SPECIFIC AIMS

Of the 5.7 million stroke survivors living in the U.S., the majority exhibits significant weakness in one upper extremity (UE).[1] This devastating impairment undermines performance of valued activities and diminishes quality of life.[2] Many promising UE rehabilitative strategies have been developed, with most emphasizing repetitive, task-specific practice (RTP) incorporating the paretic UE. However, most of these regimens[3,4,5] are only efficacious in mildly impaired individuals; a group comprising only about 20-25% of this population,[6] and already exhibiting high levels of active, paretic UE movement.

In contrast, survivors exhibiting moderate UE impairment constitute a larger proportion of the stroke population,[6] yet exhibit little to no active movement in their paretic wrists and fingers and limited active proximal movements. These diminished movement capabilities hamper participation in UE therapies emphasizing RTP, and responses to conventional rehabilitative regimens.[3,4,5] Given their relative inability to participate in practice based protocols, device-oriented approaches have been explored to facilitate increased movement capability in moderately to severely impaired stroke survivors.[7] The goal of such approaches is to assist clients exhibiting higher UE impairment levels with performing UE movements, with assistance from the devices. For example, sophisticated robotic systems have been developed to evaluate and treat patients who have sustained strokes.[8,9] However, the cost and complexity of these systems as well as their size limits their applicability in the clinical and home environments, especially with regards to enabling clients to easily perform valued activities. A device that is compact, relatively easy to use, capable of capturing the interest of the user, and can be easily integrated into valued activities remains an unmet need.

Since the 1950's, myoelectrically-controlled devices have been integrated into prosthetic limb designs,[10] and are now considered standard of care for certain patients with disarticulated UEs. Developed by Myomo, Inc. (Cambridge, MA), multi-week RTP regimens incorporating a portable, myoelectric brace have reduced paretic UE impairment and increased UE function and self-rated recovery in stroke survivors with moderate UE deficits.[11,12] These braces support the weakened or deformed arm while enabling volitional movement of the UE and protecting from joint hypermobility. The most recent device version - called the "MyoPro 2 Motion G" - uses surface electromyography (EMG) signals from the biceps and triceps brachii and forearm flexor and extensor muscle groups to assist the active muscle with movement of the paretic UE. Specifically, during active paretic UE movement attempts, the user's intention to move is detected via his/her EMG. The treating therapist can then adjust the system parameters to alter the amount of mechanical assistance that the device provides on an as needed basis, using software on a tablet or personal computer.

Multi-week RTP regimens incorporating such a device could address an unmet need for an efficacious, easily implemented, UE therapy for stroke survivors with moderate UE impairment; hundreds of thousands of new patients annually, and millions living in the community. However, a paradigm shift in stroke clinical care also requires evidence demonstrating that donning a

MyoPro has an immediate, discernible impact on UE movement and functional limitation, especially for patients who may be prescribed such a device with limited opportunities to participate in multi-week UE therapy regimens. In pilot work leading to the current study, we showed clinically-important increases in UE movement when wearing the MyoPro Motion G (+8.2 points on the upper extremity Fugl-Meyer scale; a widely used, stroke-specific measure) as well as reduced functional limitation and increased gross manual dexterity immediately after 18 subjects with chronic, stable, moderate UE impairments donned the MyoPro Motion G. As a next step, the primary study objective is to compare UE movement while wearing the MyoPro 2 Motion G versus a resting splint and no device in stroke survivors with moderate UE dysfunction. During the study, subjects will undergo general training in the operation of the EMG-controlled orthosis and the comparison orthosis, and then guided through a series of standard clinical outcome measures. These outcome measures will allow the researchers to directly compare the relative benefit of the MyoPro 2 Motion G with a resting hand splint and no device in reducing UE impairment and increasing UE dexterity and functional task performance.

Specific Aim 1: Determine the impact of the MyoPro 2 Motion G myoelectric brace on affected UE movement. 75 stroke survivors exhibiting moderate UE impairment will be administered the UE FM while wearing: (a) the MyoPro 2 Motion-G (b) a comparison resting hand splint, and (c) no device, with the order of assessment conditions randomized and counterbalanced across subjects. This study design will allow investigators to determine the immediate impact of the MyoPro 2 Motion G on increasing UE movement when compared to a commonly-prescribed device (resting hand splint) and compared to no device

Based on our supportive pilot data, *Aim 1* will test the hypothesis that wearing the MyoPro 2 Motion-G will result in the largest increases in UE movement compared to the resting hand splint and compared to no device as measured by the upper extremity section of the Fugl-Meyer Scale (UE FM); our primary outcome measure. While not a functional measure, per se, this measure is sensitive to all levels of UE impairment and is, thus, best situated to examine the changes in active UE movement likely to occur in the paretic UE that are hypothesized to occur most prominently with MyoPro 2 Motion G use. Further, functional outcomes are rigorously assessed using the battery of assessments described in Aim 2.

