Interactive Robotic Training Modes In Self-telerehabilitation

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THESIS

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This thesis is dedicated to my parents, without whom it would never have been accomplished.

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LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
AMFM	Arm Motor section of the Fugl-Meyer
ANOVA	Analysis of Variance
EA	Error Augmentation
FAS	Functional Ability Scale
HSD	Honest Significant Difference
IMI	Intrinsic Motivation Inventory
MAL	Motor Activity Log
ROM	Range of Morion
UE	Upper Extremity
VRROOM	Virtual Reality Robotic and Optical Operations Machine
WMFT	Wolf Motor Function Test
WREX	Wilmington Robotic Exoskeleton

SUMMARY

Despite the existing evidence of possible recovery long after the onset of stroke, regaining functional use of upper extremity has been an ongoing challenge. Recent neurorehabilitation studies have pointed to technological manipulation of error signals during practice to stimulate improvement in coordination for individuals with a history of stroke. This thesis contains four studies dedicated to exploring prospects of teleoperation using advanced haptic/graphic environments for hemiparetic patients. Reviewing the existing robotic rehabilitation technology, we investigated the concept of error augmentation in addition to standard therapist-guided repetitive practice and how it translates into clinical outcomes in hemiparetic stroke survivors. Development of bimanual skills plays a major role in fostering recovery in neural injuries resulting in hemiparesis, because recovery of both the affected arm, as well as the coordination of both arms, is critical to the restoration of quality of life. In the next step, using healthy subjects, we dug deeper into the bimanual movement and its underlying mechanisms. One experiment examined the intuitiveness of different bimanual reaching modes; mirror versus parallel. In a second experiment, the concept of bimanual movement was tested in a more complicated drawing task where only the left-hand was challenged with a visual transformation, and both hands must have moved either simultaneously or sequentially. These results were then employed in the design of a bimanual self-telerehabilitation experiment tested on chronic stroke survivors. The combination of these studies highlight new prospects for training and functional recovery, and opens new doors for future creative applications such as gaming or full body activity to enhance practice in a variety of fields.

1 Introduction

Functional recovery of upper extremity is a challenge in a significant number of stroke survivors and affects the quality of life to a great extent. This recovery includes grasping, holding and manipulating objects, which requires the recruitment and complex integration of muscle activity from shoulder to fingers. However, a minimal amount of recovery of the hemiparetic arm may lead to large changes in function. Although rehabilitation of the upper limb is a challenge, there are studies that have proven that motor recovery could be improved and maintained by an enhanced therapy regimen -- even several years after stroke. Therefore, finding better therapeutic strategies have been an ongoing research topic in recent years. Robotic devices combined with virtual reality technology offer opportunities for new forms of motor skills re-training that could increase the potential for motor recovery even years post-injury. In particular, tasks that require both hands to work together are critical to function but yet are less studied in robotic training to understand optimal therapy techniques for proper rehabilitation programs.

This thesis is dedicated to developing and identifying best practices for bimanual therapy using advanced haptic/graphic environments for hemiparetic patients. The second chapter reviews terminology, interventions and issues present in unimanual and bimanual rehabilitation and further describes the motivation and specific aims of the study. Chapter 3 reviews existing robotic rehabilitation technology, then investigates the concept of error augmentation in addition to standard unimanual therapy and how it translates into clinical outcomes in hemiparetic stroke survivors. Using healthy subjects, the next two chapters (Chapter 4 and Chapter 5) dig deeper into the bimanual movement and its underlying mechanisms. Chapter 4 describes an experiment that examines work load in different bimanual reaching modes mirror versus parallel. Then, in Chapter 5 the concept of bimanual movement is tested in a more complicated drawing task where only the left-hand is challenged with a visual transformation, and both hands must move either simultaneously or sequentially. In Chapter 6, we leverage these recent results and perform a bimanual self-telerehabilitation experiment on stroke survivors. Final discussion, conclusions and possible future directions are then described in Chapter 7.

2 Background

2.1 A brief introduction to stroke

A stroke occurs when there is a disturbance in the normal blood supply to the brain causing damage to the brain tissue. There are two types of stroke: ischemic, which occurs when there is a blockage in the artery that supplies blood to a specific region of the brain, and hemmorhagic, in which an intracranial blood vessel bursts and causes accumulation of blood within the skull vault. Ischemic strokes are the most common type of cerebrovascular injury, including 87% of all strokes (Go, Mozaffarian, et al., 2013).

The incidence of stroke is a leading cause of serious long-term disability (Wolf, Cobb, et al., 1992), with about 16 million first-ever annual strokes occurring worldwide (Di Carlo, 2009). On average, every 40 seconds, someone in the United States has a stroke with a predicted incidence increase of 21.9% from 2013 to 2030 (Go, Mozaffarian, et al., 2013). Up to 85% of people who survive a stroke show an initial deficit in the arm, and 3 to 6 months later, these problems persist in 55 to 75% of patients (Wade, Langton-Hewer, et al., 1983; Parker, Wade, et al., 1986; Olsen, 1990). In addition, stroke costed the United States $38.6 billion in 2009 and this cost is projected to go up to $1.52 trillion in 2050 (Go, Mozaffarian, et al., 2013), a figure which does not include the cost of informal care from family members and friends.

The disabilities that occur as a result of stroke may vary depending on lesion size and region. For instance, subcortical strokes lead to more upper limb incapacitation as compared to cortical strokes (Shelton and Reding, 2001). Earlier rehabilitation approaches were based on the notion that 90% of recovery happens within the first six months post stroke (Jorgensen, Nakayama, et al., 1995). However, more recent studies show that rehabilitation leads to significant improvements long after the onset of stroke (Prange, Jannink, et al., 2006; Kwakkel, Kollen, et al., 2008) even when the study population averages 5 years post-stroke (Lo, Guarino, et al., 2009).

2.2 Upper extremity hemiparesis is a primary impairment in stroke

While functional recovery of upper extremity is poor in a significant number of patients, 75 to 80% of survivors regain their walking ability (Herman, Leyten, et al., 1982; Skilbeck, Wade, et al., 1983; Friedman, 1990). This discrepancy might be due to several reasons. One could be the fact that three quarters of strokes occur in the region supplied by the middle cerebral artery (Feys, De Weerdt, et al., 1998). As a consequence, the upper limb will be affected in a large number of patients. Another factor might be the lack of spontaneous stimulation of the limbs during therapeutic activities. Whereas each attempt to stand or walk requires bilateral activity in the legs, most rehabilitation methods, except for a few recent ones, have focused on the affected arm therapy.

Functional recovery of the arm includes grasping, holding and manipulating objects, which requires the recruitment and complex integration of muscle activity from shoulder to fingers (Feys, De Weerdt, et al., 1998). However, a minimal amount of recovery of the hemiparetic arm may cause quite different functionality for a stroke survivor. Although the rehabilitation of the upper limb is a challenge, studies have proven that motor recovery could be improved and maintained by an enhanced therapy regimen, even several years after stroke (Sunderland, Tinson, et al., 1992). Although research shows intensive therapy, or “massed practice”, appears to have a dramatic effect on recovery (Taub, Miller, et al., 1993; Taub, Uswatte, et al., 1999), with the recent rising costs of health care and recent caps on the fees for rehabilitation, it is difficult to fund more time with therapists.

2.3 Bimanual coordination is critical to everyday living

Bimanual coordination for functional tasks is ubiquitous in everyday life; therefore arm disability caused by stroke could have dramatic consequences in daily living activities of patients. Upper extremity movements such as buttoning a shirt, zipping a jacket or tying a shoe lace are simple but essential actions that should be regained for motor recovery. Studies have shown that bilateral movements take advantage of the inherent dependencies between the arms, and furthermore, symmetrical bilateral movements have been shown to activate similar neural networks distributed in both hemispheres (Jancke, Peters, et al., 2000; Debaere, Wenderoth, et al., 2004; Carson, 2005).

The proved existence of neural plasticity, the ability of synapses and neuronal circuits to change because of activity (Seitz and Freund, 1997; Cramer, 2000; Squire and Kandel, 2000), has created a strong basis for post-stroke rehabilitation. However, in spite of the existing information about the greater brain activity during homologous arm movements, and the evidence provided in research that shows even after a hemispheric stroke, bimanual movements retain a similar underlying structure to that seen in the healthy people (Rose and Winstein, 2004), bimanual practice has not received a great deal of attention as a modality for post-stroke rehabilitation. Researchers have used bimanual training methods in order to improve the bilateral coordination between the paretic and non-paretic arm (Whitall, McCombe Waller, et al., 2000; Cunningham, Stoykov, et al., 2002; Chang, Tung, et al., 2007; Cauraugh, Kim, et al., 2008;

Cauraugh, Coombes, et al., 2009), though some existing research has shown contradictory findings (See (Cauraugh, Lodha, et al., 2010) for a review). It is important to point out that while many studies are inconclusive, only a few studies demonstrate a decrement in performance as a consequence of bimanual training, while many more show benefit. It appears that results could vary widely depending on task, feedback context, modes of practice, level of attention, the parts of the body involved, and many other yet discovered factors. *Hence, there exists a need for a consistent effective bilateral movement training paradigm that can demonstrate effectiveness over and above the current state of practice therapy.*

2.4 Robotic therapy offers new opportunities in post-stroke rehabilitation

Pioneering experiments, in which limb movements and sensory information are not merely observed but also assisted and/or perturbed, have provided a deeper knowledge of limb mechanics and neural control in both healthy and pathological conditions (Krebs, Aisen, et al., 1999; Reinkensmeyer, Dewald, et al., 1999; Patton and Mussa-Ivaldi, 2004). Robotic training with a planar robot improved patient performance, with benefits lasting at least three years (Krebs, Hogan, et al., 1998), leading to increased clinical scores in hemiparetic subjects (Volpe, Krebs, et al., 2000). This robotic therapy technology is promising because studies have shown that appropriate practice is a highly productive way to restore function to an individual recovering from stroke. It is believed that the underlying physiological mechanism for these results is an adaptive reorganization of the brain (neural plasticity), which shifts in-tact neural resources to compensate for the functional areas damaged by the injury (Cohen, Ziemann, et al., 1998; Friel, Heddings, et al., 2000). Such adaptive responses in stroke patients have been observed in the oculomotor (Weiner, Hallett, et al., 1983) and limb motor systems (Dancause, Ptitob, et al., 2002; Takahashi and Reinkensmeyer, 2003). In fact, part of impairment has been attributed to “learned non-use” that can be reversed by encouraging individuals to practice and relearn how to move their arm (Wolf, Lecraw, et al., 1989). The error-augmentation techniques under investigation focus on retraining central control and triggering motor relearning.

In the past few years, the field has exploded with a number of promising prospects in therapeutic robotics, and most notably are the studies on adaptive training. Prolonged training in the presence of appropriately designed visual distortions (Rossetti, Rode, et al., 1998; Brewer, Klatky, et al., 2005) or mechanical distortions (Emken and Reinkensmeyer, 2005; Patton, Stoykov, et al., 2006) is an exciting novel way to use this technology to provide a beneficial change in movement ability. As reported by Patton et al. 2006, when patients returned to an external environment after training in the presence of the distortions, their movement was shifted towards an improved pattern, and subjects tended to preserve this beneficial “after-effect” (Patton, Kovic, et al., 2006).

2.5 Error Augmentation and Neuro-Plasticity in Stroke Patients

There is ample evidence in the literature that alludes to error-driven learning processes as an integral part, if not central, to the acquisition of skill in human movement (Kawato, Maeda, et al., 1990; Wolpert, Ghahramani, et al., 1995). Errors that are exaggerated and thus are more noticeable may trigger responses that would otherwise not be perceived. Error augmentation has been explored in different learning processes (Patton, Kovic, et al., 2006; Patton, Stoykov, et al., 2006; Celik, Powell, et al., 2009) and has led to significant improvements only when the training feedback magnified the original errors and not when the errors were reduced or were completely absent (Patton and Mussa-Ivaldi, 2004). Also, the type of error augmentation used can significantly affect the rehabilitative results (Winstein, Merians, et al., 1999; Kording and Wolpert, 2004).

Often the affected limb recovery is influenced by the preference to use the non-affected limb. The "learned non-use" of the affected limb can become a vicious cycle of impairment, since it only leads to further detriment of the limb and in turn a higher degree of "learned non-use". This non-use cycle, however, can be circumvented by forced use of the affected arm or restricting the movement of the non-affected arm (Wolf, Lecraw, et al., 1989; Wolf, Winstein, et al., 2006). Hence, error augmentation is a potential way to promote functional motor recovery for individuals with brain injury.

2.6 The role of virtual environment in bimanual training approach

In general, virtual environments offer several advantages over conventional therapy. Properties of objects can be changed in an instant with no setup or breakdown time, the state-of-the-art graphic displays use virtual reality technology, which employs stereo-vision and head tracking to present images that correspond to the current eye location, and the see-through display adds the advantage of augmented reality, in which images are superimposed on the physical world (Figure 1). This element of surprise is critical for studying how the sensory-motor system reacts and learns to move in new situations. For rehabilitation, the robotic device can compensate, enhance, or cancel out friction or mass during the early stages of recovery. One of the most compelling advantages of virtual environments is that they can distort reality, which causes the person to immediately begin to adapt. Several studies have shown how the nervous system can be "tricked" by a given altered sensory feedback (Flanagan and Rao, 1995; Ernst and Banks, 2002; Sainburg, Lateiner, et al., 2003). Conversely, suppression of some visual feedback has slowed de-adaptation when healthy peoples' movements are unfavorably altered by the same process (Patton and Mussa-Ivaldi, 2004). Many of these results point to a single unifying theory: errors induce motor learning, and judicious manipulation of error can lead to lasting desired changes.

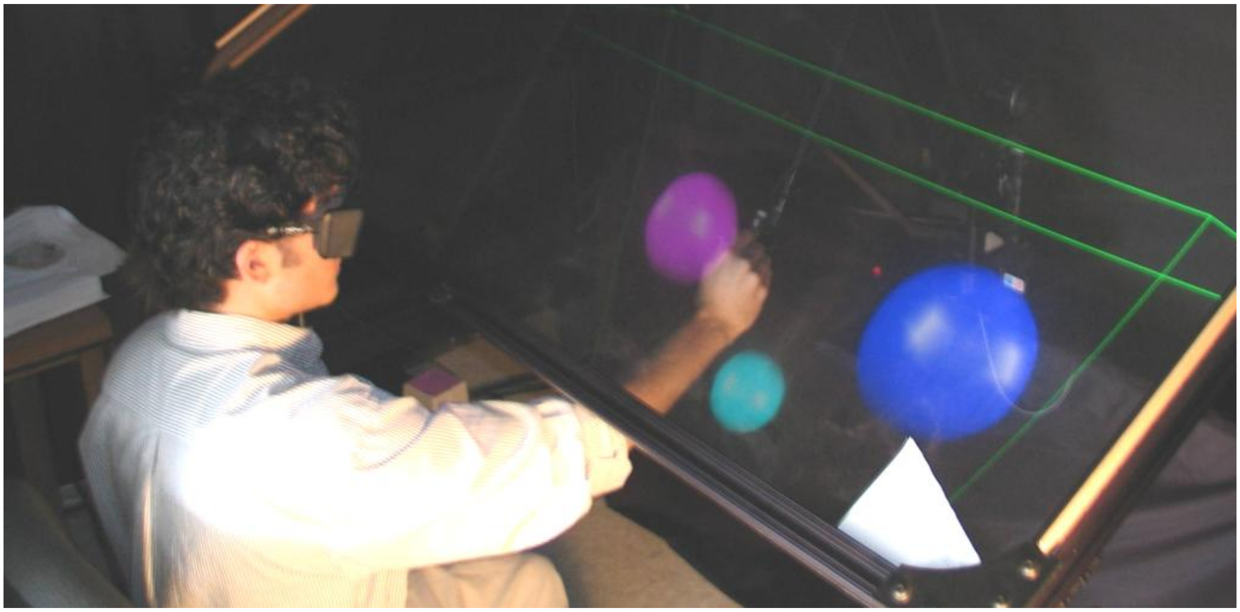

Figure 1- Components of the VRROOM apparatus. Large virtual spheres rendered both haptically by the robot and graphically by the PARIS display. Magnetic tracking sensors detect head position in space.

2.7 Plan of work

Overall, to our knowledge, no bimanual therapeutic techniques have been developed using state of the art haptic/graphic environment that allows stroke patients to train themselves while receiving distorted feedback that enhances learning. Therefore the aims of this dissertation are:

2.7.1 Aim 1: To investigate the effect of error augmentation in addition to standard therapy

Current rehabilitation training in which a therapist specifies a movement trajectory in real time was compared to a combination of haptic and visual error augmentation in addition to standard therapy. Twenty-seven chronic stroke survivors were enrolled in this 6-week cross-over study, with two weeks of practice per treatment type and one week of no treatment in between. Participants were divided into two groups where one started with one treatment type and switched to the second and the other group practiced vice versa. This novel technique combined with the standard repetitive practice allows the expert therapist to customize their approach to therapy, focus on what is critical for a particular patient's recovery and benefit from the error augmentation to emphasize more on the deficits. The results demonstrated a benefit of error augmentation to standard therapy.

2.7.2 Aim 2: To investigate parallel and mirror bimanual training modes on learning

When movement of two hands is involved, there are several options of using both at the same time: one imitates a transfer task, using the same relative position (parallel motion), another is a symmetric task, using the same joint angles (mirror motion). With twenty healthy subjects as models, and taking advantage of a virtual environment, we examined how such tasks and visual feedback mode affect learning of bimanual coordination. In a 2-by-2 design methodology, four groups of subjects each experienced a different task: mirror reaching to one visual target, mirror reaching to two visual targets, parallel reaching to one visual target and parallel reaching to two visual targets. Results revealed the lowest completion time and trajectory error for bimanual parallel reaching to two targets. Surprisingly, mirror reaching to one target happened to be the most challenging of all groups.

