with respect to measurement and outcomes as this often drives the rehabilitation process. Significant to the entire rehabilitation process is evaluation, a procedure for gathering pertinent information necessary for effective intervention planning. Evaluation serves to identify activity limitations as well as impairments that may or may not contribute to movement difficulties. This occurs on two separate levels in individuals after stroke, as impairments can be within the central or peripheral to the central nervous system. Participation in stroke rehabilitation entails a collaborative process whereby clinicians help patients to achieve improved functional performance. Thoughtful consideration occurs only when clinicians have a complete understanding of the contributions of impairments and without such; patients may not derive the most benefit even with efficacious treatment interventions.

Appendix D: Informed Consent Form

The University of Kansas Medical Center
Department of Occupational Therapy Education

Rehabilitation Outcome Following Acute Stroke: Considering Ideomotor Apraxia

Adult Informed Consent

Patient's Name _____

Principal Investigator: Dr. Jeff Radel, PhD

Co-Investigator: Andy J. Wu, MOT

INTRODUCTION

You are being asked to join a research study because you have had a stroke recently. This study will collect data to learn ways to improve patient rehabilitation after stroke.

You do not have to participate in this research study. Taking part in this research is voluntary, and you may change your mind at any time. There will be no penalty to you if you decide not to participate, or if you start the study and decide to stop early. Either way, you can still get medical care and services at this institution.

This consent form explains what you will have to do if you take part in this study. It also describes any possible risks and benefits. Please read this form carefully and ask as many questions as you need to before deciding about this research. You can ask questions now or later, or anytime during the study.

This research study will take place at the University of Kansas Hospital and at four hospitals in the St. Luke's Health System of Kansas City. Dr. Jeff Radel, PhD, is the principal investigator, and Mr. Andy J. Wu, MOT is Dr. Radel's co-investigator. We expect about 20 patients to take part in this research study, with about 10 patients from the University of Kansas Hospital and about 10 patients from St. Luke's Hospital on the Plaza and St. Luke's South Hospital.

BACKGROUND

Stroke symptoms contribute to difficulties doing activities of daily living (ADLs) such as bathing, dressing, and grooming, and this is a concern for patients, families, and therapists. Research efforts often focus on treating muscle weakness after a stroke, but often do not consider other stroke-related problems that can make daily activities difficult. Ideomotor apraxia (IMA) is one such problem, which presents as difficulty manipulating objects in daily life. This, in addition to other stroke-related problems, could slow the rehabilitation of patients after stroke.

PURPOSE

This study will compare the effectiveness of inpatient rehabilitation in two groups of people who have had a stroke recently: people who have Ideomotor Apraxia and people without Ideomotor Apraxia.

PROCEDURES

The researchers will gather relevant demographic and medical information from you or your medical chart when necessary.

Participation in this study involves several assessments **in addition** to those routinely given to all patients in the in-patient rehabilitation setting:

1. You will be asked to move your right arm to a one of several positions and then hold your arm in that position briefly. There will be a series of different positions, and this assessment will take about 15-20 minutes to complete.
2. You also will be asked to use your left arm as you pretend to use several different objects and tools. This assessment will take about 15-20 minutes to complete.

These movements are not difficult or strenuous but if you feel tired or frustrated please let the investigator know right away so we can pause and allow you to rest.

The assessments will be videorecorded for scoring by the investigators later. The videorecordings will be made of your upper body only. No information that might be used to identify you will be included in the videorecording.

RISKS

There are no known risks for participating in this study. As with any assessment of this sort, there is a possibility that you may become tired, frustrated, or anxious. Rest periods will be provided as needed.

BENEFITS

You will not benefit directly from your participation in this study. The investigators hope that the information from this research study may help to improve the treatment and recovery of patients after stroke.

COSTS

There is no cost to you for participating in this study.

PAYMENT TO SUBJECTS

There is no payment for this study.

INSTITUTIONAL DISCLAIMER STATEMENT

If you think you have been harmed as a result of taking part in research conducted by the University of Kansas Medical Center (KU Medical Center), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow for payment to persons who are injured in research at KU Medical Center.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION

The privacy of your health information is protected by a federal law known as the Health Insurance Portability and Accountability Act (HIPAA). If you choose to participate in this study, you will be asked to give permission for uses and disclosures of your health information collected in this study, as listed in the Procedures section of this consent form.

