Published in final edited form as:
NeuroRehabilitation. 2014 January 1; 35(4): 741–754. doi:10.3233/NRE-141178.

Using clinical and robotic assessment tools to examine the feasibility of pairing tDCS with upper extremity physical therapy in patients with stroke and TBI: a consideration-of-concept pilot study

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Abstract

BACKGROUND—Transcranial direct current stimulation (tDCS) may provide a safe, non-invasive technique for modulating neural excitability during neurorehabilitation.

OBJECTIVE—1) Assess feasibility and potential effectiveness of tDCS as an adjunct to standard upper extremity (UE) physical therapy (PT) for motor impairments resulting from neurological insult. 2) Determine sustainability of improvements over a six month period.

METHODS—Five participants with chronic neurologic insult (stroke or traumatic brain injury > 6 months prior) completed 24 sessions (40 minutes, three times/week) of UE-PT combined with bihemispheric tDCS delivered at 1.5mA over the motor cortex during the first 15 minutes of each PT session. Outcomes were assessed using clinical (UE Fugl-Meyer, Purdue Pegboard, Box and Block, Stroke Impact Scale) and robotic (unimanual and bimanual motor control) measures. Change in scores and associated effects sizes from Pre-test to Post-test and a six month Follow-up were calculated for each participant and group as a whole.

RESULTS—Scores on UE Fugl-Meyer, Box and Block, Purdue Pegboard, Stroke Impact Scale, and robotic measures improved from Pre- to Post-test. Improvements on UE Fugl-Meyer, Box and Block, and robotic measures were largely sustained at six months.

CONCLUSIONS—Combining bihemispheric tDCS with UE-PT in individuals with neurological insult warrants further investigation.

INTRODUCTION

Following neurological insult, sites in the intact hemisphere exert increased interhemispheric inhibition over homologous sites in the lesioned hemisphere. This inhibition may hinder functional recovery by further suppressing already reduced activity in the lesioned

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Declaration of Interest
The authors have no commercial interest relevant to the subject of the manuscript, nor any other conflicts of interest to report.

hemisphere and interfering with the normal operation of activity-dependent plasticity (Kidgell, Goodwill, Frazer, & Daly, 2013; Murase, Duque, Mazzocchio, & Cohen, 2004). Transcranial direct current stimulation (tDCS) may provide a safe, non-invasive (Russo, Wallace, Fitzgerald, & Cooper, 2013) technique for modulating neural excitability by exciting (anodal stimulation) or inhibiting (cathodal stimulation) neurons in targeted cortical areas (Kidgell et al., 2013; Pellicciari, Brignani, & Miniussi, 2013). Accordingly, tDCS may allow for better recovery by reducing interhemispheric imbalance (Bolognini, Pascual-Leone, & Fregni, 2009; Feng, Bowden, & Kautz, 2013; Murase et al., 2004; Nowak, Grefkes, Ameli, & Fink, 2009). In particular, bihemispheric stimulation, which involves placement of the source electrode over the damaged motor cortex and placement of the sink electrode over the undamaged motor cortex, may provide additional benefits over stimulation of a single hemisphere by simultaneously increasing excitability in weakened areas and decreasing excitability in regions that inhibit these areas (Vines, Cerruti, & Schlaug, 2008).

Bihemispheric tDCS holds potential as a feasible adjunct to standard rehabilitation because it is portable and requires minimal technical expertise, time, and monetary cost. Stimulation is delivered via a lightweight, portable unit that can be carried in a pocket. The unit is connected to two disposable sponge electrodes that can be held in place with a cap. Importantly, neither the unit nor the cap interferes with typical treatment activities. Placing the electrodes and programming the unit can be completed in approximately five minutes and requires minimal training. The units are also relatively inexpensive and, in many cases, already available for iontophoresis treatments in physical therapy (PT) clinics.

Multiple studies have been conducted to examine the immediate effects of a single bout of tDCS on individuals with stroke (Fusco et al., 2013; Giacobbe et al., 2013; Lefebvre et al., 2012; Lefebvre et al., 2013; O'Shea et al., 2013). However, few studies have used tDCS as an adjunct to upper extremity (UE) therapy for this population, and none have examined individuals with TBI. Most studies have included approximately five treatment sessions (Khedr et al., 2013; Lindenberg, Renga, Zhu, Nair, & Schlaug, 2010; Nair, Renga, Lindenberg, Zhu, & Schlaug, 2011; Ochi, Saeki, Oda, Matsushima, & Hachisuka, 2013), with a few longer studies including between 10 and 20 sessions (Bolognini et al., 2011; Wu et al., 2013). Follow-up periods have ranged from one week (Lindenberg et al., 2010; Nair et al., 2011) to three months (Khedr et al., 2013). As a result, numerous questions exist regarding the role of tDCS as an adjunct to PT over the course of an entire plan of care, which for UE PT, typically includes approximately 960 minutes dispersed over 24 treatment sessions (Birkenmeier, Prager, & Lang, 2010; Chang, Tung, Wu, Huang, & Su, 2007; Dickstein, Hocherman, Pillar, & Shaham, 1986; Kimberley, Samargia, Moore, Shakya, & Lang, 2010; Lang, MacDonald, & Gnip, 2007; Wang, Zhao, Zhu, Li, & Meng, 2011). Is providing stimulation throughout an entire plan of care feasible? Are there adverse effects? Does it elicit improvement in UE function? Are improvements maintained for extended periods of months and years following treatment?

Dobkin (2009) presented recommendations on staging of pilot studies in neurorehabilitation, which included guidelines for designing studies that build on each other and lead to effective multi-center randomized clinical trials (MRCT). Dobkin proposes that research on

rehabilitation techniques should progress through four stages from consideration-of-concept studies (stage 1) through proof-of-concept MRCTs (stage 4) (Dobkin, 2009). As evidence is limited in regards to the use of bihemispheric tDCS as an adjunct to UE therapy in patients with neurological insult, consideration-of-concept studies are needed prior to moving on to more advanced stages. Our objective was to carry out a consideration-of-concept pilot study aimed at: 1) assessing the feasibility and potential effectiveness of tDCS paired with standard UE PT over an entire plan of care for individuals with motor impairments resulting from neurological insult, and 2) determining the sustainability of improvements over a six month period.

METHODS

Participants

All participants signed an Informed Consent form approved by the Institutional Review Board of the University of XXX. Inclusion and exclusion criteria are presented in Table 1.