2.7.3 Aim 3: To investigate simultaneous and sequential bimanual training modes on learning.

There are studies that have shown the benefits of bimanual training, but to our knowledge, no one has investigated whether such benefits arise from simultaneous action with left and right neural centers operating in unison, or whether it is sufficient to simply have one arm follow the other in a sequential action. In this study, healthy subjects were placed into groups (10 subjects per group), in which they experienced either one of two methods of bimanual movement training (simultaneous or sequential) or no bimanual training in a control group (left hand only), while learning a left hand transformation. Results revealed that although the miscoordination between arms makes the simultaneous task significantly more difficult compared to the other groups, subjects improved in trajectory shape significantly over time in the circle drawing task, while the complex pattern was only improved in size.

2.7.4 Aim 4: To evaluate bimanual self-therapy training for stroke survivors.

Tasks that involve two arms are very important to function in hemiparetic stroke. However, few researchers have looked into the efficacy of bimanual training on post-stroke recovery (Whitall, McCombe Waller, et al., 2000; Hesse, Schulte-Tigges, et al., 2003). The integration of the most successful modes from aims 2 and 3 were tested as a therapy protocol either with the use of error augmentation or without it, in a virtual environment (aim 1) with 10 chronic stroke survivors per group. The combined bimanual-EA method of training was shown to heighten the effects of motor recovery.

3 Error augmentation enhancing arm recovery in individuals with chronic stroke: a randomized crossover design[1]

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3.1 Introduction

New technology offers opportunities to hemiparetic stroke survivors who frequently have the potential for recovery long after their course of therapy has ended (Wolf, Winstein, et al., 2006). Therapy is often terminated as third-party payers incorrectly associate a tendency to plateau in motor recovery with a similar plateau in functional improvement. Emerging interventions include intensive repetitive practice (Wolf, Winstein, et al., 2008), task-specific training (Dean and Shepherd, 1997), and interactive robotic technology (Lum, Burgar, et al., 2002; Volpe, Ferraro, et al., 2005; Sanchez, Liu, et al., 2006) to restore upper extremity motor ability and function. While these methods might offer benefits, the wide variety of technology-facilitated interventions need to be clearly evaluated and distinguished from therapist-guided repetitive practice. Recent work studying neuroplasticity during movement control supports methods that leverage the natural adaptive nature of the nervous system (Patton, Stoykov, et al., 2006). Specifically, the manipulation of error signals during practice appears to stimulate improvement in coordination for individuals with or without a history of stroke (Patton and Mussa-Ivaldi,

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2004). This study also speculated that such learning was implicit through repetition. While the mechanisms for these improvements are not yet known, we speculate that the nervous system reacts to and learns more from larger errors (Patton, Kovic, et al., 2006). Here, we implement these ideas in a clinical intervention that employs visual display and robotic technology which can deliver augmented error signals during training.

Error augmentation has shown promise because it isolates and enhances movement errors, and promotes changes in movement control (Patton, Kovic, et al., 2006). This feedback is sometimes counter-intuitive and differs greatly from the current standard level of care -- seldom does a therapist try to amplify a patient's mistakes. However, such error-driven learning processes are believed to be central to neuroplasticity and reacquisition of skill in human movement (Kawato, 1990; Desmurget, Jordan, et al., 1997). Brewer and colleagues used deceptively small visual feedback of force to encourage stroke survivors with persisting motor deficits to push harder than their original capability (Brewer, Klatky, et al., 2005). Rossetti and colleagues showed a therapeutic benefit using prisms to shift the visual field in stroke survivors with hemi-spatial neglect (Rossetti, Rode, et al., 1998). Our group showed improvement in stroke survivors' movement straightness using training forces that amplified the original errors in movement (Patton, Stoykov, et al., 2006). Several approaches have also addressed the adjacent idea of elevating resistive forces as long as the participant remains capable of moving (Lum, Burgar, et al., 2002; Emken and Reinkensmeyer, 2005). While this approach can amplify error, resistances did not directly depend on error as we propose in the present study.

Here, we hypothesized that during therapist-directed treatment, error augmentation would lead to greater functional recovery over repetitive practice alone. Individuals with chronic stroke received both standard and error augmentation treatment in a blinded, randomized crossover design.

3.2 Methods

3.2.1 Participants

This was a quadruple-blind, crossover design, registered at ClinicalTrials.gov, trial number NCT01574495. Twenty-seven adults with chronic stroke agreed to participate in the study (12 male, age range 36-88, mean age 57.92). Study participants were recruited from a registry of post-stroke individuals who contacted the lab with interest in participating due to postings in the Chicago area. This study was approved by the Northwestern University Institutional Review Boards. All participants provided informed consent according to the Declaration of Helsinki prior to commencing the study. Twenty-six individuals completed all phases of the study, and only one participant, who dropped out for reasons that did not pertain to the study, was excluded from analysis (Figure 2). Eligible participants were all adults aged 18 or over who had suffered a single cortical stroke and were at least six months post-stroke. Participation also required some recovery of proximal strength in the hemiparetic limb as confirmed by an upper extremity Fugl-Meyer score of 15-50. Exclusion criteria included multiple strokes, bilateral paresis, severe spasticity or contracture, severe concurrent medical problems, severe sensory deficits, cerebellar strokes resulting in severe ataxia, significant shoulder pain, focal tone management with Botulinim Toxin (Botox®) injection to the hemiparetic upper extremity (UE) within the previous four months, depth perception impairment (< 3/9 on Stereo Circle Test), visual field cut, cognitive impairment (Mini Mental State Examination < 23/30), or severe aphasia, affective dysfunction or hemisensory neglect that would influence the ability to perform the experiment or provide informed consent. Participants were excluded if they received any other skilled upper extremity rehabilitation in a clinical setting. We discovered that one participant (participant 14) received outpatient therapy during his entire enrollment. We included this person in our analysis to rigorously adhere to our randomization procedure for data analysis according to the intention-to-treat approach (Peduzzi, Henderson, et al., 2002; Stanley, 2007) and also because of the cross-over nature of our design. See Table I for participants' demographics and lesion characteristics.

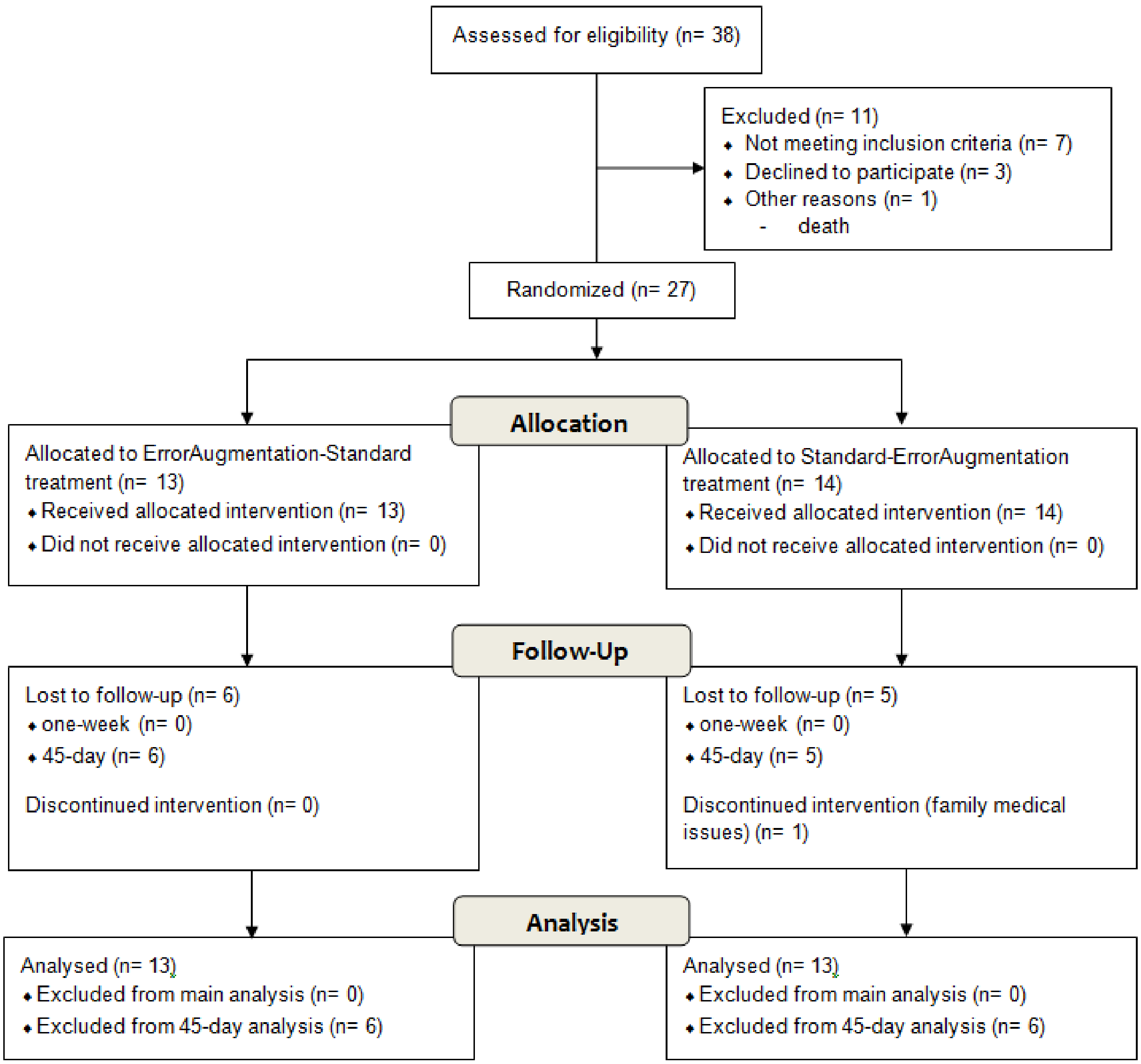

Figure 2- Subject recruitment flow diagram

Table I- Baseline demographics and clinical characteristics

Subject ID	Sex	Age	Months Post Stroke	Previously Dominant Hemisphere	Affected Hemisphere	Lesion Type	Lesion Location
001	M	57	17	Left	Left	Ischemic	Cortical
002	M	36	26	Left	Left	Ischemic	Subcortical
003	M	54	63	Right	Left	Ischemic	Subcortical
004	M	59	61	Left	Left	Hemorrhagic	Unknown
005	F	69	236	Left	Left	Ischemic	Subcortical
006	F	65	25	Left	Left	Ischemic	Cortical, Subcortical
007	F	57	259	Left	Left	Hemorrhagic	Unknown
008	M	63	158	Left	Left	Hemorrhagic	Cortical, Subcortical
009	F	88	205	Left	Left	Ischemic	Unknown
010	F	54	21	Left	Both	Ischemic	Cortical, Subcortical
011	F	51	19	Left	Left	Ischemic	Cortical
012	F	61	81	Left	Left	Hemorrhagic	Subarachnoid
013	F	65	56	Left	Left	Ischemic	Cortical
014	M	47	6	Right	Left	Ischemic	Subcortical
015	M	58	43	Left	Right	Hemorrhagic	Cortical
016	F	58	157	Left	Right	Hemorrhagic	Subcortical
017	M	63	92	Left	Right	Ischemic	Cortical
018	M	69	141	Left	Left	Ischemic	Cortical
019	M	45	32	Left	Left	Hemorrhagic	Subcortical
021	M	52	35	Right	Left	Hemorrhagic	Subcortical
022	F	56	38	Left	Left	Ischemic	Cortical, Subcortical
023	F	44	16	Left	Right	Ischemic	Subcortical
024	M	56	74	Left	Left	Ischemic	Subcortical
025	F	66	150	Left	Right	Ischemic	Unknown
026	F	54	90	Left	Right	Hemorrhagic	Subcortical
027	F	59	40	Left	Left	Ischemic	Subcortical

F, female; M, male.

3.2.2 Study Setting

The study took place solely at the Robotics Laboratory at the Rehabilitation Institute of Chicago from January 2007 to April 2012. The study used a three-dimensional haptic/graphic system called the Virtual Reality Robotic and Optical Operations Machine (VRROOM) (Patton, Dawe, et al., 2006). StereoGraphics liquid crystal shutter glasses separated left and right eye images, and Ascension Flock of Birds sensors tracked head motion for appropriate display of perspective. A SensAble Technologies Phantom Premium 3.0 robot interfaced with the participant's impaired wrist (Figure 3). A Wilmington Robotic Exoskeleton (WREX) provided anti-gravity arm support (Rahman, Sample, et al., 2000).

3.2.3 Experimental Protocol

A computer-generated list of random numbers allocated each participant to one of 2 groups. We tested two experimental robotic-assisted treatments in a crossover design: each participant received either a control treatment of repetitive practice with no error augmentation called the "*standard treatment phase*" or a treatment with the same amount of practice plus combined visual and haptic error augmentation called the "*error augmentation (EA) treatment phase*". Each phase consisted of two weeks of training with participants receiving three, 60-minute sessions per week (six sessions per experimental phase). After a week of no treatment, each group experienced the other treatment type for another two weeks.

Each session began with five minutes of passive range of motion (ROM) exercises, followed by ten to fifteen minutes of setup of the participant and therapist within the VRROOM, then six 5-minute blocks of movement training with two-minute rest periods between each treatment block (Figure 4). The treatment protocol included the practice of standardized movements for all participants (consisting of forward and side reaching, shoulder-elbow coupling, and diagonal reaching across the body) in addition to customized movements.

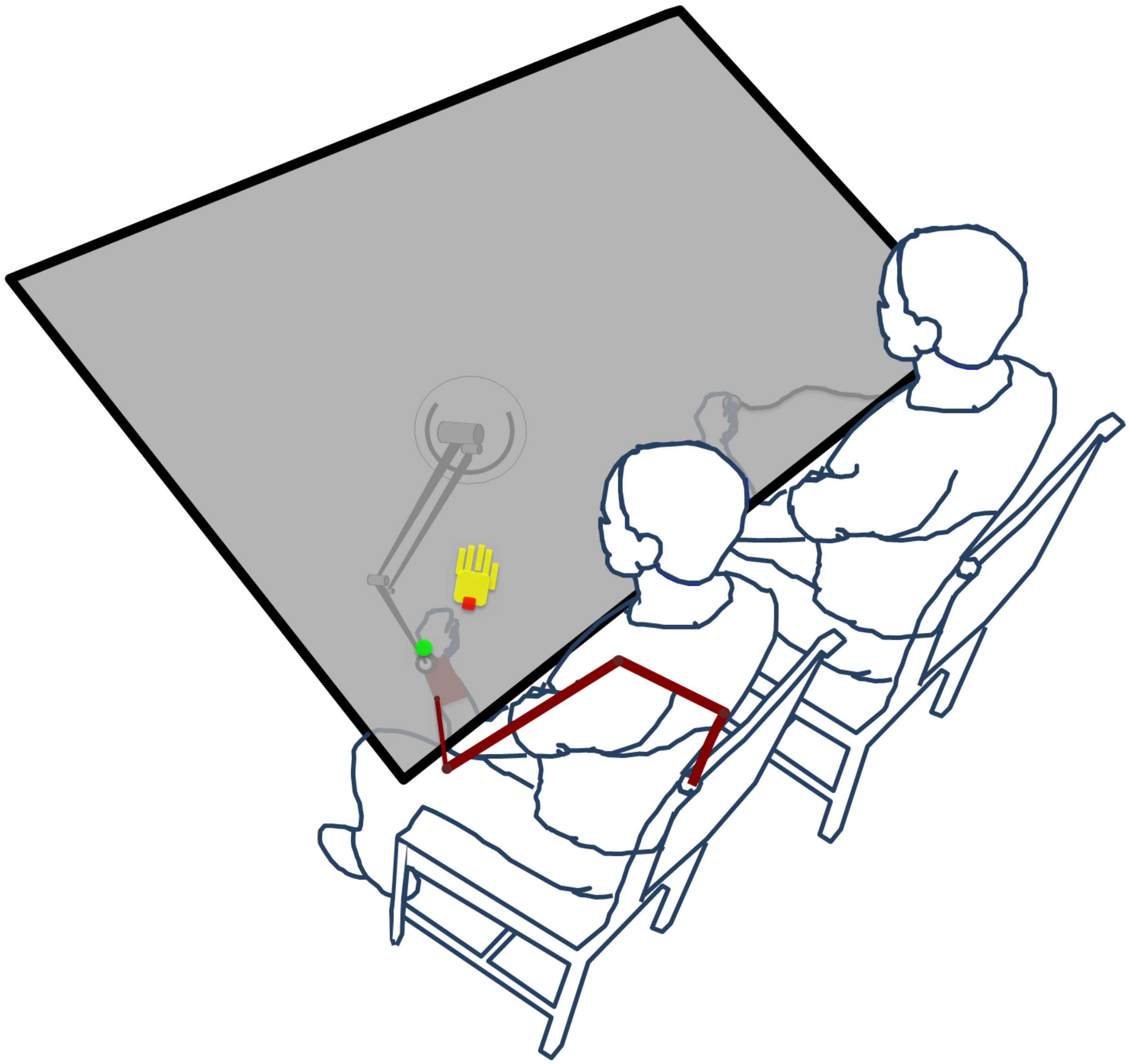

Figure 3- Experimental setup; therapist (right) and participant (left) sat side by side in front the virtual display. Robot handle is attached to participant's hand (green sphere) and therapist holds a position tracker (yellow hand)

The customized treatment blocks targeted specific areas of weakness determined by the therapist based on the previous standardized five-minute block. This allowed the clinician to customize the therapeutic approach, focusing on what was most critical for a particular participant's recovery. Between the two phases of treatment, participants received a one-week no treatment period, in which there were no upper extremity rehabilitative interventions. Quantitative assessments were performed at the beginning and end of each treatment phase (pre and post) as well as one week after post (follow-up) and 45 days after the end of the final post assessment. During this 1-week and 45-day retention period, there were also no upper extremity rehabilitative interventions.