Your study-related health information will be used at KU Medical Center by Dr. Jeff Radel and members of the research team, or by KU Medical Center officials and committees that oversee research and government officials who oversee research if a regulatory review takes place. All study information sent outside KU Medical Center will have your name and all other identifying characteristics removed, so that your identity will not be known. Because identifiers will be removed, your health information will not be re-disclosed to outside persons or groups and will not lose its federal privacy protection. Videorecordings are archived without identifying information and kept indefinitely. Videorecordings of your arm movements may be utilized for education and training, but you will not be identified.

The permission to use and disclose your health information that you give today will remain in effect indefinitely. By signing this form, you give permission for the use and disclosure of your information at any time in the future for purposes of this study. If you decide not to sign the form, you cannot be in the study.

The investigators may publish the results of the study. If they do, they will only discuss group results. Your name or other information that might be used to identify you will not be used in any publication or presentation of these findings.

QUESTIONS

You may ask any questions at this time. If you have any questions in the future, you may contact Dr. Jeff Radel, who can be reached by phone at (913) 588-7195, or in writing at Mail Stop 2003, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160, or email at jradel@kumc.edu. If you have questions about your rights as a research subject you may call or write the Human Subjects Committee, Mail Stop 1032, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160, (913) 588-1422.

SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY

You may stop being in the study at any time. Your decision to stop will not prevent you from getting treatment or services at the University of Kansas Hospital or St. Luke's Hospital of Kansas City.

You have the right to cancel your permission for researchers to use your health information. If you want to cancel your permission, Dr. Jeff Radel can be reached by phone at 913.588.7195 or by sending a written statement to Jeff Radel, PhD, Mail Stop 2003, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160. If you cancel permission to use your health information, you will be withdrawn from the study. The researchers will stop collecting any additional information about you. They may use and share information that was gathered before they received your cancellation. This will not, however, change the routine care provided to you as a patient.

This study might be stopped, without your consent, by the investigator. Your participation also might be stopped by the investigator or by the sponsor if it is in your best interest or if you do not follow the study requirements.

CONSENT

Dr. Jeff Radel or a member of the research team has given you information about this research study. That person has explained what will be done and how long it will take. He or she also explained any inconvenience, discomfort, or risks that you may experience during this study.

By signing this form, you say that you freely and voluntarily consent to participate in this research study. You have read the information and had your questions answered.

You will be given a signed copy of the consent form to keep for your records.

Print Patient's Name

Signature of Patient

Time

Date

Print Name of Person Obtaining Consent

Signature of Person Obtaining Consent

Date

Appendix E: Screening Form

Screening/Intake Form				Subject ID:			Date Collected:			Mon	Day	Year
Completed by:				Subject Initials:			Collection site:			<input type="checkbox"/> KU		<input type="checkbox"/> SLH

Date of Birth (Month/Day/Year)			Gender		Race/Ethnicity						
			<input type="checkbox"/> Female <input type="checkbox"/> Male		<input type="checkbox"/> American Indian/Alaskan Native <input type="checkbox"/> Black <input type="checkbox"/> Asian/Pacific Islander <input type="checkbox"/> Caucasian				<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> More than one race <input type="checkbox"/> Unknown or not reporting		

Stroke Onset (Month/Day/Year)			Admission Date (Month/Day/Year)			Discharge Date (Month/Day/Year)			Type of Stroke		Location (specify)	
									<input type="checkbox"/> Ischemic <input type="checkbox"/> Hemmorrhagic			

Stroke Impairments														
	0No		1Yes			0No		1Yes			0No		1Yes	
Tone					Visual Deficits					Cognitive Deficits				
Paresis					Neglect					Aphasia				
Ataxia					Balance Deficits					Dysarthria				
Endurance					Gait Deficits					Dysphagia				
Sensory Deficits					Incontinence									

Inclusion Criteria				Exclusion Criteria					
			No	Yes				No	Yes
1) Age \geq 18 years and \leq 85 years					1) History of other CNS disease besides CVA				
2) Left CVA; CT or MRI confirmed					2) History of bilateral CVA				
3) Admission to inpatient rehabilitation facility					4) History of dementia				
					5) History of major head trauma				
					6) Severe aphasia; confirmed by clinical assessment				

Appendix F: Functional Independence Measure

Functional Independence Measure	Subject ID:					Date Collected:	Mon	Day	Year			
Completed by:				Subject Initials:			(Circle visit number)					
							PRE	POST1	POST2	POST3	POST4	POST5