Intervention

During the intervention phase of the study, participants completed 24 sessions (40 minutes, three times per week) of UE PT combined with bihemispheric tDCS. The first 10 minutes of each session were dedicated to standardized strengthening activities, and the final 30 minutes were spent performing three, separate functional activities for 10 minutes each. All activities were tailored to the appropriate level for each participant with the goal of maintaining a degree of difficulty sufficient to produce adaptation. The treatment clock was started at the beginning of the session and the session was terminated once 40 minutes had elapsed, similar to the time demands in a clinical setting. A physical therapist or doctoral student in physical therapy delivered all treatments.

Strengthening Phase (10 minutes)—Participants performed one minute of five UE exercises in circuit format completed twice. Standardized exercises consisted of push-ups, pronation/supination of the affected UE, and UE therapy-ball exercises (lifting ball up/down, moving ball side-to-side, and rotating ball). Push-ups were progressed by transitioning from wall push-ups to push-ups on an elevated mat table. Forearm pronation/supination was progressed by changing the weight or lever arm of the object held by the participant. Therapy ball exercises were progressed by increasing the size of the ball (e.g. 45cm diameter to 55cm). During each strengthening activity, continuous performance for one minute was encouraged.

Functional Activities Phase (30 minutes)—Although the structure of delivery of the functional activities was standardized (i.e. three activities for 10 minutes), activities were participant-specific and modeled on clinical practice. By organizing functional activities into 10 minute blocks, we were able to address different impairments, maximize active time, and minimize time lost transitioning between activities. Activities ranged from gross to fine motor depending on participant deficits. Examples of gross motor activities included reaching for items on shelves, hitting a balloon with a racquet or hand, and simulating household chores. Activities were progressed by changing the direction or height of reaching

and hitting motions, incorporating heavier objects, or increasing the complexity of chores. Examples of fine motor tasks included flipping playing cards, manipulating small change, and writing. These were progressed by adding speed and/or accuracy components.

tDCS Parameters—During the first 15 minutes of each treatment session (10 minutes of strengthening and first five minutes of functional activities), participants received 1.5 mA of bihemispheric tDCS delivered via a dual-channel constant-current stimulator (Chattanooga Ionto Dual Channel Drug Delivery Phoresor Device, Iomed® Inc., Salt Lake City, Utah). In order to determine location of motor cortices and maintain electrode contact, the participants were fitted with a standard EEG cap (International EEG system). Saline soaked 2”× 2” sponge electrodes were then placed under the C3 and C4 electrode locations on the cap, which correspond to the left and right motor cortices, respectively. Cap sizing and electrode placement were in accordance with the international 10–20 system (Homan, Herman, & Purdy, 1987; Okamoto et al., 2004). The anodal electrode was centered over the ipsilesional motor cortex and cathodal electrode over the contralesional motor cortex. Previous studies involving individuals with chronic stroke have applied tDCS ranging from 1 to 2 mA delivered for between 10 and 40 minutes (Ang et al., 2012; Bolognini et al., 2011; Lefebvre et al., 2012; Lindenberg et al., 2010; Ochi et al., 2013). The dosage selected for this study falls within this range and has been shown to alter excitability of underlying cortical regions for 60 to 90 minutes (Nitsche & Paulus, 2001).

Outcome Measures

A unique feature of this study was supplementing traditional clinical measures with more sensitive robotic measures of UE function. Robotic assessments provide objective measures that can accurately quantify spatial and temporal parameters of UE movements in neurological populations (Balasubramanian, Colombo, Sterpi, Sanguineti, & Burdet, 2012; Debert, Herter, Scott, & Dukelow, 2012; Einav, Geva, Yoeli, Kerzhner, & Mauritz, 2011; Zollo, Gallotta, Guglielmelli, & Sterzi, 2011). Such objective measures are particularly valuable for avoiding biases that can influence longitudinal assessments used for intervention studies (Scott & Dukelow, 2011).

The schedule of assessment sessions is presented in Figure 1. Both clinical and robotic data were collected at each time point. Pre-intervention testing, Post-test, and Follow-up sessions were comprehensive, while only a subset of the clinical measures (i.e. Box and Block Test, Purdue Pegboard Test, and robotic measures) were administered during interim testing sessions. All testing was conducted by a licensed physical therapist who received training on the standardized protocols.

Clinical Measures—Fugl-Meyer Assessment of Sensorimotor Impairment UE section (UE-FM) The UE-FM is a valid and reliable measure of UE impairment following stroke and is recommended for assessing change in this population (Gladstone, Danells, & Black, 2002; J. H. Lin et al., 2009). The UE-FM assesses reflexes, range of motion, pain, light touch sensation, proprioception, movements in and out of synergy, grasp, and coordination on a 3-point ordinal scale (0 = cannot perform, 1 = performs partially, 2 = performs fully) with a maximum score of 66 points (Duncan, Propst, & Nelson, 1983). For individuals with

chronic stroke, change scores of 4.25 to 7.25 points indicate that a clinically important change has occurred (Page, Fulk, & Boyne, 2012). The UE-FM was administered at Baseline, Post-test, and all Follow-up testing sessions.

Box and Block Test (BBT): The BBT assesses manual dexterity by requiring participants to move as many 2.5 cm blocks as possible in one minute. Participants move the blocks over a partition separating two sides of a standardized test box. Normative data regarding the number of blocks moved for five-year age groups has been established (Mathiowetz, Volland, Kashman, & Weber, 1985). The measure is valid (K. C. Lin, Chuang, Wu, Hsieh, & Chang, 2010) and reliable (Chen, Chen, Hsueh, Huang, & Hsieh, 2009) for assessing UE dexterity following stroke with a minimal detectable change (MDC) for this population of 5.5 blocks (Chen et al., 2009). The BBT was administered at all assessment sessions.

Purdue Pegboard Test (PPT): The PPT is a reliable measure of fine manual dexterity that requires participants to pick up pins one at a time out of a well and place them consecutively in a row of holes (Desrosiers, Hebert, Bravo, & Dutil, 1995; Tiffin & Asher, 1948). The goal is to successfully place as many pins as possible in 30 seconds. Normative data for this measure have been established (Desrosiers et al., 1995; Tiffin & Asher, 1948). The PPT was administered at all assessment sessions.

Stroke Impact Scale-16 (SIS-16): The SIS-16 is a valid and reliable assessment of self-perceived physical function (Duncan, Lai, Bode, Perera, & DeRosa, 2003) with a minimal clinically important difference value of 9.4–14.1 points (Fulk et al., 2010). Domains covered on the SIS-16 include hand function, strength, mobility, and ADL/IADL (Duncan et al., 2003). The participant scores each item on a 1 to 5 Likert scale with higher scores indicating better self-perceived function. The SIS was administered at Baseline, Post-test, and all Follow-up testing sessions.