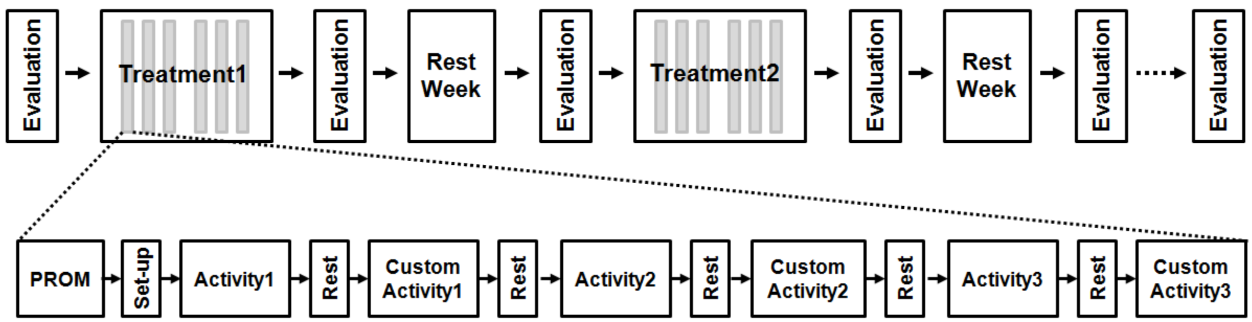

Figure 4- Schematic of the successive days of treatment for the study (top panels), and a breakdown of the successive phases of treatment in each day's session (bottom panels)

During all therapy sessions, participants were comfortably seated in a chair with the hemiparetic arm supported by the WREX^{TM} gravity-balanced orthosis. The hemiparetic hand was placed in an exotendon glove that included a wrist splint, which assisted with hand opening and neutral wrist alignment to allow for a more functional hand and wrist position. Since holding a handle is not necessarily the same as free-hand motion (Cothros, Wong, et al., 2006), we connected the robot near the wrist to allow the hand to open freely as well as allow free pronation and supination of the forearm with the WREX^{TM} swiveling wrist support. The PHANTOM^{TM} robot was attached to the forearm with the center of the handle located above the radiocarpal joint. Forces were only applied by the robot during the EA treatment phase; however, the robot was attached during both phases to assist in blinding the participant and treating therapist as well as to provide feedback regarding location within the 3D workspace. While it is difficult to determine if these responses reflect any true failure of blinding (Sackett, 2004) there were also known compromises in our attempt at blinding.

During training, participants were only able to see two cursors within the virtual environment with the view of their arms being blocked. One cursor was manipulated by the treating therapist while the other was controlled by the participant. Participants were instructed to follow the exact path of the therapist's cursor as close as possible by superimposing their cursor over the therapist's cursor as it moved throughout the workspace. During the EA treatment phase, the error vector *e*, defined as the real time difference in position between the position tracker held by the therapist and the robot handle attached to participant's wrist was visually magnified by a factor of 1.5 as part of the error augmentation. Additionally, we applied an error augmenting force of 100 N/m, pushing the participant's hand further away from the target controlled by the therapist in the virtual environment. For safety purposes, this force was designed to saturate at 4 N. To determine the sample size we chose to measure the improvement in the Fugl-Meyer clinical score as the main outcome, an improvement of at least 3.5 is commonly believed to be clinically meaningful (Wagner, Rhodes, et al., 2008). Based on a power > 80%, two-sided type I error of 0.025 (adding to 0.05), and an estimated variance of 2.5 (Patton, Kovic, et al., 2006), we obtained a sample size of 11 subjects per group, which was increased to 13 to account for factors of safety and a possible dropout rate of 10%.

3.2.4 Evaluation Procedure

Participants were evaluated inside the VRROOM with the Range of Motion test and outside the VRROOM with the clinical measures immediately prior to the start and again at the end of each treatment phase. Follow-up testing was performed at one week and at 45 days after the end of second treatment phase. The follow-up evaluation for the treatment received in the first two weeks overlapped with the evaluation of the start of the second treatment. A blinded evaluator administered all outcome measures including our primary outcome; the arm motor section of the Fugl-Meyer (AMFM) to measure impairments (Platz, Pinkowski, et al., 2005; Wagner, Rhodes, et al., 2008) as well as our secondary outcome measures, which included the Wolf Motor Function Test (WMFT) for functional ability (Wolf, Catlin, et al., 2001; Fritz, Blanton, et al., 2009) and the Box and Blocks assessment as an indicator of manual dexterity (Platz, Pinkowski, et al., 2005; Chen, Chen, et al., 2009). Range of motion was also evaluated in successive reaches from a neutral point on their lap to nine evenly-spaced targets placed at the extent of the reachable workspace (randomly presented with each target repeated three times). From this, we calculated and averaged the fraction of full arm-extension in the direction of each target. Finally, to assess perception of the experience, participants completed the Intrinsic Motivation Inventory (IMI) questionnaire (McAuley, Duncan, et al., 1989), which consists of 25 questions in four categories (interest/enjoyment, perceived competence, motivation/effort, and perceived value).

3.2.5 Statistical Analysis

To examine for treatment-related change, outcomes were analyzed using a repeated measures analysis of variance (ANOVA), with factors of evaluation day (pre versus post), treatment type (EA versus standard), and treatment order (EA first versus EA second). To examine for retention, a second repeated measures ANOVA was performed with factors of evaluation day (post versus follow-up), treatment type (EA versus standard), and treatment order (EA first versus EA second). Finally, for each treatment type, a paired t-test was used to evaluate participants' changes in performance at 45 days relative to the final post time-point. All statistical tests were evaluated using an alpha level of 0.05.

3.3 Results

The primary analysis was EA treatment effect and involved all patients who were randomly assigned. Our main outcome measure, AMFM, in an overall analysis showed significant improvement over the six weeks (paired t-test, $t=4.077$, $df=25$, $p<0.001$), such that the average gain was 2.23 ± 2.79 points. Further detailed analysis (repeated measures ANOVA) showed a significant interaction effect between treatment-type and evaluation-day ($F(1,24)=4.261$, $p<0.050$). The treatment-type by evaluation-day interaction indicated that within the two-week training phases, the EA treatment showed significantly better performance than the standard treatment. As shown in Figure 5-left, over the first phase of training, the EA treatment group showed a change in 2.08 points (pre to post) while the standard treatment group rose only 0.69. As can be seen in the same figure, during the second phase of training where each group swapped training types, although not significant, the group that received EA training showed larger improvements than the group who received standard training. As a result, EA treatment provided a therapeutic advantage that further improved the average gains by 1.00 AMFM point over repetitive practice alone. The treatment-type by treatment-order interaction ($F(1,24)=5.933$, $p<0.025$) indicated that there was significant improvement in the second two-week period, relative to the first. There was also a significant main effect in evaluation-day showing that participants improved an average of 1.12 ± 2.48 points for each two-week treatment phase over the course of training ($F(1,24)=7.013$, $p=0.014$). These improvements were unchanged after one week of no treatment ($F(1,24)=0.00$, $p=1.00$). With the 15 participants for which we were able to obtain data at a 45-day follow-up, the AMFM showed an overall improvement averaging 2.93 ± 3.37 points from the first evaluation to the 45-day follow up evaluation (paired t-test, $t=3.372$, $df=14$, $p<0.005$).

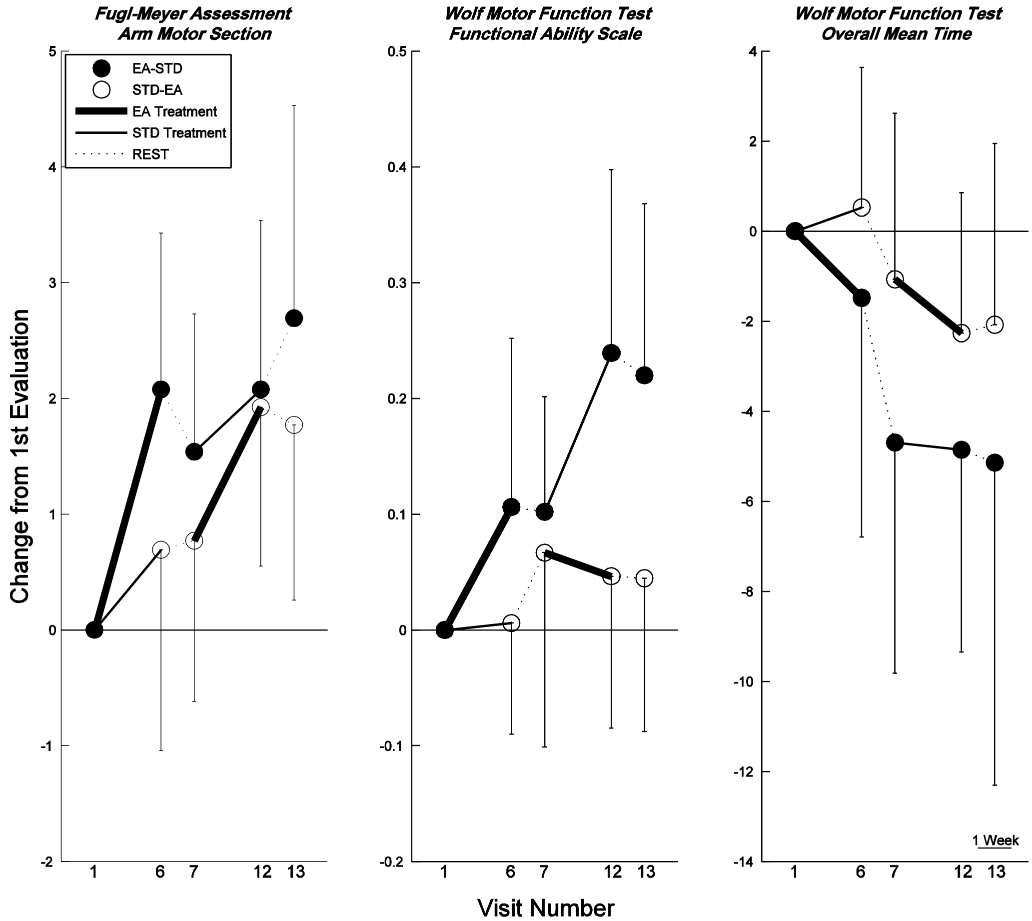

Figure 5- Clinical score changes from the first visit, AMFM score (left), WMFT score (middle), WMFT time (right). EA treatment (thick line), standard treatment (thin line), no treatment periods (dashed lines)

When we examined the final outcome of each group, as seen in Figure 5-left, the group that started with EA treatment showed 2.69 ± 3.07 points improvement while the other group showed a 1.77 ± 2.52 point increase. Interestingly, this trend was also found at the 45-day follow-up where the group receiving EA treatment first showed total improvement of 4.13 ± 4.05 points and the second group showed total improvement of 1.57 ± 1.81 from the first visit. These overall gains from beginning of the training to the end of the study occurred despite a drop in performance after returning from a one-week break such that there was no significant difference in AMFM scores for the groups training with and without error augmentation prior to starting the second phase of the training.

We found similar treatment related results in our secondary measures. Although variable, the WMFT Functional Ability Scale (FAS) improved significantly with an overall average of 0.13 ± 0.24 points over six weeks (paired t-test, t=2.735, df=25, p<0.012). This score also showed a significant interaction effect between treatment type and order of treatment (F(1,24)=7.416, p<0.012) indicating that there was higher gain in the second two-week period, relative to the first (Figure 5-middle). This effect was unchanged after one week of no treatment (F(1,24)=3.149, p>0.088). The same trend was also seen in the WMFT-Time measure where the significant interaction between treatment type and treatment order (F(1,24)=7.860, p<0.010) indicated a shorter time to complete task items in the second two-week period (Figure 5-right). These improvements were unchanged after one week of no treatment (F(1,24)=3.123, p>0.088). Finally, at the 45-day follow-up, the WMFT showed overall improvements averaging 0.21 ± 0.36 points with the FAS from the first evaluation to the 45-day follow-up evaluation (paired t-test, t=2.272, df=14, p<0.040).

The measure we constructed, Range of Motion, appears to be less sensitive to change. We failed to detect significant treatment related effects in ROM and Box and Blocks assessments. A summary of all the effect sizes reported above is shown in Table II.

Table II- Summary of effect sizes graphed in Figure 5. Each value is a change from first visit and is reported as mean ± standard deviation

Assessment type	**Fugl-Meyer Assessment** Arm Motor Section				**Wolf Motor Function Test** Functional Ability Scale				**Wolf Motor Function Test** Overall Mean Time			
Visit number	6	7	12	13	6	7	12	13	6	7	12	13
EA-STD	2.08 ±2.25	1.54 ±1.98	2.08 ±2.43	2.69 ±3.07	0.11 ±0.24	0.10 ±0.17	0.24 ±0.26	0.22 ±0.25	-1.48 ±8.86	-4.69 ±8.55	-4.86 ±7.49	-5.14 ±11.96
STD-EA	0.69 ±2.90	0.77 ±2.31	1.92 ±2.29	1.77 ±2.52	0.01 ±0.16	0.07 ±0.28	0.05 ±0.22	0.04 ±0.22	0.53 ±5.19	-1.07 ±6.16	-2.26 ±5.20	-2.08 ±6.72

Perceived value and enjoyment of the overall experience was evident in the IMI questionnaire results. The highest scores were associated with questions such as, "I would be willing to do this again because it had some value to me." Generally, all results were more in agreement with the positive questions and more in disagreement with negative questions (Figure 6). The lowest scores were reported in questions related to the perceived competence sub-scale, such as "I think I did pretty well at this activity, compared to others." The groups of IMI questions were averaged and then compared to the overall clinical outcome scores, but the series of 24 pair-wise correlations revealed no significant relationships higher than R^2=0.45.

3.4 Discussion

This blinded, randomized crossover study revealed a benefit of repetitive practice with error augmentation over repetitive practice alone. The AMFM, WMFT FAS score, and WMFT time showed significant EA-related improvements when compared to standard care. While this study does not firmly establish clinical efficacy of such interventions, it does shed light on a family of future methodologies for improving motor function after stroke.

While the effect sizes were modest and could be considered not quite clinically meaningful (de NAP Shelton, Volpe, et al., 2001), we argue that such gains might continue for longer treatment courses. In contrast to this study, typical robotic interventions include a training duration of at least six weeks or more (Lum, Burgar, et al., 2002; Stein, Krebs, et al., 2004; Volpe, Lynch, et al., 2008; Molier, Prange, et al., 2011). In the literature, constraint-induced movement therapy utilized two-week periods, with each day including six hours of training (Miltner, Bauder, et al., 1999; Taub, 2000; Wolf, Winstein, et al., 2006); others included 2 to 3 hours of training (Dromerick, Lang, et al., 2009). Our study matched several other studies in weekly dosage (1-hour treatment sessions three times per week) (Lum, Burgar, et al., 2002; Stein, Krebs, et al., 2004; Volpe, Lynch, et al., 2008). However, our study had a shorter duration of two weeks per treatment phase whereas the aforementioned studies lasted 6-8 weeks. Because error augmentation showed significant improvements during just two weeks of treatment, larger effect sizes might be obtained with higher treatment dosages or durations. Participants also reported improvements in function such as increased use of the involved extremity in daily life and improved self-care independence, which were not captured in any of the outcome measures. This could be due to the measures not being sensitive enough to these changes. In future studies, it may be beneficial to include a self-report questionnaire such as the Motor Activity Log (Uswatte, Taub, et al., 2006).

This study builds upon several other studies that highlight the prospect of augmenting error in order to enhance the learning process, and supports EA as an effective option over regular, repetitive practice for therapy. Such work has been shown to be effective in reshaping movements in individuals with stroke (Patton, Kovic, et al., 2006), altering the rate and amount of adaptation in locomotion training (Emken and Reinkensmeyer, 2005), and encouraging more force output in rehabilitation tasks (Brewer, Klatky, et al., 2005). Our work here joins other mounting evidence supporting error augmentation approaches for speeding up or enhancing learning in both healthy and brain-injured individuals.

While error augmentation can be considered a form of *anti-assistance,* it is important to distinguish it as neither *assistive* (Sanguineti, Casadio, et al., 2009) nor *resistive* in the manner that weight training resistance exercise impedes motion to foster hypertrophy, bone density, and motor unit recruitment (Enoka, 1997). Error augmentation may actually push in any direction relative to the direction of motion, depending on locations of cursor and target.

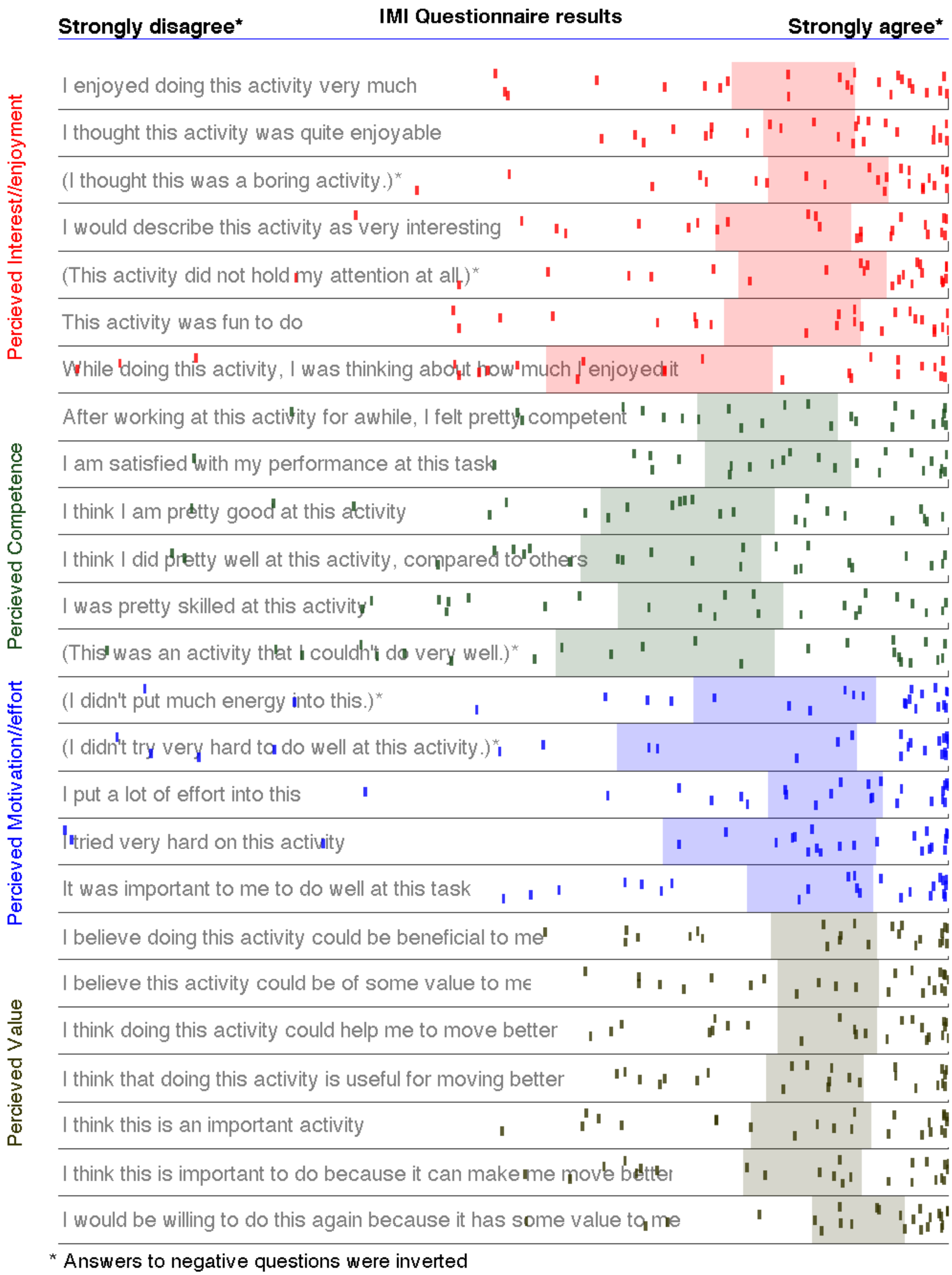

Figure 6- Intrinsic Motivation Inventory results, each tick mark shows response of a subject, different categories are shown in various colors

It is still not clear what underlying neurological mechanisms might be the reason individuals respond to error augmentation. It may be that the impaired nervous system does not react to nor does it try to learn from smaller errors, and the EA approach might promote learning by making errors more noticeable. Moreover, models of learning suggest that at least one mechanism of learning is driven by error (Kawato, 1990; Desmurget, Jordan, et al., 1997). The approach might also simply heighten motivation and/or attention, or simply intensify the signal-to-noise ratio for sensory systems, making errors more noticeable.