Self-Care

- A. Eating _____
- B. Grooming _____
- C. Bathing _____
- D. Dressing – Upper _____
- E. Dressing – Lower _____
- F. Toileting _____

Sphincter Control

- G. Bladder _____
- H. Bowel _____

Transfers

- I. Bed, Chair, W/C _____
- J. Toilet _____
- K. Tub, Shower _____

Locomotion

- L. Walk/Wheelchair _____
- M. Stairs _____

Motor Subtotal Score _____

Communication

- N. Comprehension _____
- O. Expression _____

Social Cognition

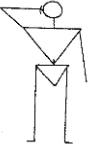



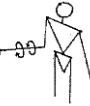
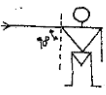
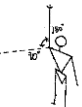


- P. Social Interaction _____
- Q. Problem Solving _____
- R. Memory _____




Cognitive Subtotal Score _____

Total Score: _____

Appendix G: Fugl-Meyer Assessment

Fugl-Meyer Assessment				Subject ID:				Date Collected:				Mon	Day	Year
Completed by:				Subject Initials:				(Circle visit number)						
								PRE	POST1	POST2	POST3	POST4	POST5	

I. Reflex Activity		none	can be elicited			
Flexors: biceps and finger flexors		0	2			
Extensors: triceps		0	2			
II. Volitional movement within synergies		none	partial	full		
	Flexor synergy: Hand from contralateral knee to ipsilateral ear.	Shoulder retraction	0	1	2	
		Shoulder elevation	0	1	2	
		Shoulder abduction (90°)	0	1	2	
		Shoulder external rotation	0	1	2	
		Elbow elbow flexion	0	1	2	
	Extensor synergy: Hand from ipsilateral ear to the contralateral knee	Forearm supination	0	1	2	
		Shoulder adduction/int.rotation	0	1	2	
		Elbow extension	0	1	2	
Forearm pronation	0	1	2			
III. Volitional movement mixing synergies		none	partial	full		
	Hand to lumbar spine	cannot be performed, hand in front of ASIS hand behind of ASIS (no compensation) hand to lumbar spine (no compensation)		0	1	2
	Shoulder flexion 0° - 90° elbow at 0° forearm in neutral	immediate abduction or elbow flexion abduction or elbow flexion during movement complete flexion 90°, maintains 0° in elbow		0	1	2
	Pronation/supination elbow at 90° shoulder at 0°	no pronation/supination limited pronation/supination complete pronation/supination		0	1	2
IV. Volitional movement with little or no synergy		none	partial	full		
	Shoulder abduction 0° - 90° elbow at 0° forearm pronated	immediate supination or elbow flexion supination or elbow flexion during movement abduction 90° maintains extension pronation		0	1	2
	Shoulder flexion 90° - 180° elbow at 0° forearm in neutral	immediate abduction or elbow flexion abduction or elbow flexion during movement complete flexion, maintains 0° in elbow		0	1	2
	Pronation/supination elbow at 0° shoulder at 30° - 90°	no pronation/supination limited pronation/supination full pronation/supination, elbow extension		0	1	2
V. Normal Reflex Activity <i>(evaluated only if full score of 6 points achieved on part IV)</i>		0	1	2		
biceps, triceps, finger flexors		0 points on part IV or 2 of 3 reflexes markedly hyperactive 1 reflex markedly hyperactive or at least 2 reflexes lively maximum of 1 reflex lively, none hyperactive		2		
VI. Wrist stability/mobility <i>(support may be provided at the elbow, no support at wrist)</i>		none	partial	full		
	Stability at 15° extension shoulder at 0°	less than 15° wrist extension wrist extension 15°, no resistance taken		0	1	2