Specific Aim 2: Determine the impact of the MyoPro 2 Motion G myoelectric brace on affected UE outcomes. All subjects will undergo a battery of assessments to compare the impact on UE outcomes when utilizing the MyoPro 2 Motion G, resting hand splint and no device as explained above. Each subject will be administered (a) a battery of functional tasks; (b) the Box and Block (B&B) Based on our supportive pilot data, *Aim 2* will test the hypothesis that wearing the MyoPro 2 Motion G will result in the largest increases in UE outcomes compared to the splint and compared to no device.

APPROACH

Subjects

Subjects will be recruited through local registries at each site. If needed, approved advertisements will be distributed to local stroke support groups and outpatient rehabilitation clinics. After being identified and signing approved consent forms, subjects will be screened using the following study criteria: **Inclusion criteria**: (a) MMT ≥1/5 in the paretic biceps, triceps, finger extensors and finger flexors; (b) score ≥ 10 ≤ 30 on the FM AND active shoulder flexion of at least 30 degrees with device weight on affected arm; (c) Ability to generate consistent, detectable EMG signal from the bicep/tricep upper arm and distal forearm flexor and extensor sensor sites with wrist in neutral, and fingers in neutral. At rest, achieve an EMG of 5 or below on myConfig (wrist and fingers in neutral and elbow extended); with gain at ≤ 10 and boost <12, able to reach a threshold of 10 at both bicep and wrist flexors/extensors; (d) a single stroke that is the cause of arm impairment, experienced >12 months ago; if there are additional asymptomatic lesions (as diagnosed by MRI), these subjects may also be included. Those with another symptomatic stroke in addition to the stroke causing arm impairment are excluded; (e) score ≥70 on the Modified Mini Mental Status Examination; (f) age ≥18< 85; (g) ≥ 6 months since previous functional or therapeutic use of an upper extremity myoelectric orthosis; (h) Height ≥5'0"; (i) Weight ≥110≤ 250 lbs.; (j) Forearm circumference (at widest part) ≤13 in.; (k) Bicep circumference ≥9 ≤15 in.; (l) Upper arm length ≥5.5 in.; (m) Wrist thickness (anterior- posterior) ≤1.75 in.; (n) ability to stand with minimal assistance **Exclusion criteria**: (a) ≥ 5 on a 0-10 Numeric Pain Rating Scale for pain in the paretic hand, arm or shoulder; (b) > 3 on the Modified Ashworth Spasticity Scale in the paretic elbow, >2 at wrist or fingers; (c) ≤ 2.5 on the Alexander Apraxia scale; (d) history of neurological disorder other than stroke; (e) change in anti-spasticity medications in the last 6 months, and/or receipt of botulinum toxin in the paretic UE in the previous 4 months; (f) elbow contracture greater than 10 degrees; (g) inability to passively extend fingers while wrist is in neutral; (h) other conditions or physical/mental attributes that may undermine safety and/or full participation in the study; (i) bilateral hemiparesis.

Apparatus

MyoPro 2 Motion G Device

The MyoPro 2 Motion G (Myomo Inc., Cambridge, MA, USA) (Figure 1) is a custom fabricated limb orthosis that is individually fabricated for the patient over a positive model of the patient requiring education, training, and experience to custom-fabricate and fit. It uses surface EMG signals from affected muscle groups to control the powered orthosis to assist with the movement of a paretic upper limb.

Figure 1: Myopro 2 Motion G

The device has been registered with the Food and Drug Administration (FDA) as a powered limb orthosis with biofeedback intended for medical purposes that is worn on the upper limb to support, to correct, or to prevent deformities or to align body structures for functional improvement.[13] The

MyoPro 2 Motion G provides powered proportional assistance for elbow flexion and extension and gross grasp motions via motors attached to the exterior of the orthosis brace. It functions by continuously monitoring the surface EMG signals of the user's bicep and tricep muscles for elbow motion and the forearm flexor and extensor muscle groups for grasp motion. These signals are filtered and processed to provide a desired joint torque proportional to the exerted effort of the user.