One insight may come from how results differed between ability (AMFM) and function (WMFT). WMFT (Figure 5, middle and right plots) did not significantly improve when applied in the second phase (weeks 4 & 5). This data suggests that the intervention had greatest impact on motor ability, and may have diminishing effects on functional ability. It may be that more functionally relevant tasks in the presence of EA can lead to continued gains in functional scores. Moreover, Figure 5 Suggests that if EA is performed in the second 2-week period, performance increases may be more difficult to detect, perhaps due to an order effect.

Although the IMI revealed a positive experience overall, some participants did not find the repetitive nature of the intervention particularly engaging. There were no gaming elements or scores for success, and the only motivational mark for success was their own view of the cursor and target in real time. Several complained about the mundane, repetitive nature of the experiment; expecting a more “exciting” experience using virtual reality. However, positive changes in clinical scores were seen even without an engaging interface. It remains to be seen whether more creative elements can be used to enhance the involvement of the participants’ attention to optimize clinical outcomes, or whether such elements might serve as a distraction from rigorous deliberate practice (Ericsson, Krampe, et al., 1993).

Although helpful in assisting arm posture, the WREX gravitational assistance device and hand-opening glove may have increased set-up time and restricted movement at extremes of the reachable workspace. Participants with less impairment may have also benefited from less inhibited reaching without this equipment. It remains to be seen whether an alternative approach could improve results with a clinical cutoff for supplementing with such assistive devices.

This study provides practical clinical evidence that enables future studies to improve arm motor recovery. The techniques associated with error augmentation may easily add to the repertoire of possible strategies for rehabilitation, likely to be most effective if combined with other rehabilitation strategies. In the search for optimal training methods, the evidence presented here points to possible future research that makes use of feedback technology to leverage the error-based adaptive tendencies of the nervous system to improve motor recovery and possibly functional reaching ability.

3.5 Acknowledgments

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4 Mirror versus parallel bimanual reaching[2]

Farnaz Abdollahi, Robert Kenyon, James Patton

4.1 Introduction

Bimanual training is particularly important in fostering recovery in neural injuries resulting in hemiparesis such as stroke, because the non-affected arm can potentially retrain the affected arm (Lum, Burgar, et al., 2002; Hesse, Schulte-Tigges, et al., 2003; Macclellan, Bradham, et al., 2005). Upper extremity movements such as buttoning a shirt or zipping a jacket are simple but essential actions that need to be regained for making progress towards motor recovery and regaining activities of daily living (ADL). And although many studies focus on perfect performance, patients most care about task completion with proper coordination of both arms (Rose and Winstein, 2004). Therefore, bimanual therapy, which gives the users the possibility of achieving their primary goal of retraining ADLs, should be of major importance to the therapist.

Several studies have demonstrated that bimanual training improves coordination between the paretic and non-paretic arms (Whitall, McCombe Waller, et al., 2000; Mudie and Matyas, 2001; Cunningham, Stoykov, et al., 2002; Stinear and Byblow, 2004; Chang, Tung, et al., 2007; Cauraugh, Kim, et al., 2008; Cauraugh, Coombes, et al., 2009); while a few have shown unwanted outcomes, such as reductions in the Fugl-Meyer or Ashworth scales (See (Cauraugh, Lodha, et al., 2010; Latimer, Keeling, et al., 2010) for a review). This discrepancy in

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performance may be due to the various ways the two limbs interact and move during bimanual training; for example, there are mirror-symmetric movements with respect to the body midline and asymmetric/alternating flexion-extension movements among others. Additionally, rigid coupling of the limbs (locking the actions of one limb to the other) often present in bimanual training could enable the paretic limb to act passively and depend mainly on the less affected limb for control, thus reducing its experience of the forces and motions associated with a particular movement. This may be why Kadivar *et al*., 2011 found no significant differences in bimanual performance (i.e. trajectory error) when one arm was rigidly forced to follow the other in parallel and mirror modes (Kadivar, 2011). Thus, it remains unclear which methods are optimal.

Placing a subject in an environment that manipulates the visual feedback may help to resolve this discrepancy in the literature. Virtual environments can allow each arm to perform independently while presenting novel visual feedback. This promotes active participation of both limbs, and hence each limb is making and learning from its own mistakes. Furthermore, using this paradigm may tell us which form of uncoupled bimanual practice provides superior results, i.e. mirror versus parallel mode. Previous robotic rehabilitation studies that used the mirror mode of bimanual practice showed a significant increase in brain activation in similar parts of both brain hemispheres as well as enhanced inter-hemispheric activation (Burgar, Lum, et al., 2000; Lum, Burgar, et al., 2002; Hesse, Schulte-Tigges, et al., 2003; Luft, McCombe-Waller, et al., 2004; Hesse, Werner, et al., 2005; Summers, Kagerer, et al., 2007; Cauraugh, Coombes, et al., 2009). However, to our knowledge, the *intuitiveness,* defined in terms of how fast and how accurate people can perform in this mode of practice, compared with the parallel mode, has not been studied in the uncoupled condition.

With two hands involved in practice, there are several approaches for coordinating both limbs. One is based on symmetry -- either transfer actions (parallel motions such as transferring a large object) or joint-similar actions (mirror motions such as opening a book). Lewis and Byblow reported that patients respond better to bimanual practices that involve in-phase and symmetric actions also denoted as mirror movements (Staines, McIlroy, et al., 2001; Lewis and Byblow, 2004; Byblow, Stinear, et al., 2012), which has been attributed to simultaneous brain activation of bilaterally homologous areas during these activities. However, these activations are not necessarily associated with functional gains, and the performance in a parallel mode was shown to be superior to mirror in a triangle drawing task (Bogaerts and Swinnen, 2001). Hence, it remains to be seen whether parallel or mirror modes might be superior in terms of trajectory error and/or task completion time with the limbs decoupled.

Besides muscle grouping and coordination, visual attention also plays a role in task difficulty in targeted reaching. Virtual reality displays allow the possibility of transforming one of the hand's feedback to the opposite side, so that subjects only need to attend to one side of their view. We hypothesize that such a "one-target" visual transformation might reduce task difficulty over managing a divided view to two targets.

The present study used healthy individuals in a virtual environment to examine how these modes of bimanual practice influence performance on a simple reaching task. We investigated how different modes, symmetry and feedback, might influence performance and rate of learning (change of performance across time). Specifically, we focused on differences in bimanual reaching due to mirror versus parallel arm movements. We investigated the performance of uncoupled, bimanual point-to-point reaching under four conditions; mirror reaching to one target (the "one-target" visual transformation), mirror reaching to two targets, parallel reaching to one target, and parallel reaching to two targets. This study showed lowest completion times and trajectory errors for parallel movements reaching to two targets, identifying the least challenging mode for bimanual practice, which may suggest the most appropriate mode for self-therapy in future neurorehabilitation interventions.

4.2 Methods

4.2.1 Participants

Twenty healthy right-handed individuals (12 male, age range 19-53, mean age 28 ± 9) with corrected 20/20 vision were invited to participate and consented using approved Institutional Review Boards from both Rehabilitation Institute of Chicago and University of Illinois at Chicago guidelines for protection of human subjects Internal Review Boards according to the Declaration of Helsinki. A pilot study determined the effect size and inter-group variance to be 1.21 and 1.41 seconds, leading us to a power estimate of 5 subjects in each of four treatment groups (described below) based on Cohen's method for ANOVAs with a targeted power of 0.8 and significance levels of 0.05. Participants were naïve to the apparatus and had no history of previous musculoskeletal or neurological injury. The handedness of each individual was assessed using the modified Edinburgh Handedness Inventory (Oldfield, 1971). Subjects were excluded if they scored less than 90 percent on the right-handedness test or if they had depth perception impairment of less than 8 out of 9 on graded circle test (Stereo Optical Company, Chicago, IL, USA).

4.2.2 Study setting

All experiments in this study were performed in a three-dimensional, large-workspace haptics/graphics system called the Virtual Reality and Robotic Optical Operations Machine

(Figure 7) (Scharver, Evenhouse, et al., 2004). A cinema-quality digital projector (Christie Mirage 3000 DLP) displays the stereo images that span five-foot-wide 1280x1024 pixel display resulting in a 110º wide viewing angle in a see-through augmented reality display. In this study, vision of the arms was occluded so that only cursors (representing hand locations) and targets were shown. Infra-red emitters synchronize separate left and right eye images through LCD shutter glasses. Ascension Flock of Birds^{TM} magnetic sensors tracked motion of the head to track the head position and re-render the environment when necessary so that the subject had the proper real-time view angle. Another sensor served as the position tracker of the right hand. A 6-degree of freedom PHANTOM Premium 3.0 robot (SensAble Technologies) provided tracking of the left hand.

4.2.3 Experimental protocol

Subjects were seated in a chair in front of the VRROOM. Hand position for left and right hands were obtained using a PHANTOM robot in left hand and a Flock of Birds position tracker in the right hand. These instruments are highly precise devices making it safe to assume they had similar accuracy and signal-to-noise ratios. Hand position data were sampled at 100 Hz. The PHANTOM robot only recorded forces and exerted no forces during the experiment. Targets were displayed in the virtual environment such that the average distance that both hands were required to travel remained the same (Figure 8). Targets were placed to avoid crossing the midline in one of four randomly chosen locations, and were displayed on the screen as a sphere that the subject was instructed to move the cursor inside of. Alternating trials were at the initial position to ensure repeatable task requirements during training. All subjects were instructed to make straight and fast movements from the initial target to the final target. A movement (or trial) was considered complete when both cursors arrived at the appropriate target and halted for 0.5

seconds. Upon completion, the target(s) would vanish and the next target in the sequence would appear.

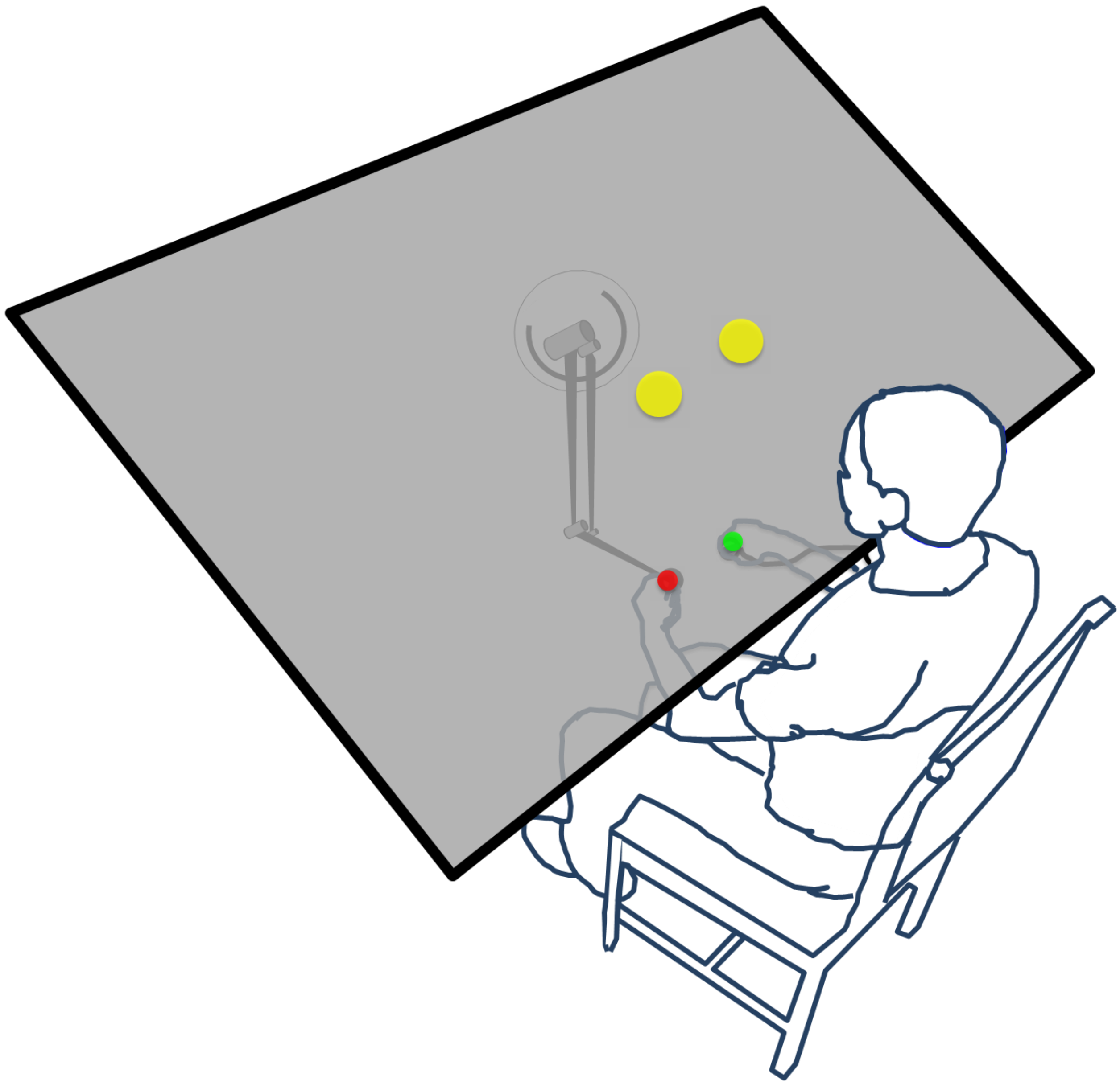

Figure 7- Experimental setup. The subject was instructed to move the cursors tracking their hands (small red and green dots) within the targets (yellow spheres) and then return

Participants were divided into four separate groups in a 2-by-2 design. Each group experienced one of the bimanual movement modes (either mirror or parallel) and one of the target requirements (move to either one or two targets) in a single session. For the one-target condition, the right hand's cursor was transformed to be near the left, with the goal of having the cursors representing each hand moving side by side (Figure 9, top). This required subjects to visually attend to one area in the workspace. The remaining groups were required to move towards two targets while experiencing veridical feedback about the location of each hand, but had to attend to two areas (one for hand on each side) at the same time – the "two-target" groups.

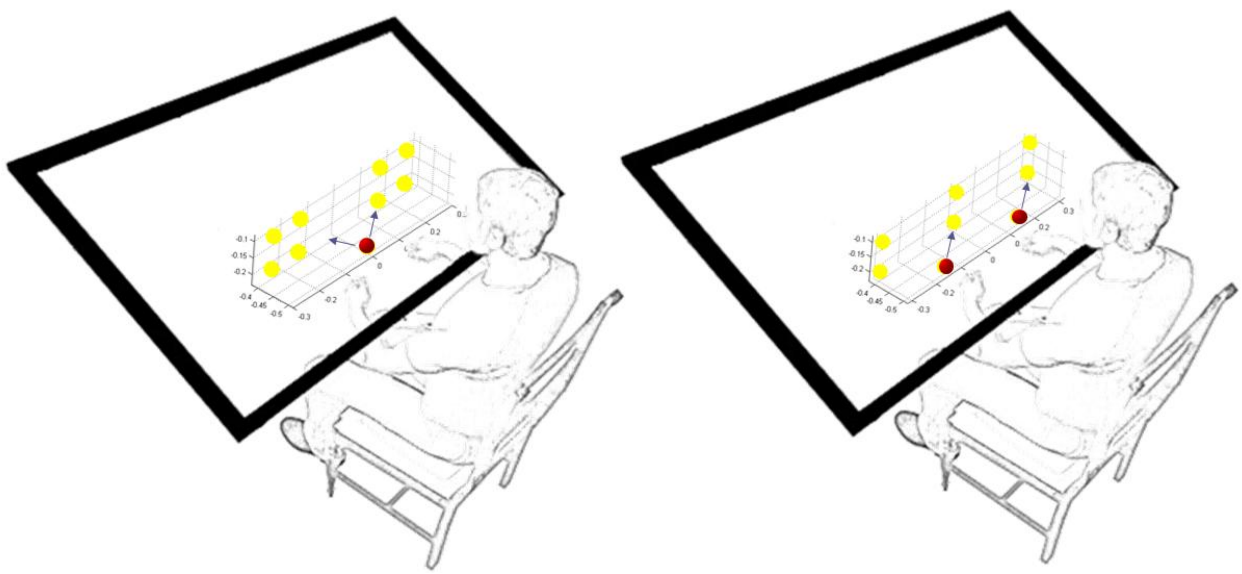

Figure 8- Four different target locations per hand (yellow) with home target(s) (red); Mirror (left) and Parallel (right); the arrows show the movement pattern in each group; the numbers represent the x, y and z coordination of the targets

For the purposes of familiarization and to check the effects of bimanual movements on unilateral performance, subjects began with 40 unilateral movements per hand to randomly placed targets before and after the bimanual task. Each session consisted of 200 bimanual practice trials; 100 of these trials were center-out reaches to randomly placed targets. These outward trials were evaluated for their performance.