Robotic Measures—Robotic assessments were performed using the KINARM End-Point Lab (BKIN Technologies, Kingston, Ontario, Canada). Participants sat at the robot and grasped handles linked to robotic motors with each hand (see Figure 2A). Arm movements were performed in a horizontal plane in response to targets presented with an augmented reality display. Robotic measures were collected at all assessment sessions. The following standardized tasks were used to quantify the participants' UE sensorimotor functioning.

Visually Guided Reaching Task: The visually guided reaching task is a reliable, sensitive measure of UE visuomotor control following stroke (Coderre et al., 2010). Participants generated reaching movements from a central target to four peripheral targets (2.0 cm diameter circles) located 10 cm away (see Figure 2 B and C). Participants were instructed to reach as quickly and accurately as possible to the targets as they appear. Targets were presented in a block design with five randomized blocks for a total of 40 trials. Each participant repeated the task twice, once with each hand. Four measures were used to quantify distinct aspects of task performance: speed maxima count, path length ratio, movement time, and initial direction error. These are defined in Table 2.

Object Hit Task: The object hit task is designed to assess bimanual coordination and spatial awareness (Tyryshkin et al., 2014). Participants used 5 cm paddles displayed on top of the robot handles to hit away balls (2.0 cm diameter circles) moving towards them from the top of the workspace. Participants were instructed to use both hands to hit as many balls away as possible with the paddles. The workspace (80 cm wide) was divided into 10 bins containing 30 balls each for a total of 300 balls. The time and location that balls were released was randomized, but the speed each ball moved was constant. The task took a fixed amount of time, and difficulty increased over time by progressively increasing the number of balls and their speed (See Figure 2 D–F). Four measures were used to quantify distinct aspects of task performance: total hits, hit bias, miss bias, and movement area bias (Table 2).

Data Analysis

Change in outcome measure scores from Pre-test to Post-test and Pre-test to Follow-up 3 were calculated for each participant and the group as a whole. Effect size data was included as this may help inform sample sizes of future studies. To maintain consistency of effect size interpretation across all measures, positive effect size values represent improvement and negative values represent decline. For measures in which a positive effect size indicated decline, the sign on the effect size was reversed.

RESULTS

Participants

Eight individuals who met all inclusion and exclusion criteria participated in the study. Three participants did not complete the intervention; one dropped out due to unrelated health issues and two dropped out due to unexpected scheduling/transportation issues. Baseline characteristics of the remaining five participants are presented in Table 3.

Follow-up Assessment Sessions

Table 4 shows the timing of the Follow-up assessment sessions of each participant. Although follow-up testing was planned for two, four, and six months following completion of intervention, scheduling difficulties resulted in a number of minor deviations from the planned protocol. Notably, Participant 1 completed Follow-up 2 at five months post-intervention and was unable to complete Follow-up 3. Because of the proximity in time (see Table 4), data from Follow-up 2 was carried forward and included in the data analysis for Follow-up 3 for this patient only. Participant 5 completed 14 sessions of an unrelated sensory intervention study focused solely on proprioception between Follow-ups 2 and 3.

Individual Participant and Group Outcomes

Due to the small diverse sample, results are presented for each participant separately, as well as for the group as a whole. Data from Pre-test, Post-test, and Follow-up 3 were selected for presentation. These time points provide information on participant performance prior to, immediately following, and six months following intervention.

Clinical Outcomes—Table 5 and Figure 3 show individual and group data on clinical outcome measures. The greatest improvement immediately following intervention was seen

on the UE-FM (mean change = 7.6, effect size = 0.47). Individual participant results on the clinical measures were variable, with some participants demonstrating change on specific measures and others demonstrating little to no change on the same measure.

Robotic Outcomes—Table 6 and Figures 4 and 5 show individual and group data on robotic outcome measures. At the group level, the participants exhibited consistent Pre- to Post-test improvements on the reaching task and object hit task. Despite their heterogeneity, individual participants showed improvements in performance on the reaching and/or object hit task that were consistent with the changes in the group data.

DISCUSSION

This consideration-of-concept pilot study provides preliminary information regarding the feasibility and potential effectiveness of bihemispheric tDCS as an adjunct to UE therapy for patients with a chronic neurological insult. Feasibility of the approach was demonstrated by the easy incorporation into treatment sessions. The delivery of stimulation did not hinder participants' ability to engage in our treatment activities, nor did it result in complaints of skin irritation or discomfort. We cannot conclude, however, whether daily treatments would be as well-tolerated.

In addition to feasibility, another goal of consideration-of-concept pilot studies is to determine if novel intervention strategies warrant further investigation (Dobkin, 2009); in other words, does it demonstrate the *potential* to provide an effective approach. As the effect sizes for a majority of the clinical and robotic measures were in a direction indicating improvement, tDCS demonstrates potential and warrants further investigation. This is particularly true given that the treatment combination that can be easily implemented into clinical practice.

Clinical Outcomes

The largest improvement on the clinical measures was seen on the UE-FM. Using a clinically important difference estimate of 4.25 points (Page et al., 2012), three participants demonstrated a meaningful change immediately following the intervention and two maintained the improvements at six months. Gross manual dexterity improved slightly over the course of the intervention and was largely maintained at six months, as seen by performance on the BBT. In contrast, fine manual dexterity did not improve. Scores for all participants on the PPT were largely unchanged at Post-Test and Follow-up 3 compared to performance prior to the intervention. The differences observed between gross and fine manual dexterity may be due to the selected treatment activities. A review of the treatment logs revealed that more time during the functional training portion of the treatment sessions was dedicated to gross rather than fine manual dexterity activities. The Pre-Test PPT scores further indicate that four of the five participants presented with fairly significant fine motor impairments, thus trainers selected treatment activities addressing gross manual dexterity, as they were challenging but achievable.

Robotic Outcomes

The reaching task required participants to perform controlled reaching movements with their affected UE. Participants performed the task with smoother movements following the intervention and at Follow-up 3, as seen by reductions in speed maxima counts. Not only were movements smoother, they were straighter and exhibited greater initial accuracy following the intervention and at six months, as captured by decreased path length ratios and decreased initial direction errors, respectively. The aforementioned improvements were not at the expense of speed; although accuracy improved, speed remained similar from Pre- to Post-test and actually increased slightly between Pre-test and Follow-up 3. Overall, the results from the reaching task indicate that participants demonstrate improved control and coordination of reaching movements with their affected UE following the intervention. Of clinical importance is the maintenance of improvements at six months.