The signal processing of the measured surface EMG is accomplished through a system that is comprised of the MyoPro's EMG sensors, analog signal–processing components, and digital signal–processing components. The signal-processing algorithm enables bidirectional control for each joint or degree of freedom through the use of antagonistic EMG signals or unilateral active assist combined with a competing passive force for a single EMG signal source. The parameters of the device system settings, include gain (amount of assistance provided to the user), activation thresholds, and range of motion, can be adjusted for each individual based on their level of impairment and physiology through a custom software interface, MyConfig. These settings are adjusted by a treating therapist or a Certified Prosthetist and Orthotist (CPO) and may require regular updating as the user receives therapy and is trained on operation of the MyoPro 2 Motion G.

Comparison Device

The Comfy Dorsal Hand Splint (Comfy Splints, Lenjoy Medical Engineering, Inc.) (Figure 2) was chosen for the comparison device, as splints are among the most commonly-prescribed products post-stroke and are used to place the affected arm in a functional position and prevent deformity. The dorsal splint was chosen (as opposed to a palmar splint) as it leaves the digits free for object manipulation and task performance.

Figure 2: Comfy Dorsal Hand resting splint

Outcome Measures

Outcome measures were chosen to span the International Classification of Function (ICF), as well as incorporate reliable and valid measures that are commonly used by rehabilitation clinicians. All outcome measures will be administered three times (with the MyoPro 2 Motion G, with the resting hand splint and with no device).

Primary Outcome Measure (Aim 1): Like any orthosis, the MyoPro attaches to the affected body structure with the goal of supporting the affected arm, facilitating active assisted movement of the affected extremity, and, ultimately, facilitating increased participation in valued activities. Accordingly, UE movement (orthotic-assisted UE movement when the brace is donned) was chosen as the primary construct of interest. Further, due to the more impaired nature of our sample, patients would be unsuccessful attempting items on distally-based measures that we and others have commonly used in UE trials with minimally-impaired subjects (e.g., Action Research Arm Test; Wolf Motor Function Test). As such, the upper extremity section of the *Fugl-Meyer Scale (FM)* will assess whether changes occur in upper extremity movement, as anticipated in Hypothesis 1.

Secondary Outcome Measures (Aim 2):

- Demonstration of orthotic-assisted increases in motor ability alone is not sufficient to warrant clinical use of a device. Indeed, increases in orthotic-assisted UE movement must translate into improvements in functional outcomes. Additionally, the MyoPro 2 Motion G provides full active assisted ROM at the elbow to facilitate increased ability to carry out proximally-based functional tasks. While useful in assessing distal functional abilities, many distally based measures may not fully quantify an increased ability to carry out more proximally-based, gross motor tasks involving the elbow.

  As such, investigators will administer a battery of proximally-based, commonly-performed *functional tasks* (ICF: activity). This battery was used in our preliminary work leading to the current application, and consists of: (a) stabilizing a mixing bowl while stirring, (b) simulated drinking, (c) picking up a laundry basket, (d) putting an item in a laundry basket, (e) opening deodorant, (f) opening a pill bottle, (g) cutting a block of cheese, and (h) sweeping. Quality of movement on each task and sub-task will be rated using a 6-point ordinal scale (0=performs no part of task, does not attempt with the affected arm; 5=performs normally) and performance of each task will be timed, with 60 seconds allotted for each subtask. This battery will provide valuable information regarding proximal and gross distal functional abilities as well as speed of task completion.

  Importantly, in pilot work leading to this study, our sample size was not large enough to fully determine the battery's psychometrics, but internal consistency was demonstrated. While not a primary aim of this study, the study biostatistician will perform full psychometric analyses to determine the measurement properties of this instrument, as described later.