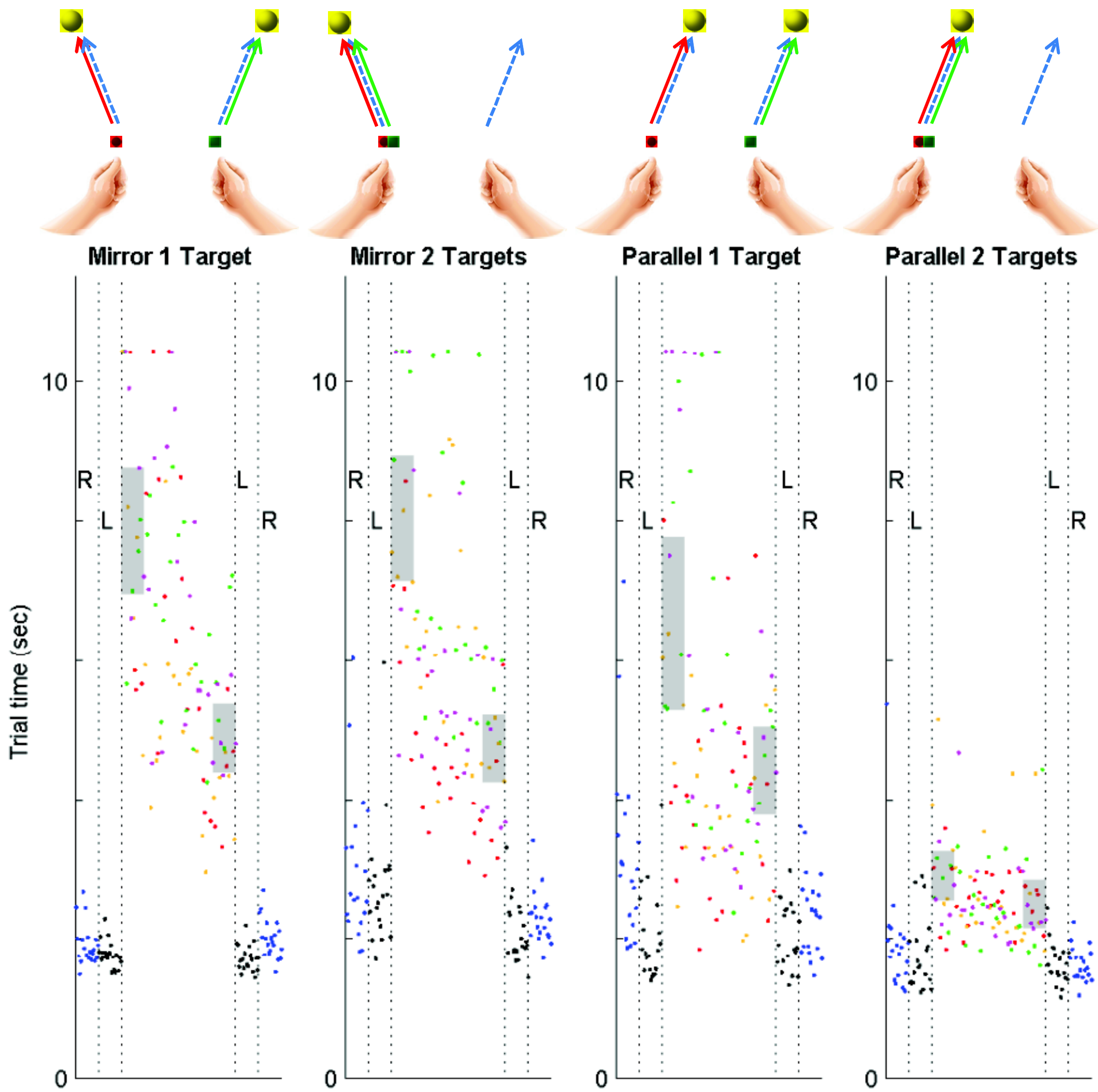

Figure 9- Group description (top); hand movement (dashed arrow), cursor movement (solid arrow). Sample learning curves for movement time (bottom); right hand (blue), left hand (black), bimanual (each color shows a different reaching direction), blocks used for data analysis (gray)

4.2.4 Evaluation procedure

Because movement speed and accuracy are believed to intimately tradeoff (Fitts, 1964), we assessed both movement time and trajectory error as primary measures of interest. Each trial's movement time was calculated from the time that both cursors left the home position until the time they both entered their target radius and remained there for 0.5 sec. Each trial's trajectory error was summarized using the typical measure of maximum perpendicular distance to the ideal line to the target (Thoroughman and Shadmehr, 2000).

4.2.5 Statistical analysis

Learning curves were only plotted for all trials, but the aforementioned measures were calculated only for the first and last 20 movements in the practice phase (gray shaded area, Figure 9, bottom). Repeated measures ANOVA was performed on both measures with main (between) factors being movement type (mirror vs. parallel) and number of targets (one vs. two) and the within factors being location of targets and different evaluation times in each trial. Statistical alpha levels were 0.05 to detect significance.

4.3 Results

The key findings of this study were that movement time and trajectory error were lowest for subjects reaching to two separate targets in parallel (Figure 10). Movement time was significantly lower for groups reaching in parallel ($F(1,16)=16.53$, $p<0.001$) and for groups reaching to two targets ($F(1,16)=8.94$, $p<0.01$). Trajectory errors were lowest for the parallel two-target group, indicated by a significant interaction effect between movement type and number of targets for both hands ($F_{right}(1,16)=130.45$, $p<0.001$ and $F_{left}(1,16)=39.37$, $p<0.001$).

Movement times changed least across practice for the parallel two-target group, indicated by a significant interaction amongst movement type, number of targets and practice ($F(1,16)=5.03$, $p<0.05$). Movement time was an average of 1.43 seconds shorter across practice for the groups reaching in parallel, indicated by a significant interaction between movement type and practice ($F(1,16)=12.86$, $p<0.01$) (Figure 10, top). Furthermore, movement time was an average of 1.49 seconds shorter across practice for groups reaching to two targets, as indicated by a significant interaction between number of targets and practice ($F(1,16)=14.07$, $p<0.01$). As Figure 10 (top) shows, the parallel two-target group begins with low movement time and exhibits a "floor effect" where there is little opportunity for improvement beyond their initial movement time (Everitt, 2002).

Trajectory error results differed from movement time results. There was no significant change in trajectory error across practice for 16 of the 20 subjects from the beginning to the end of trials within each group (individual t-test, Figure 10, indicated by dashed lines). The right hand trajectory errors changed an average of 8 mm less across practice for the groups reaching in parallel, indicated by a significant interaction between movement type and practice ($F(1,16)=5.16$, $p<0.05$). The parallel two-target group showed a lower average error for both hands compared to all other groups even after training (Figure 10, middle and bottom). Finally, different target locations did not significantly affect movement time or trajectory errors.

Further insight can be derived by inspecting how speed and accuracy interact across practice. Most subjects' left hands increased speed while error remained constant (Figure 11, red arrows point to the right). Slopes of these red arrows were not significantly different from zero ($p>0.8$). Right hands showed no particular trend.

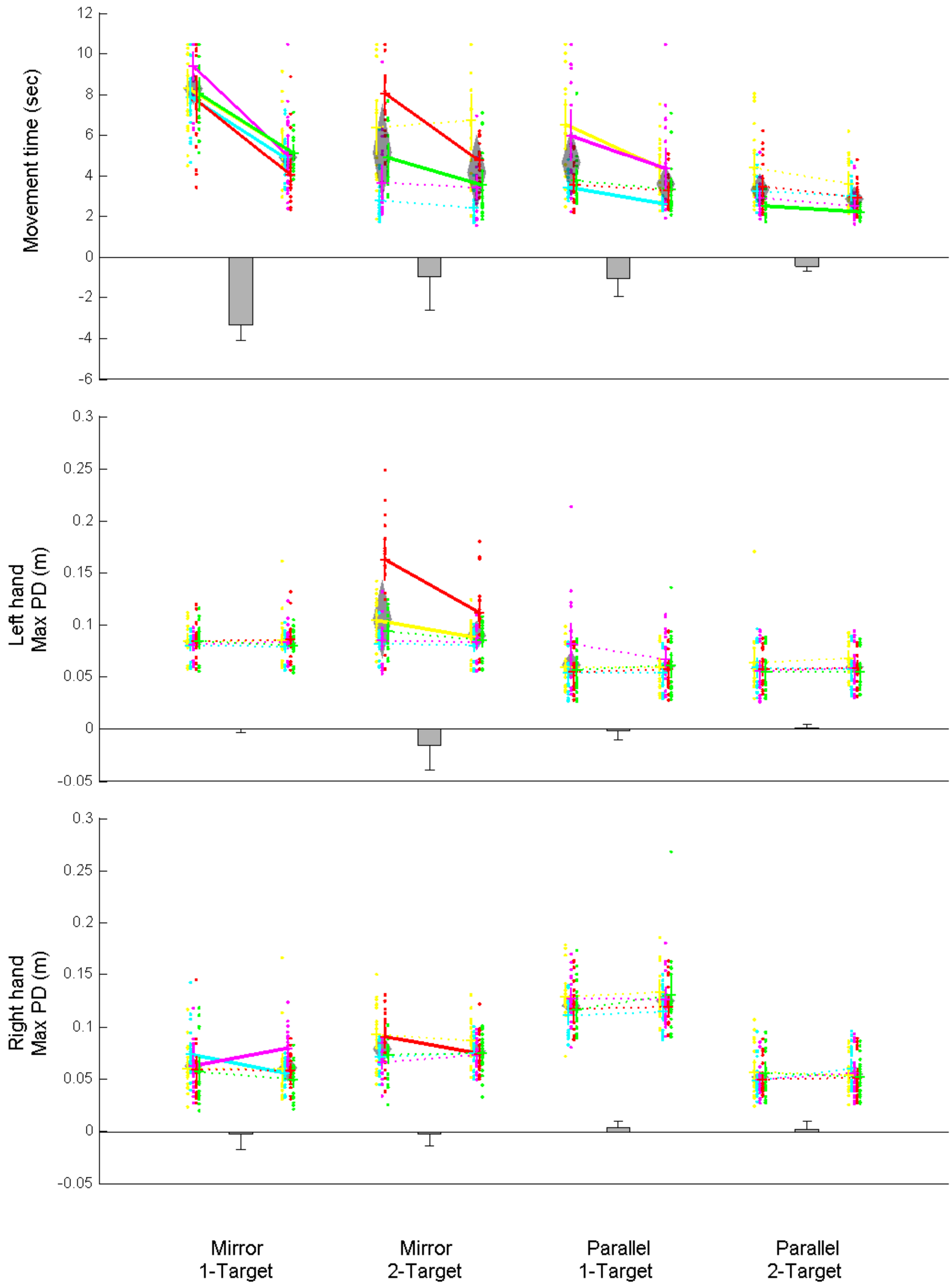

Figure 10- Mirror vs. Parallel; significant changes (solid lines), no significance (dash lines); subject order within each group (color code)

4.4 Discussion

This work shows that there are significant differences between how subjects perform bimanual targeted-reaching tasks under differing visual feedback modes. Among the four groups tested the mode that involved parallel reaching to two targets clearly showed the lowest errors and shortest completion times at the beginning and throughout the experiment. In repetitive practice, errors did not tend to change across trials. Subjects tended to maintain lower left hand than right hand errors while increasing the average speed (and reducing completion times) of the left. While this paper does not attempt to understand any underlying neurophysiological processes, it reveals behavioral evidence that can inform choices in future bimanual applications.

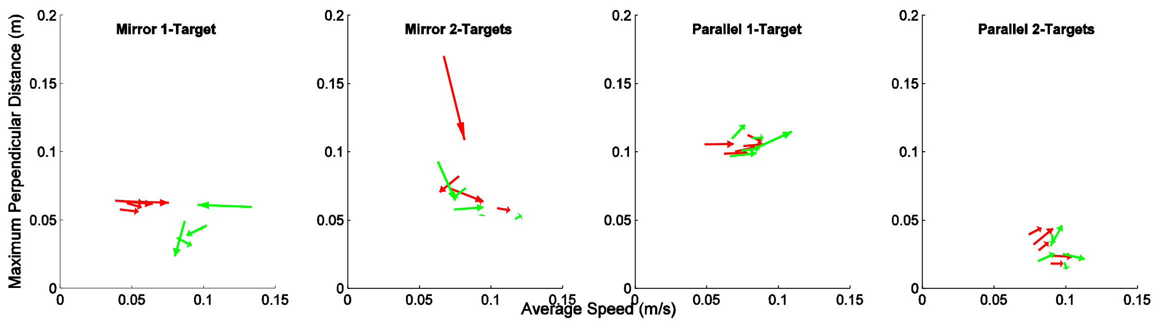

Figure 11- Speed-accuracy trade-off; left hand (red arrows), right hand (green arrows). The tail and head of each arrow represents a subject's average speed/accuracy combinations at the beginning (trials 1-20) and end (trials 80-100) phases of practice

The very small change in both completion time and trajectory error observed in the group performing parallel reaching to two targets suggested that there was little (if any) learning. This lack of change maybe due to a floor effect because error was low at the start and throughout the trials. In addition, we speculate that this is the most familiar or intuitive mode of bimanual activity making it easiest for subjects to execute. This is consistent with "directional compatibility," in which limbs are more coordinated when endpoint directions agree (Bogaerts and Swinnen, 2001). We also speculate that other modes were more difficult, making them initially less familiar, fostering learning, and leading to improvement across training. This was especially dramatic for the mirror transformation, which had the largest errors, slowest completion times, but showed the largest amount of change (learning) across practice. Nevertheless, no other groups' final errors were as low as the mode involving parallel reaching to two targets, suggesting that this mode is, by far, the most intuitive.

One issue not investigated in this initial study is the persistence of any learning effects. Depending on the bimanual training application, retention may be required at different times. Hence, the appropriate time for follow-up tests and the durability of learning should be evaluated in future use of our results in a particular application.

Our results differ from a related study by Kadivar *et al*, 2011, in which no difference between bimanual parallel and mirror modes was found. Our results, which detected significant differences, may have been due to differences in task between these two studies -- their task coupled the limbs through a robotic interface, while ours allowed each hand to move independently. Our study also calculated error differently -- we used maximum perpendicular distance from the line to the target, while Kadivar and colleagues averaged this distance and divided by path length. Such dividing by path length can mask error. For example, a movement with several reversals might result in a deceptively low value if divided by its long length. Our data showed similar trends for both of these measures, but normalized average error produced more variable results.

Contrary to our assumption that attending to only one visual target area would simplify the task, we observed longer movement times in the "one-target" modes that involved cursor transformations. This poor performance may result from the subject's need to reinterpret or mentally transform the conflict between the movements of the hands and its associated visual feedback (Miles and Eighmy, 1980; Krakauer, Pine, et al., 2000; Tong and Flanagan, 2003). Such conflict may place a further burden on a subject's attention that lengthens completion time. Furthermore, of these two transformed modes (one-target), mirror feedback showed longest completion times of all and hence was deemed the most difficult. Although participants in this group significantly improved in movement time, the final performance was still not as good as other groups even after 200 trials. The remaining "two-target" feedback modes performed significantly better, which suggests that attending to two different visual areas is easier than mentally transforming visual cues. This separation of targets to different areas of visual space may also involve parallel computations in separate somatotopic areas of visual cortex that require less competing neural resources (Debaere, Wenderoth, et al., 2003; Swinnen and Wenderoth, 2004). Also, such visual transformations are not commonly encountered in the physical world, while simultaneous attention to two areas is a frequent ecological challenge to humans in tasks such as typing, drawing, and playing video games (Thoroughman and Shadmehr, 2000). Parallel modes, now possible with such virtual reality technology, may provide the most intuitive feedback for training environments.

Our mirror (one target) approach also differed from approaches that use physical mirrors to display limb actions (Altschuler, Wisdom, et al., 1999; Sathian, Greenspan, et al., 2000; Yavuzer, Selles, et al., 2008; Nojima, Mima, et al., 2012). In previous mirror approaches, reflection of one hand replaced the visual feedback of the other. Here, we transformed the right hand cursor so that it appeared on the same side as the left cursor, which we speculate to be more challenging. Such a mirror transformation could provide a "feedback puzzle" that may promote learning. Such complex challenges may encourage recovery better than intuitive ones

(Guadagnoli and Lee, 2004), but these more challenging tasks might also be discouraging to some individuals. Hence, the results of this study serve merely as a guide to identify training modes that are either challenging or intuitive.

Nearly all participants kept error constant across training while decreasing completion times (with the exception of one subject with very high initial error). Participants improved speed rather than accuracy, which is one choice in the scheme of speed-accuracy tradeoff (Fitts's law) (Fitts, 1964). Some have shown increasing speed in the course of learning a skill (Atkeson and Hollerbach, 1985), while others have shown error reduction (Balasubramanian, Howe, et al., 2009). Therefore, changes in speed or accuracy may depend on the task. Interestingly, each group's error was maintained at a different level. We speculate that each bimanual task requires its own level of information processing until a competent strategy is learned. Therefore, subjects hold error constant, begin slowly and speed up as they train. It remains to be seen whether these error levels reflect physiological limits in sensorimotor pathways or simply a different "tolerance" for error in each feedback condition.