The object hit task was used to provide information regarding bimanual coordination and spatial awareness. Perhaps the most clinically relevant outcome from this task pertains to relative use of the affected UE compared to the unaffected UE. As measured by the hit bias, participants demonstrated greater use of their affected UE following intervention, and this improvement was maintained at Follow-up 3. Furthermore, the balls missed were more evenly distributed between the two sides of the screen, providing further evidence for increased use (and possibly improved hitting accuracy) of affected UE. These changes in hit bias and miss bias likely contributed to produce the overall increase in the number of balls hit by participants following the intervention. Observational analysis of participant hand tracings produced during performance of the task also indicated that participants were performing the task with greater control and coordination of their affected UE following intervention.

Limitations

There are limitations specific to this study that must be taken into consideration. First, our dropout rate was high even though several measures were taken to help with adherence (e.g. personal calendars, phone calls, etc.). Second, the follow-up schedule for Participant 1 did not occur at the predetermined two month interval. This participant's final follow up occurred at five months rather than at six months. A qualitative comparison of the other participants suggests that the additional month would not have dramatically influenced the results. The data for Follow-up 3 of Participant 5 should also be interpreted with caution. This participant completed 14 sessions of a sensory intervention focused solely on UE proprioception between Follow-up 2 and 3. Although this was not a motor intervention, we acknowledge the sensory intervention may have impacted UE function at Follow-up 3. Finally, we used a mixed group of participants with stroke and TBI. While this limits the applicability to one group or the other, the fact that we saw improvements in patients with both stroke and TBI suggests that this intervention holds potential as a broad treatment for individuals with neurological insult. This is of particular clinical importance where inpatient and outpatient rehabilitation units must treat a broad population of neurological patients with heterogeneous brain lesions.

Future Studies

Prior to moving on to the next stage of pilot studies, a development-of-concept trial, it may be appropriate to conduct further consideration-of-concept studies (Dobkin, 2009). Although our study indicates feasibility and potential effectiveness of using tDCS as an adjunct to standard PT, additional investigations need to examine dose-response characteristics, individual differences in response, and sensitivity to electrode placement. Using consideration-of-concept studies to determine these details will allow for better study design of subsequent development-of-concept studies. Once the aforementioned issues have been adequately investigated, the findings of these studies can be incorporated into future development-of-concept studies that include a proper control group, adequate sample, randomization of participants, and blinding of assessors.

Conclusions

In keeping with recommendations on staging of pilot studies, a consideration-of-concept study was conducted to investigate the feasibility and potential effectiveness of a novel intervention strategy combining bihemispheric tDCS with UE therapy in individuals with neurological insult. The addition of tDCS to UE therapy was found to be clinically feasible, as the unit did not hinder participants' ability to perform treatment activities and stimulation was well-tolerated. The intervention also demonstrated potential effectiveness. Improvements in UE function were seen on both clinical and robotic measures following 24 sessions of UE therapy combined with bihemispheric tDCS. Many of these improvements, though small, were maintained at a six month follow-up. Combining bihemispheric tDCS with UE therapy in individuals with neurological insult warrants further investigation, including additional consideration-of-concept and development of concept studies before moving on to a proof-of-concept MRCT.

Acknowledgements

The authors would like to thank the Doctorate of Physical Therapy students who assisted with delivery of the intervention and our lab coordinators Angela Ross, Amanda Estep, and Kristen Hadley who handled the scheduling of participants and trainers. We would also like to thank the participants who contributed their time and effort. Addie Middleton, PT, DPT is funded by a NIH T32 pre-doctoral research training grant via the National Institute of General Medical Sciences.

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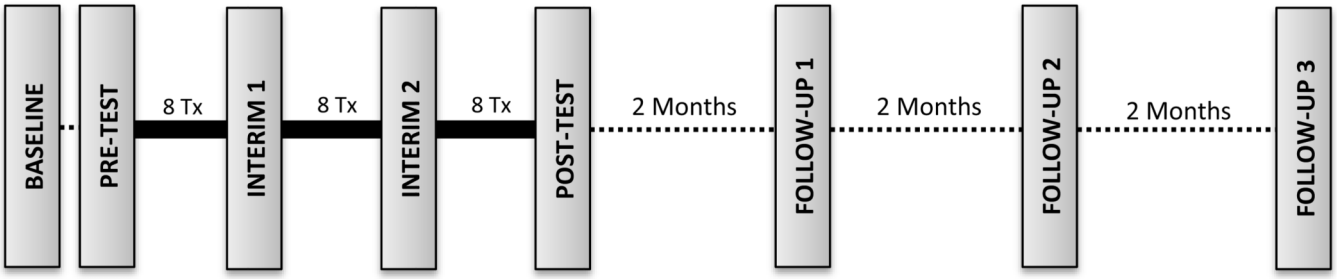