- The *Box and Block Test (B&B)* (ICF: activity) is suggested to determine whether changes occur in UE *gross manual dexterity*. During the test, the subject is seated in front of a wooden box with a partition in the middle, and is asked to move colored blocks from one side of the box, over the partition, to the other side. The number of blocks moved in one minute is recorded. The test's test-retest reliability and validity have been shown in stroke.[14,15]

Table 1: Screening and Outcome Measures

Measure	Measurement Domain	Timepoint(s) Administered
Screening Measures		
Manual Muscle Test (MMT)	Arm muscle strength	Visit #1 (screening)
Passive and Active Range of Motion (PROM/AROM)	Upper Extremity Physiology/ Kinesiology	Visit #1 (screening)
0-10 Numeric Pain Rating Scale	Pain in paretic UE	Visit #1 (screening)

Alexander Apraxia Scale	Perceptual impairment/Apraxia	Visit #1 (screening)
Modified Mini Mental Status Examination	Gross cognitive status	Visit #1 (screening)
Screening and Demographics Forms	Treatment history	Visit #1 (screening)
Patient Health Questionnaire-9 (PHQ9)	Depression severity	Visit #1 (screening)
Modified Ashworth Scale	Upper Extremity (UE) spasticity	Visit #1 (screening)
Upper Extremity (UE) Fugl-Meyer *(primary outcome measure)*	Upper Extremity Impairment	Visit #1 (Screening), Visit #2, Visit #3, Visit #4
Outcome Measures		
Upper Extremity (UE) Fugl-Meyer *(primary outcome measure)*	Upper Extremity Impairment	Visit #1 (Screening), Visit #2, Visit #3, Visit #4
Box and Blocks Test	UE gross manual dexterity	Visit #2, Visit #3, Visit #4
Battery of functional tasks	Activities of Daily Living	Visit #2, Visit #3, Visit #4

Suggested Procedures for Standardization of Raters on UE Outcome Measures:

At least one "rating" therapist who is blinded to randomization assignments should be identified and hired for this study from each site. Each individual will undergo extensive inservicing using uniform procedures to assure that outcome testing has high intra-rater and inter-rater reliability (i.e., the therapist scores each measure in a way that is consistent with him/herself, as well as with raters at other sites). Specifically, before the first subject is enrolled at each site, it is recommended that the rating therapist at each site be "certified" on the FM by demonstrating his/her rating skills on these measures during videotaped testing standardization sessions. During the videotaped session, he/she performs the measure in its entirety on a subject with stroke, and completes a case report form indicating his/her scores for each FM item. When a therapist completes the videotaped certification session, the testing videos and accompanying completed case report forms are then uploaded to a secure ftp site or to Google documents. Each rater's video from each site is reviewed externally by a single individual hired for the trial. Appropriate mastery of the testing content is attained when there is 90% agreement between the tester's score on each measure with the manual of procedures. Certification would last for 6 months and procedures for carrying out each test of interest would be detailed in a standardized manual of procedures.

This same methodology has been used in stroke rehabilitation trials by this laboratory for over a decade, including two ongoing multicenter studies for which this laboratory is organizing all outcome training and testing. Moreover, this same methodology of "certifying" raters has been used in most multicenter stroke rehabilitation studies in which UE behavioral measures have been administered, including Everest, ExCITE, and, most recently, ICare.

Data Collection Procedures

Study Protocol Overview:

All subjects will be requested to participate in 4 study visits lasting no more than 3 hours each, as well as three training sessions of approximately 1 hour each (Table 2). During the first study visit, the study will be explained to the subject and written informed consent will be obtained. Then, all screening measures (listed in Table 1) will be administered and, if the subject meets all inclusion criteria, they will move on to the educational sessions. Between visits #1 and #2, the subjects will receive two education sessions, (1 one-hour training session and 1 two-hour training session) on both the MyoPro 2 Motion G and comparison splint. During study visits #2, #3 & #4, the subject will undergo all outcome measures (Table 1) in all three conditions (one condition per visit to minimize fatigue) in randomized order. A summary of the study timeline nd a more detailed description of the study design follows.

Timeline for each research subject:

Subjects will have a maximum of 3 weeks to complete all visits beginning from the date of consent. There should not be more than one visit and/or testing session completed in the same day to reduce the likelihood of patient fatigue.

Description of Study Visits:

Visit 1 (Consent, screen): During the first visit, each volunteer will sign an informed consent for participation in this study. Next, subjects will undergo all screening measures as listed in inclusion criteria. For each subject, a study team member who will be trained on the use of the MyoPro 2 Motion G device will help don the device to their paretic UE, and select appropriate locations on their arm for the external EMG sensors. If a subject meets all inclusion criteria, they will continue on to undergo training sessions.