	elbow at 90°, forearm pronated	maintains position against resistance			
	Repeated wrist flexion/extension shoulder at 0° elbow at 90°, forearm pronated	cannot perform limited active range of motion full active range of motion, smoothly	0	1	2
	Stability at 15° extension shoulder at 30° - 90° elbow at 0°, forearm pronated	less than 15° wrist extension wrist extension 15°, no resistance taken maintains position against resistance	0	1	2
	Repeated wrist flexion/extension shoulder at 30° - 90° elbow at 0°, forearm pronated	cannot perform limited active range of motion full active range of motion, smoothly	0	1	2
	Circumduction	cannot perform jerky movement or incomplete complete and smooth circumduction	0	1	2
VII. Hand (<i>support may be provided at the elbow to keep 90° flexion, no support at the wrist</i>)			none	partial	full
	Mass flexion (<i>from full active or passive extension</i>)		0	1	2
	Mass extension (<i>from full active or passive flexion</i>)		0	1	2
Grasp					
A	Hook: extend MCP, flex PIP/DIP digits II - V test against resistance	cannot be performed can hold position but weak maintains position against resistance	0	1	2
B	Radial/Thumb: thumb adduction test with paper	cannot be performed can hold paper but not against tug can hold paper against tug	0	1	2
C	Pincer: pulpa approximation of digit I and II test with pencil	cannot be performed can hold pencil but not against tug can hold pencil against tug	0	1	2
D	Cylindrical: opposition of digit I and II test with bottle	cannot be performed can hold bottle but not against tug can hold bottle against tug	0	1	2
E	Spherical: fingers and thumb opposed test with ball	cannot be performed can hold ball but not against tug can hold ball against tug	0	1	2
VIII. Coordination/Speed (<i>nose to knee in rapid succession 5 times, eyes closed</i>)			marked	slight	none
Tremor			0	1	2
Dysmetria	pronounced or unsystematic slight and systematic no dysmetria		0	1	2
Time	more than 5 sec slower than less-affected side 2-5 seconds slow than less-affected side maximum difference of 1 second between sides		0	1	2

Appendix H: Florida Apraxia Battery gesture-to-verbal command subtest

Florida Apraxia Battery				Subject ID:				Date Collected:				Mon	Day	Year	
Completed by:				Subject Initials:				(Circle visit number)							
								PRE				POST			

Gesture-to-verbal command: Ask the patient to "Show me how to use _____"
 If BPT error, prompt **once** "Show me how as if you were holding the _____"

Command	Score	Errors (circle if observed)													
		P	R	N	A	IC	BPT	EC	M	S	T	O	NR	UR	
Scissors to cut paper	_____														
Salt shaker to salt food	_____														
Spoon to stir coffee	_____														
Hammer to pound a nail	_____														
Comb to fix your hair	_____														
Knife to carve a turkey	_____														
Screwdriver to turn a screw	_____														
Pencil to write on paper	_____														
Key to unlock a door	_____														
Razor to shave your face	_____														
Total	_____														

Errors	Error Types	Descriptions
Content	(P) Perseverative	Response includes all/part of a previous response
	(R) Related	An accurate pantomime associated with a target
	(N) Nonrelated	An real and accurate pantomime not associated with target
Spatial	(A) Amplitude	Amplification reduction or irregularity of amplitude/position in space
	(IC) Internal Configuration	Abnormality of finger/hand posture with target tool
	(BPT) Body part as tool	BPT that cannot be corrected when requested
	(EC) External Configuration	Abnormality of finger/hand/arm relationship to object receiving the action
Timing	(M) Movement	Any disturbance of the characteristic action required to complete the goal
	(S) Sequencing	Movement structure recognizable but addition, deletion or inaccurate order or sequence
	(T) Timing	Alteration of timing/speed (including increase, decrease or irregular)
Other	(O) Occurrence	Repetitive production of single movement or single production of multiple movements
	(NR) No response	Subject makes no response to request
	(UR) Unrecognizable	Shares no spatial or temporal features of target

Appendix I: Florida Apraxia Battery pantomime-to-photograph matching subtest

Florida Apraxia Battery				Subject ID:			Date Collected:			Mon	Day	Year
Completed by:				Subject Initials:			(Circle visit number)					
							PRE			POST		

Pantomime-to-photograph: Ask the patient to “Show me the one I am pretending to use”

<i>Action + target tool</i>	<i>Score 1 or 0</i>	<i>Semantic category</i>	<i>Errors (circle one) Function associate</i>	<i>Motoric</i>
Scissors to cut paper	_____	Shears	Paper	Pliers
Salt shaker to salt food	_____	Pepper grinder	Chips	Baby powder
Spoon to stir coffee	_____	Fork	Cup & saucer	Pencil
Hammer to pound a nail	_____	Wrench	Nail	Potato masher
Comb to fix your hair	_____	Brush	Hair	Hat
Knife to carve a turkey	_____	Peeler	Fork	Saw
Screwdriver to turn a screw	_____	Chisel	Screw	Key
Pencil to write on paper	_____	Ruler	Notepad	Needle
Key to unlock a door	_____	Key ring	Lock	Screwdriver
Razor to shave your face	_____	Electric shaver	Shaving cream	Blusher brush
Total	_____			

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