These results have implications in rehabilitation, where bimanual interactions can assist a person in re-learning movement skills (Lum, Lehman, et al., 1995). Our results suggest that parallel reaching to two targets may be the optimal method for such self-telerehabilitation because it is the most familiar (least challenging) mode of practice. To the patient, however, improvement in bilateral symmetry may not be as important as completing a functional tasks, some of which are asymmetric. It is also possible that intuitive modes for healthy may not be equally intuitive for brain injured individuals. It remains to be seen whether these results translate effectively to neurorehabilitation. Nevertheless, the initial findings presented here in healthy subjects can help identify environments for rehabilitation or in any training situation requiring bimanual practice.

4.5 Acknowledgements

We thank Daniel Evestedt of SenseGraphics for his technical programming assistance.

5 Simultaneous versus sequential bimanual drawing[3]

Farnaz Abdollahi, Robert Kenyon, James Patton

5.1 Introduction

Development of bimanual skills plays a major role in fostering recovery in neural injuries resulting in hemiparesis, because recovery of both the affected arm, as well as the coordination of both arms, is critical to the restoration of quality of life. Research has revealed a tendency for individuals to synchronize bilateral movements and establish a coordinative structure (Kelzo, Southard, et al., 1979; Swinnen, 2002; Wiesendanger and Serrien, 2004). In the case of hemiparetic stroke, it is possible that deficits in bimanual coordination are caused by the brain lesion directly, or by the patients' attempt to compensate for it (Gordon, 1987; Beer, Dewald, et al., 1999; Mudie and Matyas, 2000; Dewald, Sheshadri, et al., 2001). In either case, given that bimanual movements use unique neural resources (Brinkman, 1981; Brinkman, 1984; Sadato, Yonekura, et al., 1997; Donchin, Gribova, et al., 1998; Schaal, Sternad, et al., 2004), bimanual training could better facilitate learning by utilizing extra cortical areas.

Rather than simple simultaneous bimanual motion, there may be an advantage to practicing sequentially, when one arm performs an action after the other. This avoids the common "crosstalk" problem in simultaneous bimanual studies, in which learning to control one arm can interfere with the other (Swinnen and Walter, 1988; Franz, Zelaznik, et al., 1991; Heuer, 1996;

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Heuer, Kleinsorge, et al., 2004). Some studies have shown the complete transfer of skill between *unimanual* (single arm) and *bimanual* movements despite varying amounts of interference (Wang, Mordkoff, et al., 2010), while others point to limitations of this skill transfer (Nozaki, Kurtzer, et al., 2006). However, all studies appear to agree on both the presence of separate controllers for each arm, and also on each arm having access to the information learned by its opposite (Sainburg and Wang, 2002). Hence, separate controllers suggests *sequential* practice mode while coordination suggests *simultaneous* practice mode. Only a controlled experiment can determine whether either of these approaches might provide benefit in bimanual training.

While multiple studies have shown the tendency of the non-dominant hand to change movement dynamics and become more synchronized with the dominant hand in presence of large distortions or high frequency movements (MacKenzie and Patla, 1983; Swinnen, Young, et al., 1991; Byblow, Carson, et al., 1994; Semjen, Summers, et al., 1995), others have presented results where both hands merge to a more stable state when tasks are of differing natures (Franz, Zelaznik, et al., 1991). These findings however, investigated the model parameters of arm controllers and not the behavioral aspect of re-learning coordination when the natural symmetry is purposely broken, i.e. with a transformation applied to the space of one arm.

In a motor learning process, both error and variability in movement reduction is shown to be a prerequisite for skilled motor performance (Abernethy and Sparrow, 1992; 1993). Hence, depending on the error metric, decreasing average error can result from increased accuracy and also trial-to-trial consistency. Thus, learning a drawing task could be viewed both in terms of the “shape error”, i.e. how close the shape is drawn compared to the template shape, and the “shape variability”, i.e. how consistent people are when learning to draw a shape.

It is our belief that if positive learning results are not obtainable in healthy volunteers, there is little point in attempting to use such modes for rehabilitation in any patient population. We have already determined that parallel movements are superior to mirror movements in previous work (Abdollahi, Kenyon, et al., In press). The present study examined whether *simultaneous* or *sequential* bimanual practice modes foster better learning when healthy individuals learn a drawing task where the left hand experienced a spatial “*stretch*” transformation. We examined both error and trial-to-trial variability of error resulting from bimanual modes of practice (simultaneous vs. sequential) also compared to a control group that practiced unimanually (left hand only). The results of this study suggest the most appropriate mode for self-therapy in future neurorehabilitation interventions.

5.2 Methods

5.2.1 Participants

Thirty healthy right-handed individuals (17 female, age range 18-34, mean age 24.6±3.5) with corrected 20/20 vision were invited to participate and consented using approved Institutional Review Boards from both Rehabilitation Institute of Chicago and University of Illinois at Chicago guidelines for protection of human subjects Internal Review Boards according to the Declaration of Helsinki. Subjects were randomly assigned to the three groups described later in this section. Participants were naïve to the apparatus and had no history of previous musculoskeletal or neurological injury. Subjects were excluded if they had depth perception impairment of less than 8 out of 9 on graded circle test (Stereo Optical Company, Chicago, IL, USA).

5.2.2 Study setting

All experiments in this study were performed in a three-dimensional, large-workspace haptics/graphics system, the Virtual Reality and Robotic Optical Operations Machine (Figure 12) (Scharver, Evenhouse, et al., 2004). A cinema-quality digital projector (Christie Mirage 3000 DLP) displayed the stereo images that span five-foot-wide 1280x1024 pixel see-through augmented reality display resulting in a 110º wide viewing angle in a display. In this study, vision of the arms was occluded so that only cursors (representing hand locations) and templates were shown. Infra-red emitters synchronized separate left and right eye images through LCD shutter glasses. Ascension Flock of Birds™ magnetic sensors tracked motion of the head to track the head position and re-render the environment when necessary so that the subject had the proper real-time view angle. Another two sensors served as position trackers one for each hand. The software application was based on the open-source platform H3DAPI (SenseGraphics, Kipsta, Sweden).

5.2.3 Experimental protocol

Subjects were seated in a chair in front of the VRROOM display. Hand position for left and right hands were obtained using two Flock of Birds position trackers. Hand position data were sampled at used for real-time feedback at100Hz. Two drawing templates (one simple and one complex) were presented to the participants, in alternating order, with one template for each trial (Figure 13). The right hand was represented with a green sphere and the left hand was represented with a red sphere as virtual "*pens*". The template was visible during the entire trial.

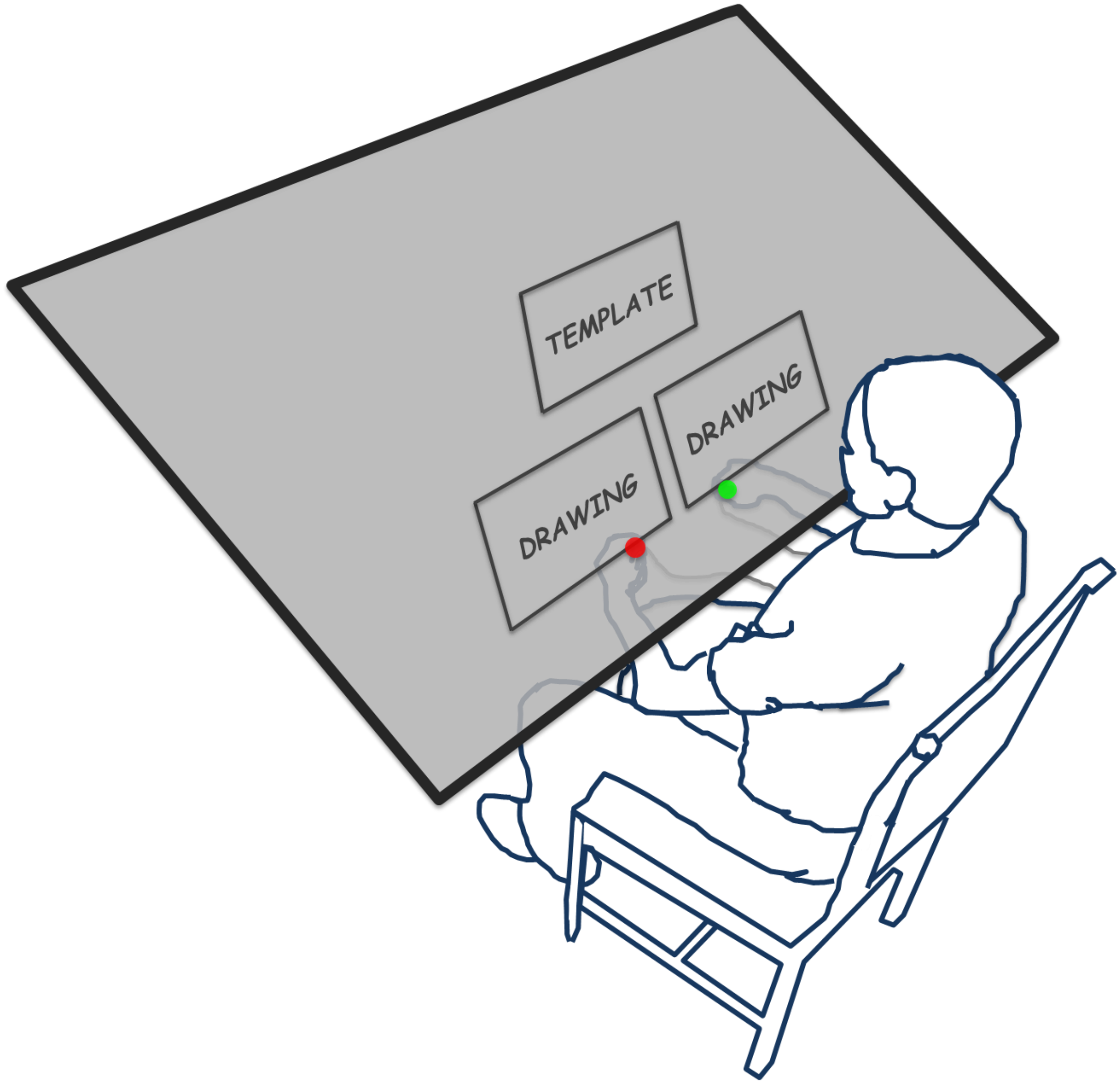

Figure 12- Experimental setup. The subject was instructed to draw the displayed template with cursors tracking their hands (small red and green dots) within the specified area

Depending on their assigned group, subjects were instructed to draw the presented template in the right or left box with the corresponding hand. A target was present to signal the beginning and end of movement. The pen (i.e., the cursor) started to leave a trace on the screen once it was placed inside the start target (displayed in yellow and visible only prior to movement onset). A movement (or trial) was considered complete when subject entered the start point target, drew the shape and returned to the end target to signal the end of movement (displayed in yellow and visible 1 second after the start of the movement). The start and end targets were at the exact same spot for each shape to assure the formation of a closed loop. They would have disappeared when the “pen” (i.e. the cursor) entered and halted for 0.5 seconds. Upon completion, the target(s) would vanish, and the next starting target and template in the sequence would appear.

Participants were divided into three separate groups, with 10 subjects per group. The first two groups each experienced one of the bimanual movement modes (either simultaneous or sequential) and the third group practiced with left hand only. During the practice phase, the left hand cursor was transformed by a linear $(0.6x, 0.8y)$ factor. Subjects in bimanual groups were instructed to match the drawing of the left hand with the one from the right hand, and as a secondary goal, to try to match the drawing of both hands with the template in shape and size. The third group served as the unimanual control, and received the same instructions for their left hand only. The participants were aware of the left hand transformation and one-to-one correlation of right hand representation. The “*Simultaneous*” group moved both hands at the same time and the start and end targets were set such that they only disappeared when both hands were in place to assure the simultaneous start and end of movements. The “*Sequential*” group alternated drawing between right and left hands, always starting from the right hand. The “*Left Only*” group only drew only with the left hand while they rested their right hand. Visual feedback, presented at the end of each trial, showed subjects what was drawn in addition to the original template.

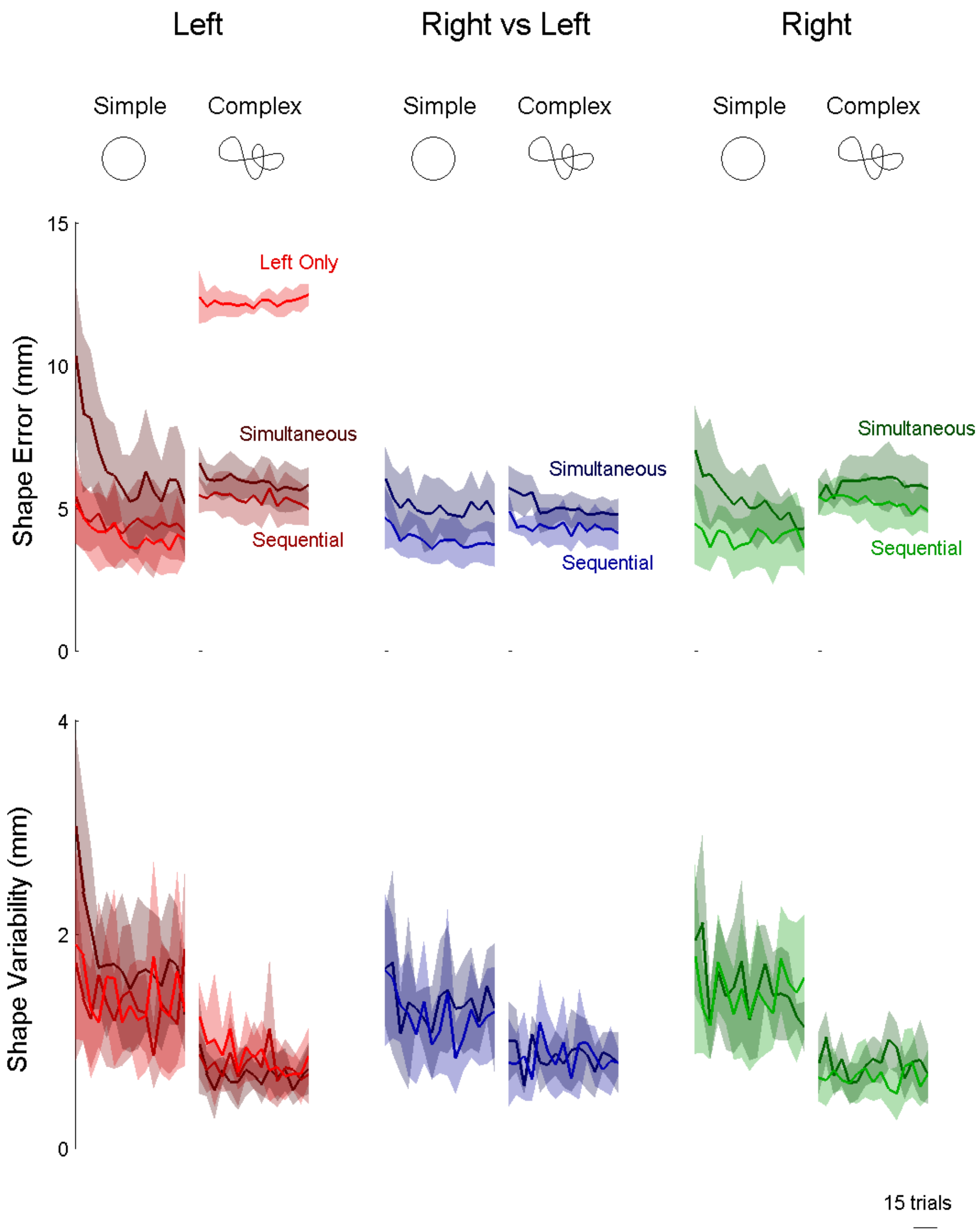

Figure 13- Group description (top); Average data across subject (bottom); average performance (solid lines), 95 percent confidence interval (shaded area)

For the purposes of familiarization and to check the effects of bimanual movements on unilateral performance, subjects began with 4 unilateral movements per hand per template before and after the main task. Each session consisted of 152 practice trials per hand half drawing each shape.

5.2.4 Evaluation procedure

We chose shape error and shape variability as the primary measures of interest in order to capture the spatial features of each movement. Shape error was defined as the distance between two trajectories, where for a given A and B trajectories with m and n samples respectively, the shape error was defined as (Conditt, Gandolfo, et al., 1997):

$$\varepsilon(A,B) = \frac{\sum_{i=1}^{m} d_{A\rightarrow B}^{i} + \sum_{j=1}^{n} d_{B\rightarrow A}^{j}}{m+n}$$

, where $d_{A\rightarrow B}$ is a vector of the minimum distance between each point in trajectory A to all points in trajectory B, and where $d_{B\rightarrow A}$ is a vector of the minimum distance between each point in trajectory B to all points in trajectory A. Shape variability was defined as the standard deviation of shape error (Basteris, Bracco, et al., 2012). In order to correct for the sample bias in the beginning and end of each movement, the trajectories were interpolated and resampled with a 1 sample/mm rate. Trials were excluded from the calculations if the length of the trajectory was less than 40% of the template. Further, in order to make fair comparisons amongst groups, error measures for each trial (ε_t) were normalized by the grand mean and standard deviations of subject means ($\bar{\varepsilon}_s$) across the group,

$$\varepsilon_t^Z = \frac{\varepsilon_t - \sum_s \bar{\varepsilon}_s / S}{std(\bar{\varepsilon}_s)}$$

While learning curves were plotted for all trials cross each condition (Figure 13), the aforementioned measures were calculated using only the first and last 10 movements of the practice phase (5 trials per shape), establishing a measures of change across practice (Figure 14). Repeated measures ANOVA was performed on both measures for three different categories (right hand vs. template, left hand vs. template and right hand vs. left hand) with main (between) factors being practice mode (simultaneous vs. sequential vs. left only) and the within factors being different shapes (simple vs. complex) and different evaluation times (beginning vs. end). Tukey Honest Significant Differences (HSD) post-hoc analysis as well as separate t-tests were performed where appropriate. All statistical alpha levels were 0.05 to detect significance.

5.3 Results

Here we divide our analysis into three categories, related to the separate goals of the task – in order to understand how well each hand could individually draw the template, as well as how the left and right hands matched each other. Speed was analyzed and determined to not to differ significantly, and hence all the results below are related to error and error variability.