The evaluation process to examine the subjects' eligibility will be performed by the PI and/or study coordinator at each site. The orthosis fitting process will be done in accordance with good orthotics practices outlined in the American Academy of Orthopaedic Surgeons (AAOS) Atlas of Orthoses and Assistive Devices. After the evaluation and fitting process, the study therapist will tune the settings on the EMG system, teach the subject the donning and doffing process for the orthosis, and educate the user on the capabilities and functionality of the MyoPro 2 Motion G brace.

Two Education sessions: Subjects will return to complete two education sessions. Training sessions #1 will last 2 hours, with 1 hour of training on the MyoPro and 1 hour of training on the splint. Training session #2 will last one hour, with 30 minutes of additional training on the MyoPro and 30 minutes additional training on the splint.

> **MyoPro 2 Motion G training:** MyoPro 2 Motion G training will consist of simple repetitions of activating the myoelectric system by attempting to flex muscle groups and seeing the system response. These exercises teach the users to understand the relationship between their EMG signal and the motions and forces generated by the device. The users will practice basic movements, including flexing and extending the elbow, opening and closing the hand unit, and grasping objects with the hand. This requires a great deal of cognitive effort and often some adjustments to the device and its

interface with the individual's muscles by the study therapist. Subjects will be taught the donning and doffing process for the orthosis, as well as learn the capabilities and functionality of the MyoPro 2 Motion G brace.

Splint training: Tasks performed in comparison device training sessions will be identical to those performed during MyoPro 2 Motion G training (i.e., flexion/extension of the elbow and fingers, object manipulation) to ensure training between devices is uniform. Subjects will also undergo training on how to adjust the device depending on which task is being practiced. Subjects will be taught the donning and doffing process for the orthosis, as well as learn the capabilities and functionality of resting splint.

Visit 2 (Assessment): Subjects will perform all aforementioned outcome measures in the first assessment condition to which they were randomized (i.e., MyoPro 2 Motion G, splint, or no device). Randomization will be performed by a study coordinator hired for this study using a computer-generated randomization table, and will be revealed to the study therapist prior to the study visit. A latin square will be used to counterbalance the order of conditions.

Visit 3 (Assessment): Subjects will perform all aforementioned outcome measures in the second condition to which they were randomly assigned.

Visit 4 (Assessment): Subjects will perform all aforementioned outcome measures in the third condition to which they were randomly assigned.

Data Analyses

Power and Sample Size Justification:

For the past 9 months, members of the study team have collected data comparing the effect of wearing the MyoPro Motion G versus not wearing the MyoPro Motion G on UE movement in moderately impaired stroke survivors. This work showed a mean change of 8.72 ± 7.1 points on the UE FM when subjects wore the MyoPro Motion G (Table 3). From this work, we have formed the primary study hypothesis, which is that subjects will exhibit significantly higher scores on the UE FM when using the MyoPro 2 Motion G compared to scores when using the splint and no device.

Table 3: Pilot Data Leading to the Current Trial

condition	Method	Mean	99% CL Mean		Std Dev	99% CL Std Dev		99% UMPU CL Std Dev	
with		27.2778	21.9152	32.6403	7.8501	5.4157	13.5603	5.3232	13.2488
without		18.5556	14.2528	22.8583	6.2987	4.3454	10.8803	4.2712	10.6304
Diff (1-2)	Pooled	8.7222	2.2498	15.1947	7.1168	5.4042	10.2156	5.3562	10.1038
Diff (1-2)	Satterthwaite	8.7222	2.2318	15.2127					

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	34	3.68	0.0008
Satterthwaite	Unequal	32.475	3.68	0.0008