Figure 1.
Flow of assessment and treatment sessions. Tx, treatment sessions

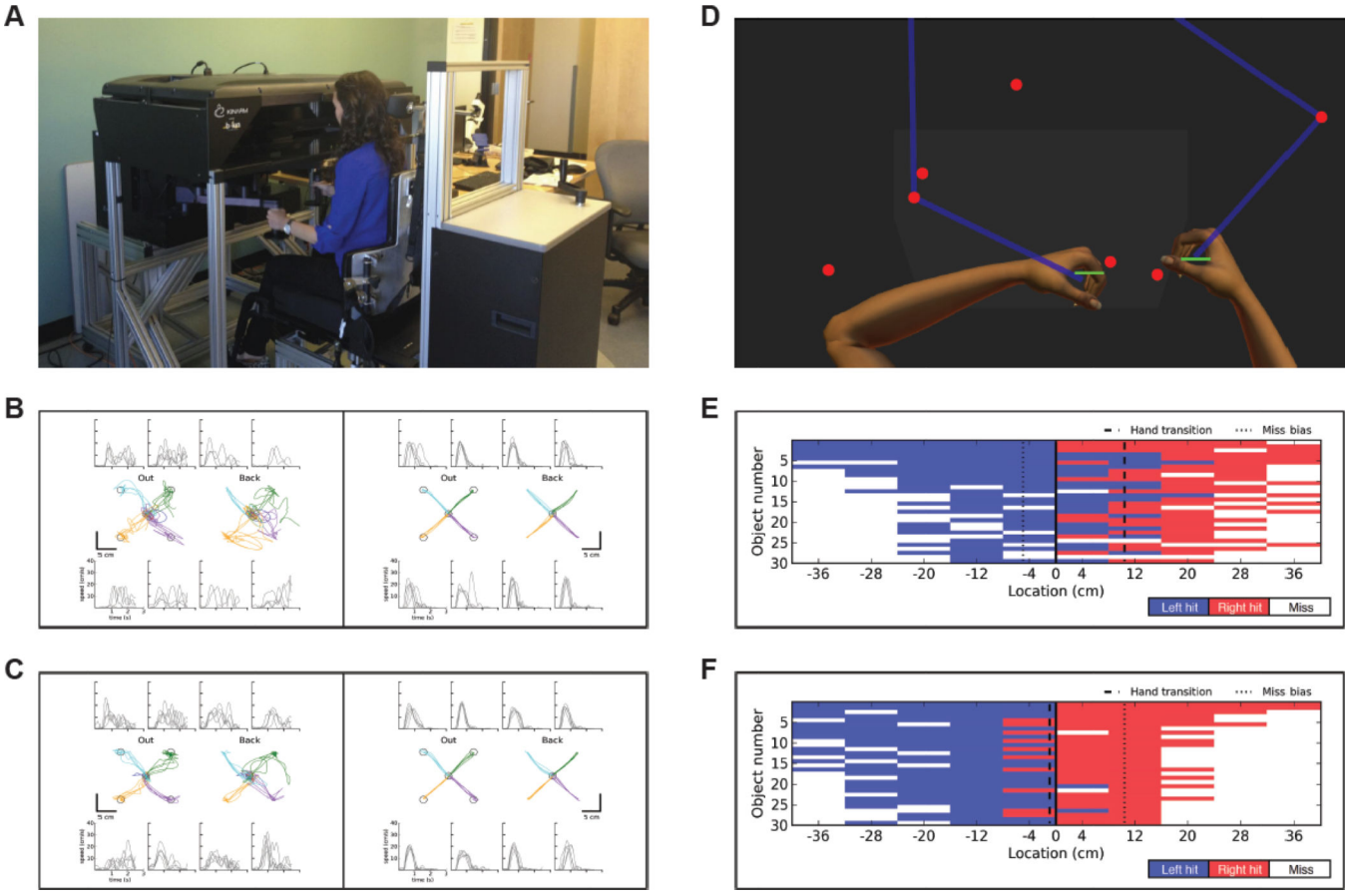

Figure 2.

Robotic Assessment. **A**, Individual seated at the KINARM End-Point Lab (BKIN Technologies, Kingston, Ontario, Canada). While sitting in a modified wheelchair base that can be raised and lowered with a hydraulic system, participants grasp two handles linked to robotic motors that can apply loads to either hand. Small discs are mounted underneath each handle to provide the hands with gravitational support. A video monitor and semitransparent mirror located above the hands are used to project visual targets onto the same plane as the hands. **B,C**, Hand paths and hand-speed profiles of Participant 5 during performance of the visually guided reaching task with the affected left hand (left half) and less affected right hand (right half) at Pre-test (B) and Post-test (C). Hand paths (center row) depict each reaching movements from the central target out to the four peripheral targets (first and third plots) and from the peripheral targets back to the central target (second and fourth plots). The hand-speed profiles (top and bottom rows) correspond to reaching movements to and from the closest peripheral target in each plot. Each line on the graph represents a single trial. **D**, Overhead reproduction of Participant 2 (right upper extremity affected) performing the object hit task. Participants use paddles (5 cm) attached to each hand to hit away as many balls as possible as they move towards them from the top of the screen. **E, F**, Performance of Participant 2 on the object hit task at Pre-test (E) and Post-test (F). Balls move along 10 vertical paths (columns) with 30 balls (rows) in each path for a total of 300 balls. Blue areas represent hits with the left hand (less affected) and red areas represent hits

with the right hand (affected). White areas represent misses. At Pre-test, Participant 2 frequently uses her left hand to hit balls on the right side of the screen (E), whereas hand and use is more symmetrical at Post-test (F). This is shown measured by the hand transition parameter (dashed line), which is on the right during the Pre-test and relatively central during the Post-test.