5.3.1 Left hand vs. the template

As expected, all groups' left hand performance improved with practice ($F(1,27)=8.98$, $p<0.01$). Importantly, in regards to our central question, the left hand performance improved for the *simultaneous* practice mode more than the *sequential* practice mode (Figure 14A; shape error $t=-2.39$, $df=18$, $p<0.01$). However, the *simultaneous* practice mode was not significantly different from the *left only* practice mode ($p=0.07$).

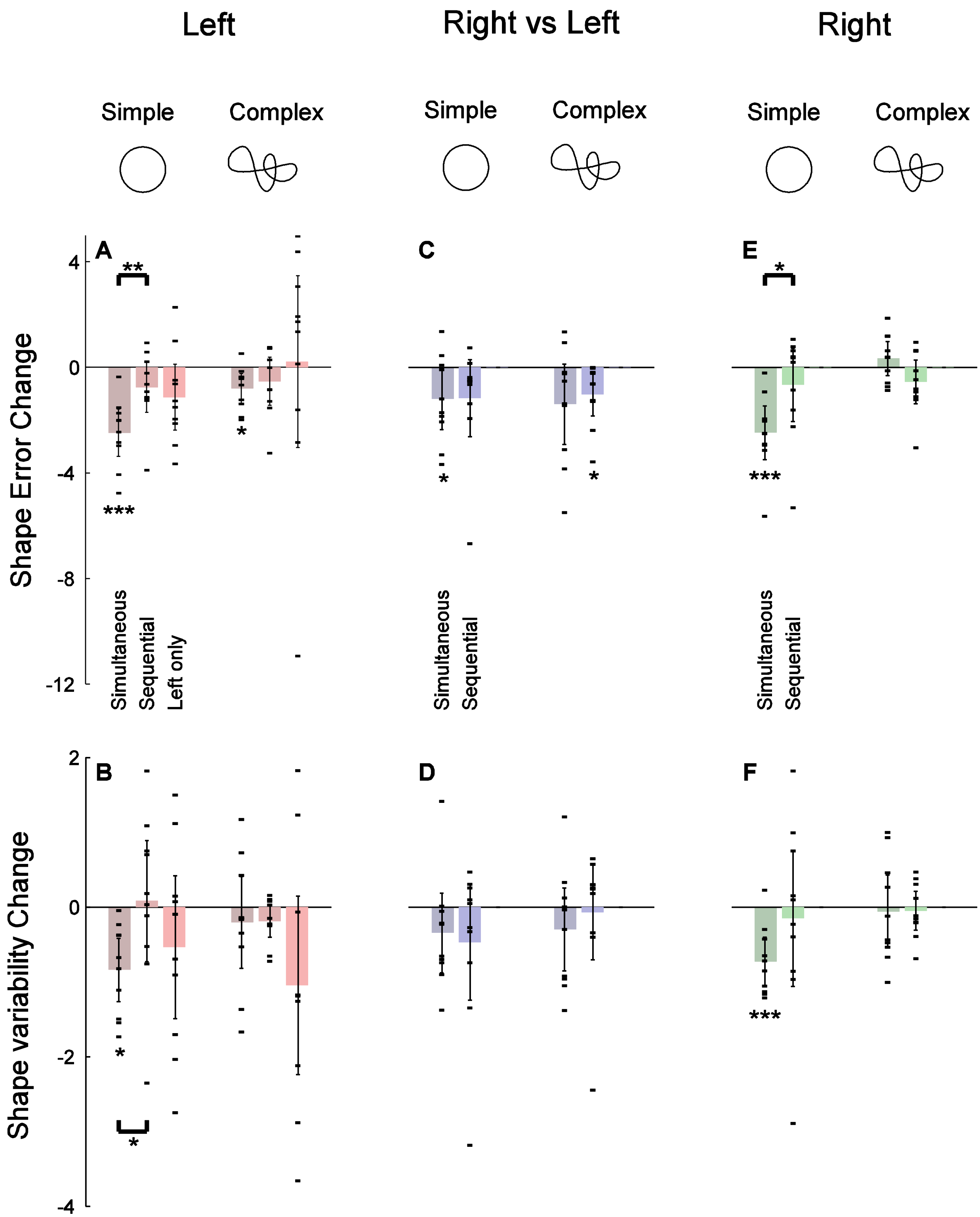

Figure 14- Simultaneous vs. Sequential change from beginning (trials 1-5) to end (trials 72-76) of practice; Left hand error (A) and variability (B) compared to template, Right hand error (E) and variability (F) compared to template and Left hand compared to Right hand in error (C) and variability (D)

All groups also became more consistent with practice (F(1,27)=10.10, p<0.01). Notably, left hand performance became more consistent when drawing the simple shape in *simultaneous* practice mode (Figure 14B; shape variability t=-4.41, df=9, p<0.05), which was also significantly different from *sequential* practice mode (t=-2.25, df=18, p<0.05). However, no significant trends were observed with the complex shape.

Ironically, for the complex shape only, error varied the most from one trial to the next for the *left only* practice mode (shape-practice mode interaction: F(2,27)=24.20, p<0.001). The left hand was less consistent throughout, evidenced by post-hoc comparisons between the *left only* practice mode and the other two groups (p<0.001 for both comparisons). Apparently, the left hand has more trial-to-trial variability when it is working by itself and attempting more complex shapes.

5.3.2 Right hand vs. the template

Similarly, all groups' right hand performance improved with practice (F (1,18)=12.68, p<0.01). Particularly, right hand performance in drawing the simple shape improved more in the *simultaneous* practice mode compared to *sequential* practice mode (Figure 14E; 3-way interaction of time-shape-practice mode (F(1,18)=9.60, p<0.01).

Strikingly, the drawing of the simple shape exhibited more variability (trial-to-trial) than the complex shape (Figure 14F; F(1,18)=23.56, p<0.001). Shape variability only significantly decreased across practice for the right hand when practicing the simple shape in the *simultaneous* practice mode (t=-5.00, df=9, p<0.001).

5.3.3 Left hand vs. right hand

Left and right hand trajectories became more similar across practice (Figure 14C; D (1,18)=13.41, p<0.01). However, more detailed analysis revealed that the *simultaneous* practice mode made the greatest improvement with practice when drawing the simple shape (t=-2.30, df=9, $p<0.05$). The *sequential* practice made the greatest improvement with practice when drawing the complex shape (t=-2.76, df=9, $p<0.05$). No change was detected in shape variability between hands for either group (Figure 14D).

5.4 Discussion

This work shows that there are significant differences between how subjects perform bimanual drawing under differing arm training modes. Among the three groups tested, both shape error and shape variability declined for both hands in the simultaneous group for simple drawing task. The complex shape results were, however, less clear. Subjects tended to maintain a similar relationship between left and right hand trajectories among both simultaneous and sequential groups while improving across practice.

The significant differences between left hand shape error and shape variability between the sequential and simultaneous groups suggested that when dealing with a transformation practicing with the other hand is more beneficial than practicing with each hand alternately. This difference could come from the fact that when both hands are discoordinated, the extra neural areas in brain activated by bimanual movements could help both hands refill their controllers with more accurate information. Thus, we speculate that, in hemiparesis, simultaneous practice is superior to sequential practice.

Our hypothesis was similar to ideas proposed in the neurorehabilitation literature, which states that non-affected arm can potentially retrain the affected arm (Lum, Burgar, et al., 2002; Hesse, Schulte-Tigges, et al., 2003; Macclellan, Bradham, et al., 2005). Average left hand performance improved across practice, however the *simultaneous* practice mode was near to (p=0.07) but not significantly different from the *left only* practice mode. It may require additional investigations to reveal the clear advantages of bimanual practice over training with one arm alone.

Interestingly, the variability was highest for the left hand only (control) group compared to both simultaneous and sequential groups. This behavior could suggest that having both hands involved in the learning process increases performance consistency in both limbs. In addition, we speculate that stability increases with further involvement of brain areas when learning a complicated, unfamiliar movement. The left hand only group did show the most improvement in shape variability of the complex shape, indicating that this aspect of the task is an important enough element to the nervous system.

The most critical of these results are the implications in neurorehabilitation, where simultaneous bimanual movements can assist a person in regaining limb coordination and movement skills (Lum, Lehman, et al., 1995; Jancke, Peters, et al., 2000; Krebs, Volpe, et al., 2009). Our recent results suggest that parallel practice of both arms (Abdollahi, Kenyon, et al., In press)may be the optimal method for self-rehabilitation because it increases coordination and improves task performance in both limbs. To the patient, completing functional tasks is more important than getting a perfect performance in one hand (Rose and Winstein, 2004), which might be better achieved using a single hand practice. It is also possible that these practice modes for healthy volunteers may not be equally transferable to brain-injured individuals. It remains to be seen whether these results translate effectively to neurorehabilitation, but these initial findings from healthy subjects can help identify optimal environments for neurorehabilitation and the variety of other training situations that require bimanual practice.

5.5 Acknowledgments

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6 Enhanced self-teleoperated arm therapy for individuals with chronic stroke[4]

Farnaz Abdollahi, Emily Case, Molly Listenberger, Robert Kenyon, James Patton

6.1 Introduction

Despite the existing evidence of possible recovery long after the onset of stroke (Taub, Uswatte, et al., 1999), regaining functional use of upper extremity has been an ongoing challenge (McCombe Waller and Whitall, 2008). Emerging interventions including intensive repetitive practice (Wolf, Winstein, et al., 2008), task-specific training (Dean and Shepherd, 1997), and interactive robotic technology (Lum, Burgar, et al., 2002; Volpe, Ferraro, et al., 2005; Sanchez, Liu, et al., 2006) all aim to restore upper extremity motor ability and function. And although many of these studies focus on perfect performance, patients most care about task completion with proper coordination of both arms (Rose and Winstein, 2004). While these methods might offer benefits, many daily activities require a coordinated participation of both arms that might be more achievable through self-therapy.

A number of studies have investigated the efficacy of bimanual training on the recovery of affected limb (Mudie and Matyas, 2000; Whitall, McCombe Waller, et al., 2000; Cauraugh and Kim, 2002; Hesse, Schulte-Tigges, et al., 2003; McCombe Waller and Whitall, 2004). Others have stated that bimanual training engages extra parts of the brain (Sadato, Yonekura, et al.,

[4] Submitted to Journal of Neural Engineering

1997; Donchin, Gribova, et al., 1998), hence it allows the possibility for additional “solo” training to occur after the one-on-one therapist time has run out. It remains to be tested whether such solo training might lead to added benefit to the therapy process if the proper technology is employed.

One reason why the prospects of bimanual training have not been fully understood is that it is a broad topic with many choices on the specific manner in which people practice. One can choose to move with hands physically coupled or uncoupled, in a mirror mode or in a parallel mode, with both hands moving together or in sequence. Previously parallel reaching has been shown to imply less of a challenge in healthy individuals compare to reaching in a mirror mode (Abdollahi, Kenyon, et al., In press). Our group has also investigated the possible advantage of simple simultaneous bimanual motion over practicing sequentially, when one arm performs an action after the other. Consequently, our work has shed light on the most likely successful mode for self-rehabilitation: simultaneous movements in parallel mode. However, it remains to be tested whether these healthy study behaviors would translate to stroke population.

The manipulation of error signals during practice appears to stimulate improvement in coordination for individuals with or without a history of stroke (Patton and Mussa-Ivaldi, 2004). In simple terms, if one perceives larger mistake, they are motivated and naturally inclined to reduce the errors. Such error-driven learning processes are believed to be central to neuroplasticity and reacquisition of skill in human movement (Kawato, 1990; Desmurget, Jordan, et al., 1997). Which is supported by the neuroplasticity supporting methods that leverage the natural adaptive nature of the nervous system during movement control (Patton, Stoykov, et al., 2006).

While the mechanisms for these improvements are not yet known, based on our recent study (Abdollahi, Case, et al., In press), we speculate that the nervous system reacts to and learns more from larger errors (Patton, Kovic, et al., 2006). In that study our group took the error augmentation ideas and expanded them to the application of a therapist-patient-machine trio that works together to restore reaching ability. The therapist held a tracking device and provided a cue to the patient, which unbeknownst to them, had their errors instantaneously, magnified both visually and haptically (through robot-applied forces). Error augmentation demonstrated an advantage over and above repetitive practice alone. The obvious next question, however, is whether the cue might come from the patient's non-effected arm, allowing for self-rehabilitation. Here, we expand on this novel concept to test a self-rehabilitation system that employs visual display and robotic technology with augmented error signals during training.

Our aim in the current study was to examine the effect of error augmentation on a self-therapy approach for individuals with hemiparesis caused by stroke. Specifically, we wished to determine if error augmentation applied during a bimanual reaching and coordination task would lead to greater functional recovery over repetitive practice alone. We hypothesized that individuals with chronic stroke would benefit more from error augmentation treatment than the standard repeated reaching.

6.2 Methods

6.2.1 Participants

Twenty-two adults with chronic stroke agreed to participate in the study (8 Female, age range 26-77, mean age 53.86). Study participants were recruited from a registry of post-stroke individuals or who contacted the lab with interest in participating due to postings in the Chicago area. This study was approved by both the Northwestern University and University of Illinois at

Chicago Institutional Review Boards. All participants provided informed consent according to the Declaration of Helsinki prior to commencing the study. Twenty-two individuals began the study, with twenty individuals completing all phases of the study. Two participants dropped out due to medical reasons unrelated to the study and were excluded from analysis (Figure 15). Eligible participants were all adults aged 18 or over who had suffered a single cortical stroke and were at least six months post-stroke. Participation also required some recovery of proximal strength in the hemiparetic limb as confirmed by an upper extremity Fugl-Meyer score of 25-50. Exclusion criteria included multiple strokes, bilateral paresis, severe spasticity or contracture, severe concurrent medical problems, severe sensory deficits, cerebellar strokes resulting in severe ataxia, significant shoulder pain, focal tone management with Botulinim Toxin (Botox®) injection to the hemiparetic upper extremity within the previous four months, depth perception impairment (< 3/9 on Stereo Circle Test), visual field cut, cognitive impairment (Mini Mental State Examination < 23/30), or severe aphasia, affective dysfunction or hemisensory neglect that would influence the ability to perform the experiment or provide informed consent. Participants were excluded if they received any other skilled upper extremity rehabilitation in a clinical setting. See Table III for participants' demographics and lesion characteristics.

6.2.2 Study Setting

The study used a three-dimensional haptic/graphic system called the Virtual Reality Robotic and Optical Operations Machine (Patton, Dawe, et al., 2006). A cinema-quality digital projector (Christie Mirage 3000 DLP) displays the stereo images that span five-foot-wide 1280x1024 pixel display resulting in a 110º wide viewing angle in a see-through augmented reality display. In this study, vision of the arms was occluded so that only cursors (representing hand locations) and targets were shown. Infra-red emitters synchronize separate left and right eye images through

StereoGraphics liquid crystal shutter glasses. Ascension Flock of Birds sensors tracked head motion for appropriate display of perspective another sensor served as the position tracker of the non-affected wrist. A SensAble Technologies Phantom Premium 3.0 robot interfaced with the participant's impaired wrist (Figure 16). A Wilmington Robotic Exoskeleton provided anti-gravity arm support (Rahman, Sample, et al., 2000).

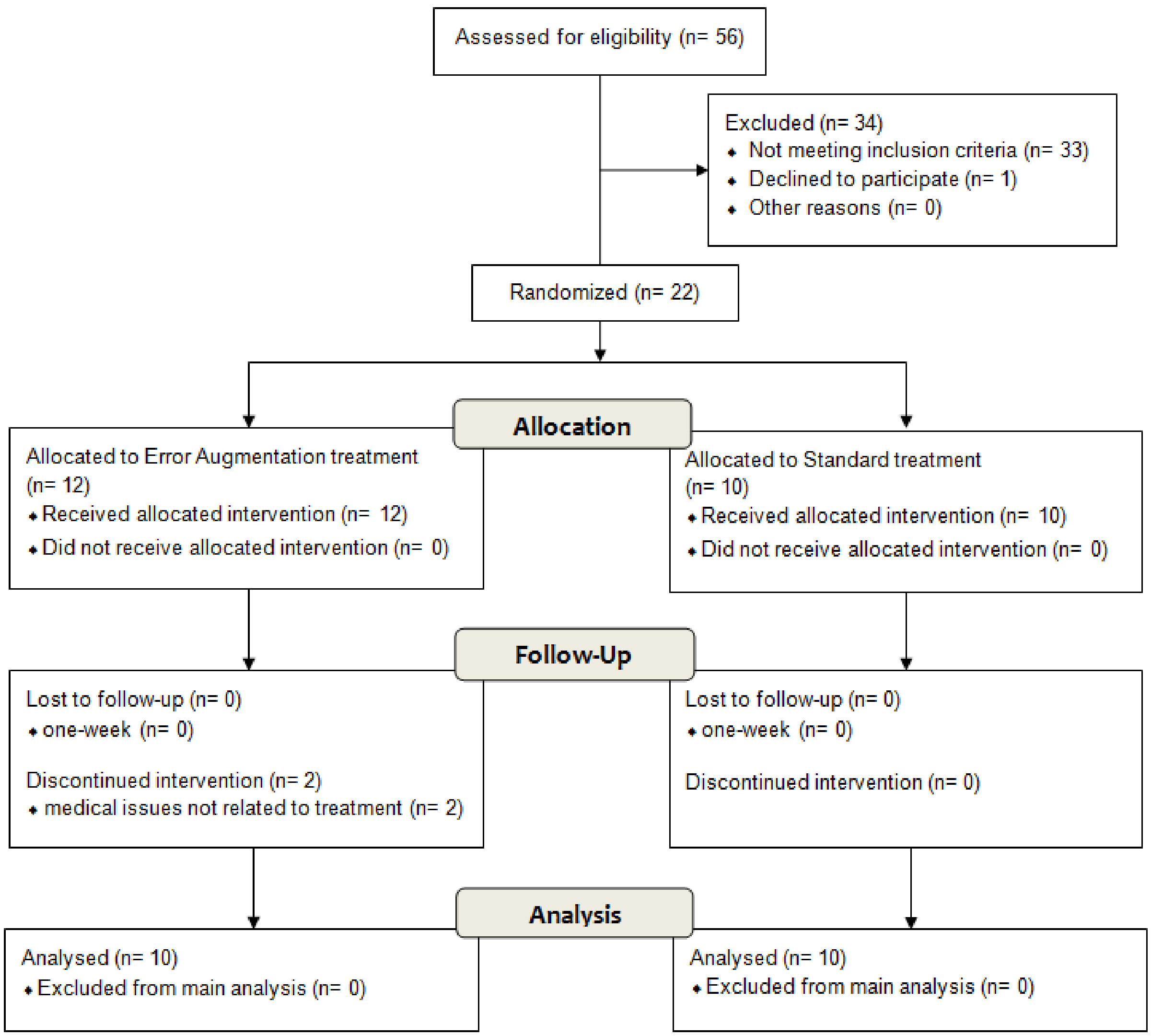

Figure 15- Subject recruitment flow diagram

Table III- Baseline demographics and clinical characteristics

Subject ID	Sex	Age	Months Post Stroke	Previously Dominant Hemisphere	Affected Hemisphere	Lesion Type	Lesion Location
201	M	62	54	Left	Right	Ischemic	Cortical, Subcortical
202	M	57	203	Right	Right	Hemorrhagic	Cortical
204	F	53	144	Left	Right	Hemorrhagic	Cortical, Subcortical
205	M	66	17	Right	Left	Ischemic	Brain Stem
206	M	54	48	Right	Left	Ischemic	Subcortical
207	F	58	238	Right	Right	Ischemic	Unknown
208	M	54	30	Left	Right	Ischemic	Cortical, Subcortical
209	M	61	66	Left	Left	Ischemic	Cortical
210	M	26	6	Left	Right	Hemorrhagic	Cortical, Subcortical
211	M	62	105	Left	Left	Hemorrhagic	Brain Stem
212	M	56	23	Left	Left	Ischemic	Subcortical
213	F	53	51	Left	Left	Hemorrhagic	Cortical
214	F	46	102	Left	Right	Hemorrhagic	Unknown
215	F	65	142	Left	Right	Ischemic	Cortical
216	M	42	31	Left	Right	Hemorrhagic	Cortical, Subcortical
217	M	66	38	Left	Right	Hemorrhagic	Cortical, Subcortical
218	F	51	51	Right	Left	Ischemic	Unknown
219	M	48	38	Left	Right	Ischemic	Cortical, Subcortical
220	M	69	31	Left	Left	Ischemic	Subcortical, Brain Stem
222	F	33	29	Left	Left	Ischemic	Cortical

F, female; M, male.