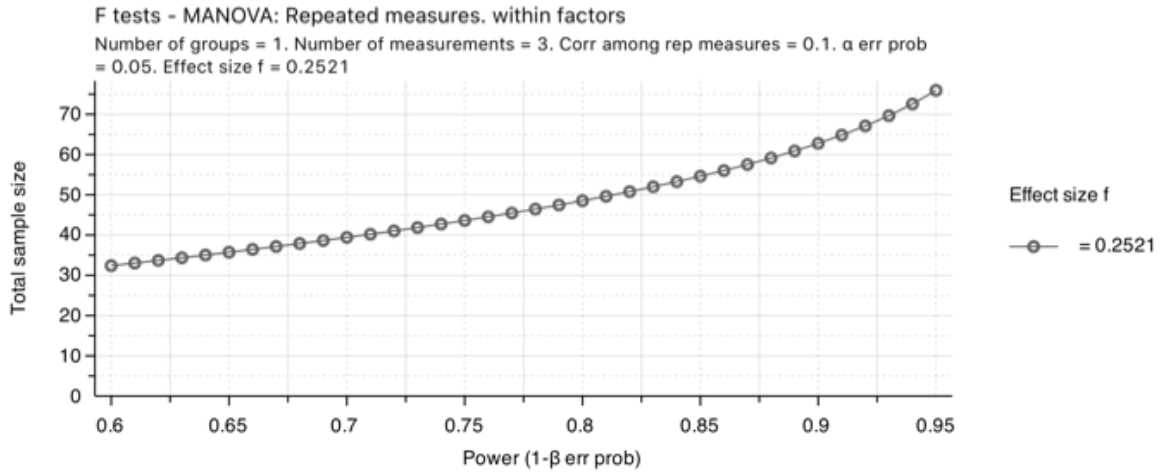
Equality of Variances				
Method	**Num DF**	**Den DF**	**F Value**	**Pr > F**
Folded F	17	17	1.55	0.3729

Based on the above work, we have taken a very conservative estimate of effect size (Table 4), and estimate that a sample size of n=49, will provide approximately 80% power to detect a medium effect size of *f*=0.2521 when alpha is set to 0.05 for repeated measures MANOVA with 1 group and 3 measurements, using the *F*-distribution. (Figure 2). Given a liberal attrition rate of 20% and the need to examine age-associated differences in depth (i.e., covariates such as age and time since stroke), we plan to enroll up to a total of 75 participants (*n* = 75) *to* ensure adequate power for the planned analyses.

Table 4: Point Estimate and 95% Confidence Interval Effect Size, *d* and *f*

	Effect Size		
	Point Estimate	**95% Lower Bound**	**95% Upper Bound**
d	1.22667	0.50413	1.93409
f	0.6134	0.2521	0.9670

Figure 2: Differences Between Independent Means and Power/Sample Size Estimates



Desired Power	Required Sample Size
0.600000	32.393509
0.610000	33.035972
0.620000	33.689708
0.630000	34.355391
0.640000	35.033746
0.650000	35.725556
0.660000	36.431665
0.670000	37.152989
0.680000	37.890523
0.690000	38.645352
0.700000	39.418662
0.710000	40.211754
0.720000	41.026061
0.730000	41.863165
0.740000	42.724820
0.750000	43.612981
0.760000	44.529834
0.770000	45.477833
0.780000	46.459755
0.790000	47.478749
0.800000	48.538415
0.810000	49.642895
0.820000	50.796985
0.830000	52.006284
0.840000	53.277389
0.850000	54.618146
0.860000	56.037995
0.870000	57.548430
0.880000	59.163657
0.890000	60.901520
0.900000	62.784876
0.910000	64.843687
0.920000	67.118332
0.930000	69.665121
0.940000	72.566040
0.950000	75.947367

Data Analyses:

Primary Study Hypothesis: Subjects will exhibit significantly higher scores on the UE FM when using the MyoPro 2 Motion G compared to scores when using the splint and no device.

Secondary Study Hypotheses:

Hypothesis 2a: Subjects will exhibit significantly higher scores on the B&B when using the MyoPro 2 Motion G compared to scores when using the splint and no device.

Hypothesis 2b: Subjects will exhibit significantly higher quality scores and decreased time on the battery of functional tasks when using the MyoPro 2 Motion G compared to scores when using the splint and no device.

We will evaluate primary and secondary study hypotheses using repeated measures MANOVA. The independent variable is device usage and has three levels: (1) performance with MyoPro 2 Motion G, (2) performance with the resting hand splint, and (3) performance without device. The multiple dependent variables include: (1) UE movement as measured by the UEFM (primary hypothesis), (2) dexterity as measured by the B&B (hypothesis 2a), and (3) functional movement as measured by the novel battery (hypothesis 2b). A significant main effect and/ or interaction effect will be investigated in greater detail using univariate tests. These analyses are powered to permit inclusion of 1-2 covariates such as participant age and time since stroke. Post-hoc analyses will include a specific contrast for participants aged 65 and over.