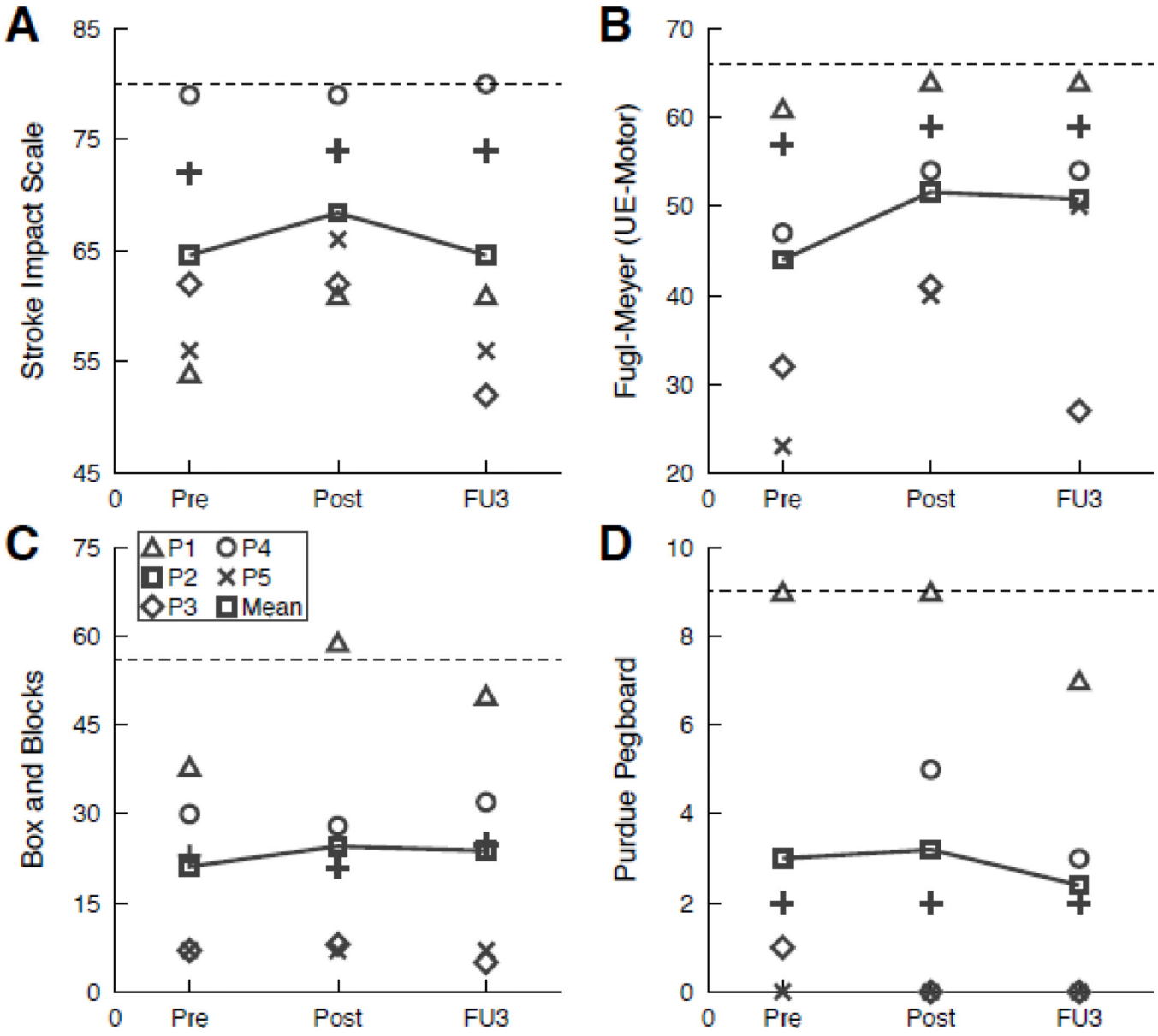

Figure 3.

Individual and group outcomes on clinical measures. Results presented for Stroke Impact Scale (A), Fugl-Meyer Assessment of Sensorimotor Impairment UE section (B), Box and Blocks Test (C), and Purdue Pegboard Test (D). Dashed lines in A and B show maximum attainable score (normal). Dashed lines in C and D show the lower limit of normal range. For all measures, increases in score indicate improvement. Abbreviations: UE, upper extremity; Pre, Pre-test; Post, Post-test; FU 3, Follow-up 3.

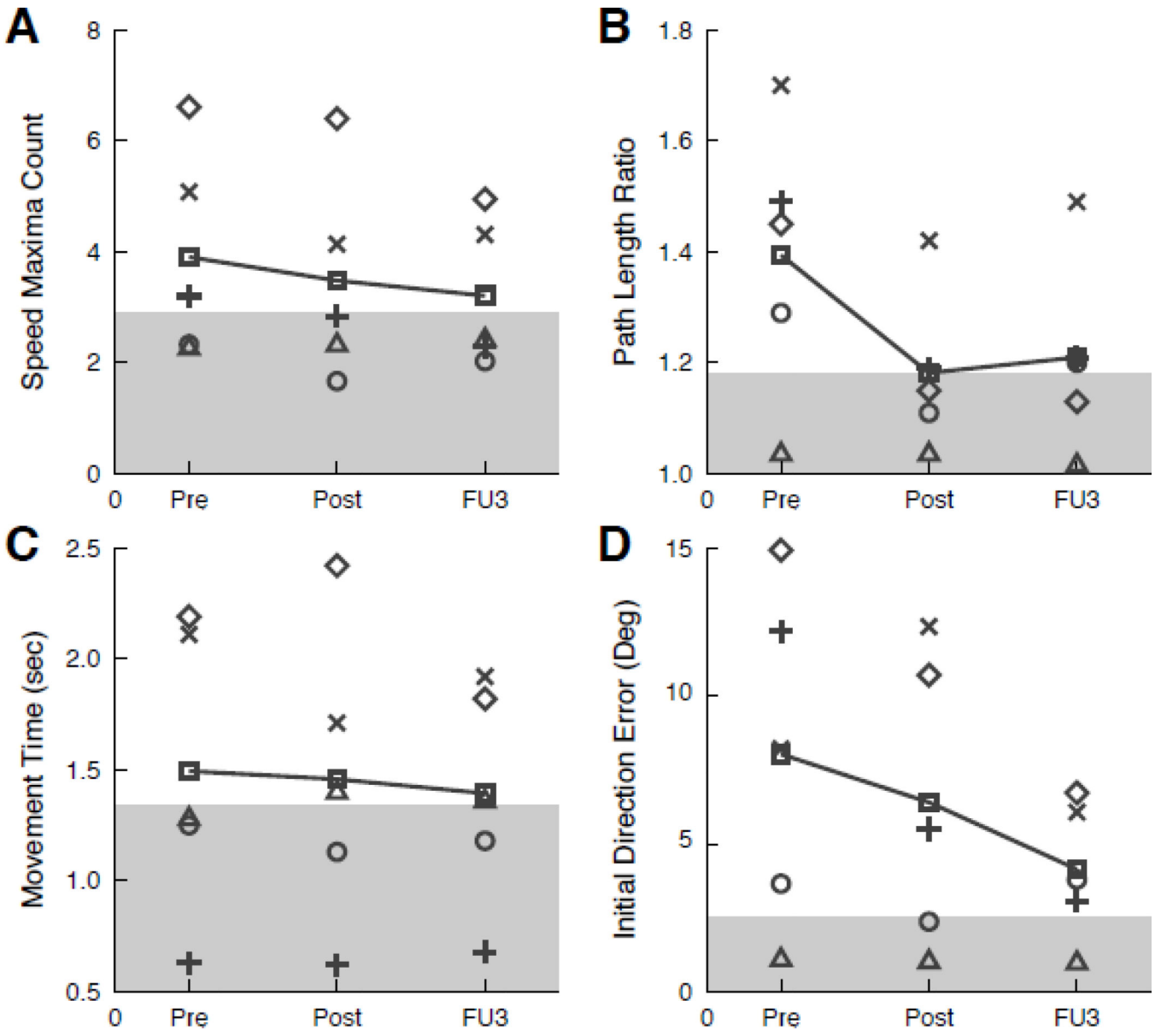

Figure 4.

Individual and group outcomes on visually guided reaching task. Results presented for speed maxima count (A), path length ratio (B), movement time (C), and initial direction error (D). For all measures, movement towards normal range (grey shaded areas) is indicative of improvement. Abbreviations and symbols same as Figure 2.

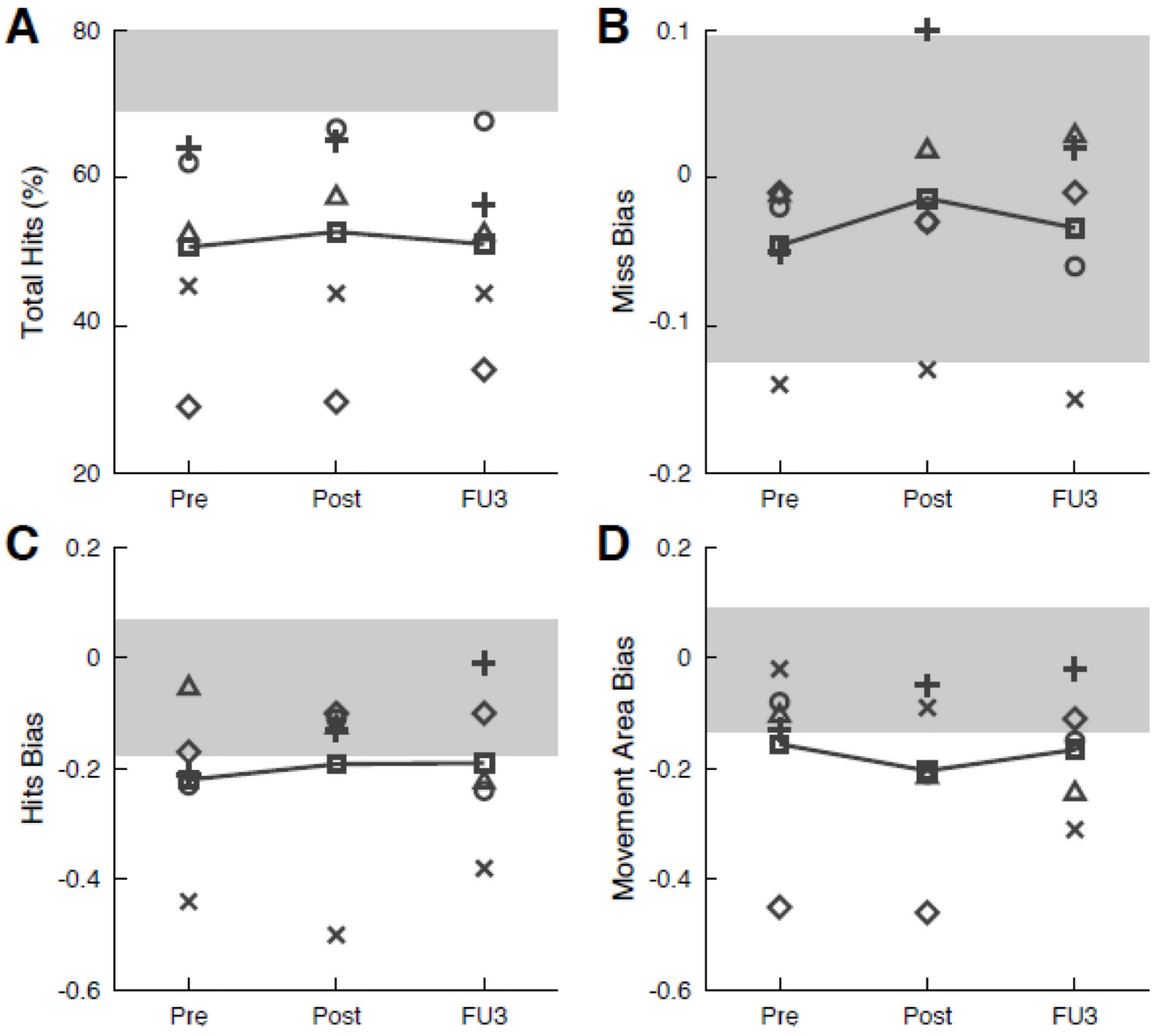

Figure 5.

Individual and group outcomes on object hit task. Results presented for total hits (A), miss bias (B), hit bias (C), and movement area bias (D). For all measures, movement towards normal range (grey shaded areas) is indicative of improvement. Abbreviations and symbols same as Figure 2.

Table 1

Inclusion and Exclusion Criteria

Inclusion Criteria

• 18 years of age or older
• Medical history of neurologic insult > 6 months prior
• More than half normal passive range of motion in the affected upper extremity
• Ability to:
  ◦ Follow simple instructions
  ◦ Sit independently without back or arm support for 10 minutes
  ◦ Lift the affected hand from their lap to a table
  ◦ Release a mass flexion grasp
  ◦ Verbalize presence and location of pain

Exclusion Criteria

• History of health problems placing them at significant risk of an adverse event during:
  ◦ tDCS (e.g., epilepsy, sensitive scalp)
  ◦ Rehabilitation (e.g., acute heart or respiratory disorder)
• History of a neurological condition other than stroke or TBI
• Upper extremity pain greater than 5/10 on a visual analog scale
• Presence of musculoskeletal problems not related to neurological insult that could limit participation in the intervention or become a confounding factor

Table 2

Parameters of Robotic Assessment

	Parameter	Definition	Direction of Improvement
Visually Guided Reaching	**Speed Maxima Count**	Number of speed peaks between two targets.	Count closer to 1
	Path Length Ratio	Distance hand travels to reach a target divided by straight-line distance to target.	Ratio closer to 1
	Movement Time	Time from movement initiation to termination.	Decreased time
	Initial Direction Error	Angle between line representative of straight path between targets and line corresponding to actual direction hand travels on initiation of reaching motion.	Angle closer to 0°
Object Hit	**Total Hits**	Number of balls successfully hit away with paddle.	Increased hits
	Miss Bias	Indication of location of misses. Negative- more misses on side of screen corresponding to affected UE and vice versa. Calculated as the mean of the distance of each missed ball from center.	Distance closer to 0
	Hit Bias	Indication of hand use. Calculated as (hits with affected − hits with unaffected)/(hits with affected + hits with unaffected).	Ratio closer to 0
	Movement Area Bias	Indication of amount of area covered by one hand relative to the other. Calculated as (area covered by affected − area covered by unaffected)/(area covered by affected + area covered by unaffected).	Ratio closer to 0

Table 3

Baseline Characteristics of Study Sample

Participant	Diagnosis	Age (years)	Time since Stroke/TBI (months)	Affected UE	Gender	MAS elbow flexors	MAS wrist flexors	MOCA
1	Stroke	57	15	R	F	0	0	21
2	Stroke	69	50	R	F	0	0	23
3	Stroke	59	253	R	F	3	1+	11
4	TBI	39	206	L	M	1+	0	23
5	TBI+Stroke	38	9	L	M	0	1	24

TBI, traumatic brain injury; UE, upper extremity; MAS, Modified Ashworth Scale; MOCA, Montreal Cognitive Assessment; R, right; L, left; F, female; M, male

Table 4

Timing of Follow-up Assessment Sessions

Participant	Post to FU1	FU1 to FU2	FU2 to FU3	Post to FU3
1	77	80	–	157*
2	71	77	62	210
3	98	56	64	218
4	58	56	63	177
5	44	77	63	184
AVERAGE	70	69	63†	197.25

Results presented in days.