Psychometric Analyses of Functional Test Battery

In addition to analyses of functional tasks, we will perform psychometric analyses on the battery of functional tasks. This is expected to produce a validated functional outcome measure that can be used in people with moderate UE impairments resulting from stroke and other disorders, which will fill a gap in the field.

To determine reliability, we will use multiple measures of internal consistency, including Cronbach's α, as well as ordinal α and Gugiu's bootstrap reliability. While Cronbach's α has been traditionally used in psychometric analyses, it is based on assumptions of interval level items and, thus, relatively poorly situated to measure reliability of measures that are comprised of items that use ordinal level scales, as is the case with our functional battery. The latter easures in combination with Cronbach's α are expected to provide a more rigorous ascertainment of internal consistency.

To ascertain dimensionality we will use latent parallel analyses (LPA) in which we: (a) generate a polychoric correlation matrix for battery items; (b) using the polychoric correlation matrix as input for LPA; (c) conducting Monte Carlo simulations to create 250 random datasets designed to match the number of respondents (n=75) and distributional characteristics of battery items; and (d) compute, extract, and compare eigenvalues for the real and random datasets.

Lastly we will ascertain convergent validity between the functional battery items and the UE FM using the Pearson correlation coefficient (*r).*

References

[1] Broeks JG, Lankhorst GJ, Rumping K, Prevo AJ: The long-term outcome of arm function after stroke: results of a follow-up study. Disabil Rehabil 1999;21:357–364

[2] Mayo N. Activity, participation, and quality of life 6 months poststroke. Arch Phys Med Rehabil 2002;83:1035–1042.

[3] Wolf SL, Winstein CJ, Miller JP, Taub E, Uswatte G, Morris D., et al. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. JAMA 2006;296:2095-2104.

[4] Page SJ, Levine P, Leonard A. Mental practice in chronic stroke: Results of a randomized, placebo controlled trial. Stroke 2007;38:1293-7.

[5] Page SJ, Boe S, Levine P. What are the "ingredients" of modified constraint-induced therapy? An evidence based review, recipe, and recommendations. Restor Neurol Neurosci 2013;31:299-309.

[6] Wolf SL, Binder-MacLeod SA. Electromyographic biofeedback applications to the hemiplegic patient: changes in upper extremity neuromuscular and functional status. Phys Ther 1983;63:1393–1403.

[7] Stein J, Narendran K, McBean J, Krebs K, Hughes R: Electromyography controlled exoskeletal upper-limb–powered orthosis for exercise training after stroke. Am J Phys Med Rehabil 2007;86:255–261.

[8] Fasoli SE, Krebs HI, Stein J, Frontera WR, Hogan N. Effects of robotic therapy on motor impairment and recovery in chronic stroke. Arch Phys Med Rehabil 2003;84:477-82.

[9] Milot MH, Spencer SJ, Chan V, Allington JP, Klein J, Chou C, Bobrow JE, Cramer SC, Reinkensmeyer DJ. A crossover pilot study evaluating the functional outcomes of two different types of robotic movement training in chronic stroke survivors using the arm exoskeleton BONES. J Neuroeng Rehabil 2013;10:112.

[10] McLean L & Scott RN. The Early History of Myoelectric Control of Prosthetic Limbs (1945 – 1970). In A. Muzumdar (Ed.), Powered Upper Limb Prostheses (pp1-2). 2004.

[11] Page SJ, Hill V, White S. Portable upper extremity robotics is as efficacious as upper extremity rehabilitative therapy: a randomized controlled pilot trial. Clin Rehabil 2013;27:494-503.

[12] Page SJ, Hermann VH, Levine PG, Lewis E, Stein J, DePeel J. Portable neurorobotics for the severely affected arm in chronic stroke: a case study. J Neurol Phys Ther 2011;35:41-6.

[13] Kim G, Rivera J, Stein J. Combined Clinic-Home Approach for Upper Limb Robotic Therapy After Stroke: A Pilot Study. Arch Phys Med Rehabil 2015 Dec;96(12):2243-8.

[14] Desrosiers J, Bravo G, Hébert R, Dutil É & Mercier L. Validation of the box and block test as a measure of dexterity of elderly people: reliability, validity and norms studies. Archives of Physical Medicine and Rehabilitation 1994;75:751-755.

[15] Cromwell F. Occupational therapists manual for basic skills assessment: primary prevocational evaluation. 1994. Pasadena, (CA): Fair Oaks Printing; 29-31.