Abbreviations: Post, post-test; FU, follow-up

*Post to FU2 presented for participant 1

†Average for participants 2–5

Table 5

Participant and Group Outcomes on Clinical Measures

	Participant	Pre	Post	FU 3*	Δ Pre to Post {Effect Size}	Δ Pre to FU 3 {Effect Size}
Stroke Impact Scale	**1**	54	61	61	7	7
	2	72	74	74	2	2
	3	62	62	52	0	−10
	4	79	79	80	0	1
	5	56	66	56	10	0
	GROUP	64.6 (10.67)	68.4 (7.83)	64.6 (11.95)	3.8 *{0.36}*	0 *{0}*
Fugl-Meyer (UE-Motor)	**1**	61	64	64	3	3
	2	57	59	59	2	2
	3	32	41	27	9	−5
	4	47	54	54	7	7
	5	23	40	50	17	27
	GROUP	44 (16.22)	51.6 (10.74)	50.8 (14.31)	7.6 *{0.47}*	6.8 *{0.42}*
Box and Block (Affected UE)	**1**	38	59	50	21	12
	2	23	21	25	−2	2
	3	7	8	5	1	−2
	4	30	28	32	−2	2
	5	7	7	7	0	0
	GROUP	21 (13.84)	24.6 (21.17)	23.8(18.65)	3.6 *{0.26}*	2.8 *{0.20}*
Purdue Pegboard (Affected UE)	**1**	9	9	7	0	−2
	2	2	2	2	0	0
	3	1	0	0	−1	−1
	4	3	5	3	2	0
	5	0	0	0	0	0
	GROUP	3 (2.30)	3.2 (3.83)	2.4 (2.88)	0.2 {0.06}	−0.6 {−0.17}

Pre, pre-test; Post, post-test; FU3, follow-up 3; Δ, change; UE, upper extremity

* FU3 results for Participant 1 are FU2 results carried forward

† Participant 5 participated in 14 sessions of a sensory intervention between post-test and

Table 6

Participant and Group Outcomes on Robotic Measures

		Participant	Pre	Post	FU 3*†	Δ Pre to Post {Effect Size}	Δ Pre to FU 3 {Effect Size}
OBJECT HIT TASK (BILATERAL)	Total Hits	1	158	173	158	15	0
		2	192	195	169	3	−23
		3	87	89	102	2	15
		4	186	200	203	14	17
		5	136	133	133	−3	−3
		GROUP	151.8 (42.64)	158 (46.75)	153 (38.02)	6.2 *{0.15}*	1.2 *{0.03}*
	Miss Bias	1	−0.01	0.02	0.03	0.03	0.04
		2	−0.05	0.10	0.02	0.15	0.07
		3	−0.01	−0.03	−0.01	−0.02	0.01
		4	−0.02	−0.03	−0.06	−0.01	−0.04
		5	−0.14	−0.13	−0.15	0.01	−0.01
		GROUP	−0.05 (0.05)	−0.01 (0.09)	−0.04 (0.08)	0.03 *{0.63}*	0.01 *{0.24}*
	Hit Bias	1	−0.05	−0.12	−0.22	−0.07	−0.17
		2	−0.21	−0.13	−0.01	0.08	0.20
		3	−0.17	−0.10	−0.10	0.07	0.07
		4	−0.23	−0.11	−0.24	0.12	−0.02
		5	−0.44	−0.50	−0.38	−0.06	0.06
		GROUP	−0.22 (0.14)	−0.19 (0.17)	−0.19 (0.14)	0.03 *{0.19}*	0.03 *{0.21}*
	Movement Area Bias	1	−0.10	−0.21	−0.24	−0.11	−0.14
		2	−0.13	−0.05	−0.02	0.08	0.10
		3	−0.45	−0.46	−0.11	−0.01	0.34
		4	−0.08	−0.21	−0.15	−0.13	−0.07
		5	−0.02	−0.09	−0.31	−0.07	−0.29
		GROUP	−0.15 (0.17)	−0.20 (0.16)	−0.15 (0.12)	−0.05 *{−0.30}*	0.01 *{0.04}*

		Participant	Pre	Post	FU 3*†	Δ Pre to Post {Effect Size}	Δ Pre to FU 3 {Effect Size}
REACHING TASK (AFFECTED UE)	Speed Maxima Count	1	2.31	2.37	2.46	0.06	0.15
		2	3.20	2.84	2.30	−0.36	−0.90
		3	6.61	6.40	4.95	−0.21	−1.67
		4	2.33	1.67	2.03	−0.66	−0.31
		5	5.08	4.14	4.31	−0.94	−0.77
		GROUP	3.91 (1.89)	3.49 (1.86)	3.21 (1.32)	−0.42 *{0.22}*	−0.70 *{0.37}*
	Path Length Ratio	1	1.04	1.04	1.02	0.00	−0.02
		2	1.49	1.19	1.21	−0.30	−0.28
		3	1.45	1.15	1.13	−0.30	−0.32
		4	1.29	1.11	1.20	−0.18	−0.09
		5	1.70	1.42	1.49	−0.28	−0.20
		GROUP	1.39 (0.24)	1.18 (0.14)	1.21 (0.18)	−0.21 *{0.85}*	−0.18 *{0.74}*
	Movement Time (sec)	1	1.29	1.41	1.37	0.12	0.08
		2	0.63	0.62	0.68	−0.01	0.05
		3	2.19	2.42	1.82	0.23	−0.37
		4	1.25	1.13	1.18	−0.12	−0.07
		5	2.11	1.71	1.92	−0.40	−0.19
		GROUP	1.49 (0.65)	1.46 (0.67)	1.39 0.50	−0.04 *{0.06}*	−0.10 *{0.15}*
	Initial Direction Error (degrees)	1	1.17	1.10	1.06	−0.07	−0.11
		2	12.18	5.50	3.06	−6.68	−9.12
		3	14.92	10.70	6.72	−4.22	−8.20
		4	3.65	2.37	3.79	−1.29	0.14
		5	8.21	12.34	6.07	4.13	−2.14
		GROUP	8.03 (5.72)	6.40 (4.97)	4.14 2.30	−1.62 *{0.28}*	−3.89 *{0.68}*

Pre, pre-test; Post, post-test; FU3, follow-up 3; Δ, change; UE, upper extremity; sec, seconds

*FU3 results for Participant 1 are FU2 results carried forward

†Participant 5 participated in 14 sessions of a sensory intervention between post-test and FU3