6.2.3 Experimental Protocol

A computer-generated list of random numbers allocated each participant to one of 2 groups matching screen Fugl-Meyer scores as close as possible. We tested two experimental robotic-assisted treatments where each participant received either a control treatment of repetitive bimanual reaching with no error augmentation called the "*standard treatment*" or a treatment with the same amount of practice plus combined visual and haptic error augmentation called the "*error augmentation treatment*". Each phase consisted of two weeks of training with participants receiving three, 45-minute sessions per week (six sessions per experimental phase). After a week of no treatment, each participant went through a follow-up evaluation.

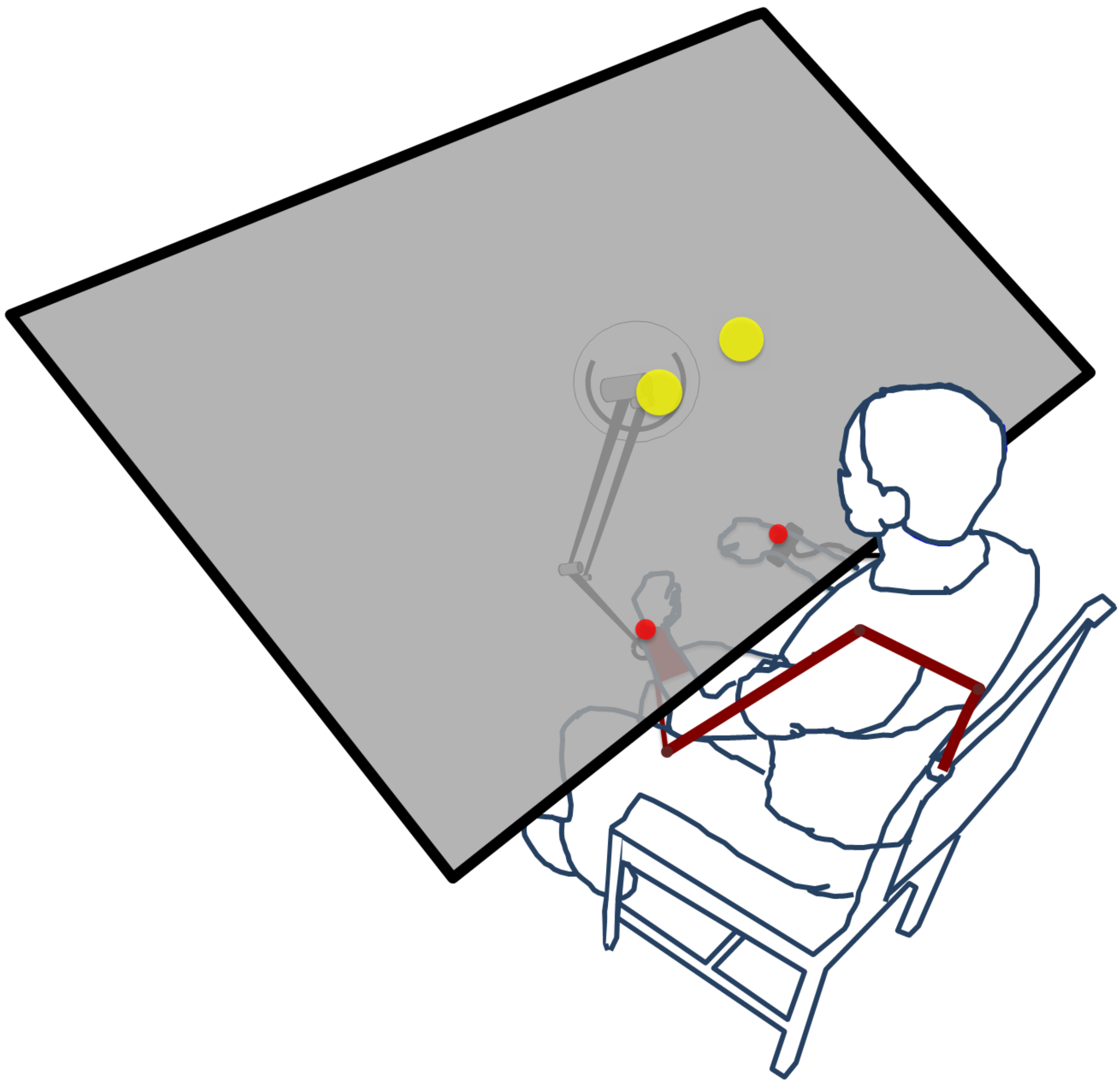

Figure 16- Experimental setup. The patient was instructed to move the cursors tracking their wrist centers (small red dots) within the targets (yellow spheres) and then return

Each session began with five minutes of setup of the participant within the VRROOM, then six 5-minute blocks of movement training with two-minute rest periods between each treatment block (Figure 17). The treatment protocol included the practice of bimanual reaching movements for all participants in addition to free movements. The free treatment blocks targeted participant's idea of good therapy based on their need with the possibility of choosing the previous standardized five-minute block practice. This allowed the patient to customize their own therapeutic approach, focusing on what was most critical for their particular weakness areas. After the end of treatment phase, participants received a one-week no treatment where there were no upper extremity interventions. Quantitative assessments were performed at the beginning and end of the treatment phase (pre and post) as well as one week after the post assessment (follow-up).

During all therapy sessions, participants were comfortably seated in a chair with the hemiparetic arm supported by the WREX™ gravity-balanced orthosis. The hemiparetic hand was placed in an exotendon glove that included a wrist splint, which assisted with hand opening and neutral wrist alignment to allow for a more functional hand and wrist position. Since holding a handle is not necessarily the same as free-hand motion (Cothros, Wong, et al., 2006), we connected the robot near the wrist to allow the hand to open freely as well as allow free pronation and supination of the forearm with the WREX™ swiveling wrist support. Both the PHANTOM™ robot and position tracker were attached to the affected and non-affected forearms respectively, with the center of the devices located above the radiocarpal joint. Forces were applied by the robot during the EA treatment; however, the robot was attached during both treatments to assist in blinding the participant as well as to provide feedback regarding location within the 3D workspace. While it is difficult to determine if these responses reflect any true failure of blinding (Sackett, 2004) there were also known compromises in our attempt at blinding.

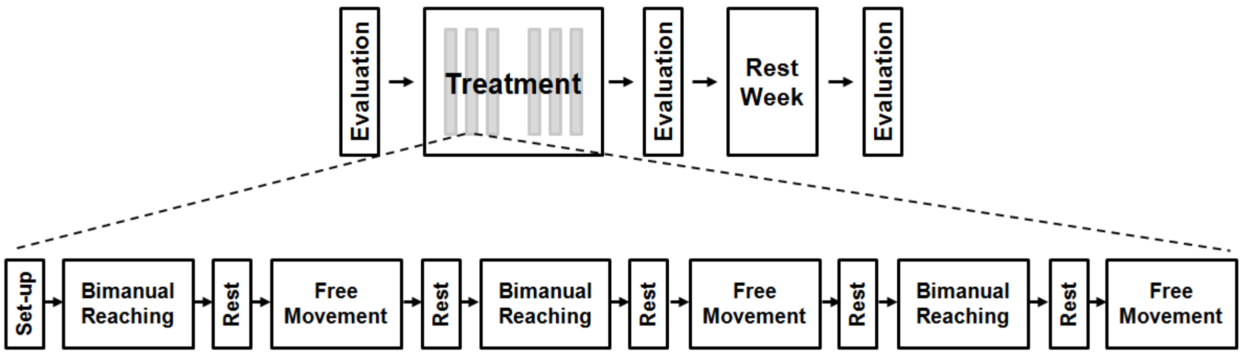

Figure 17- Schematic of the successive days of treatment for the study (top panels), and a breakdown of the successive phases of treatment in each day's session (bottom panels)

During training, participants were only able to see two cursors within the virtual environment with the view of their arms being blocked. Each cursor displayed the movement of each arm. Participants were instructed to keep moving their arms together as much as possible while reaching to targets throughout the workspace. For the EA treatment, the error vector *e*, defined as the instantaneous difference in position between the participant's wrists was visually magnified by a factor of 1.5 as part of the error augmentation. Additionally, an error augmenting force of 100 N/m was applied pushing the participant's affected hand further away from the non-affected hand. For safety purposes, this force was designed to saturate at 4 N.

6.2.4 Evaluation Procedure

Participants were evaluated inside the VRROOM with the level progress and outside the VRROOM with the clinical measures immediately prior to the start and again at the end of the treatment. Follow-up testing was performed one week after the end of treatment. A blinded evaluator administered all outcome measures including our primary outcome; the arm motor section of the Fugl-Meyer (AMFM) to measure impairments (Platz, Pinkowski, et al., 2005; Wagner, Rhodes, et al., 2008) as well as our secondary outcome measures, which included the Wolf Motor Function Test (WMFT) for functional ability (Wolf, Catlin, et al., 2001; Fritz, Blanton, et al., 2009), Motor Activity Log (MAL) for quality of arm use in activities of daily living (van der Lee, Wagenaar, et al., 1999; Oswatte, Taub, et al., 2006) and the Box and Blocks assessment as an indicator of manual dexterity (Platz, Pinkowski, et al., 2005; Chen, Chen, et al., 2009). Finally, to assess perception of the experience, participants completed the Intrinsic Motivation Inventory questionnaire (McAuley, Duncan, et al., 1989), which consists of 25 questions in four categories (interest/enjoyment, perceived competence, motivation/effort, and perceived value).

6.2.5 Statistical Analysis

To examine for treatment-related change, outcomes were analyzed using a repeated measures analysis of variance, with factors of time (pre vs. post vs. follow-up) and treatment type (EA vs. standard). Finally, Tukey HSD post-hoc analysis was performed when necessary to evaluate detailed changes in participants' performance. All statistical tests were evaluated using an alpha level of 0.05.

6.3 Results

Our main outcome measure, AMFM, in an overall analysis showed significant improvement over the three weeks ($F(2,36)=3.96$, $p<0.05$), such that the average gain was 2.90 ± 5.24 points. Further detailed analysis failed to detect a significant difference between standard and EA treatments (Figure 18A). However, the group that received EA treatment improved significantly from the pre treatment evaluation to the one-week follow-up with an average gain of 3.50 ± 3.47 ($t=3.19$, $df=9$, $p<0.05$). Interestingly, this group also improved significantly over the no treatment period with an average gain of 2.60 ± 3.50 ($t=2.35$, $df=9$, $p<0.05$).

We found similar treatment related results in our secondary measures. Although variable, the WMFT Functional Ability Scale (FAS) improved significantly with an overall average of 0.24 ± 0.32 points over three weeks ($F(2,36)=5.11$, $p<0.05$). Further detailed analysis failed to detect a significant difference between standard and EA treatments (Figure 18B). However, the group that received EA treatment improved significantly from the post treatment evaluation to the one-week follow-up with an average gain of 0.23 ± 0.17 ($t=4.27$, $df=9$, $p<0.01$).

The same trend was also seen in the MAL-Quantity measure where the overall analysis showed significant improvement over the three weeks ($F(2,36)=16.07$, $p<0.001$), such that the average gain was 0.59 ± 0.56 points. Although, further detailed analysis failed to detect a significant difference between standard and EA treatments, this result indicated an increase in amount of affected arm use in daily activities over the three-week period (Figure 18C). Nevertheless, the group that received EA treatment improved significantly from the post treatment evaluation to the one-week follow-up with an average gain of 0.30 ± 0.20 ($t=4.78$, $df=9$, $p<0.01$). This increase was significantly different from the standard group change over the same one-week period ($t=2.27$, $df=18$, $p<0.05$).

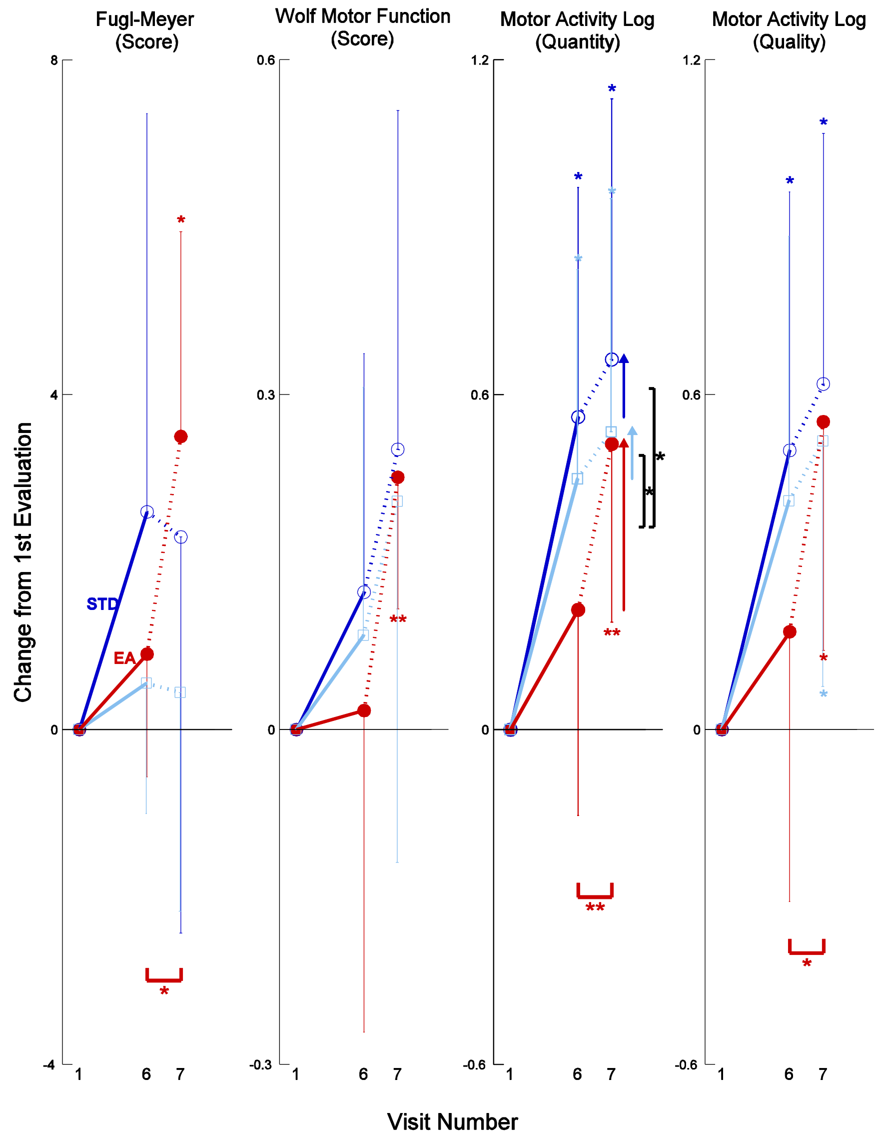

Figure 18- Clinical score changes from the first visit, AMFM score (A), WMFT score (B), MAL quantity (C) and MAL quality (D). Solid line shows the EA treatment (red) and the standard treatment (blue) and dashed lines are the no treatment periods

A similar trend was also seen in the MAL-Quality measure where the overall analysis showed significant improvement over the three weeks (F(2,36)=10.71, p<0.001), such that the average gain was 0.59 ± 0.60 points. Although, further detailed analysis failed to detect a significant difference between standard and EA treatments, this result indicated an increase in quality of affected arm use in daily activities over the three-week period (Figure 18D). Yet, the group that received EA treatment improved significantly from the post treatment evaluation to the one-week follow-up with an average gain of 0.38 ± 0.42 (t=2.82, df=9, p<0.05).

The measure we constructed, Level Progress, also showed significant improvement over the two-week treatment period (t=6.14, df=19, p<0.001). Further detailed analysis failed to detect a significant difference between standard and EA treatments (Figure 19). We failed to detect significant treatment related effects in WMFT-Time and Box and Blocks assessments.

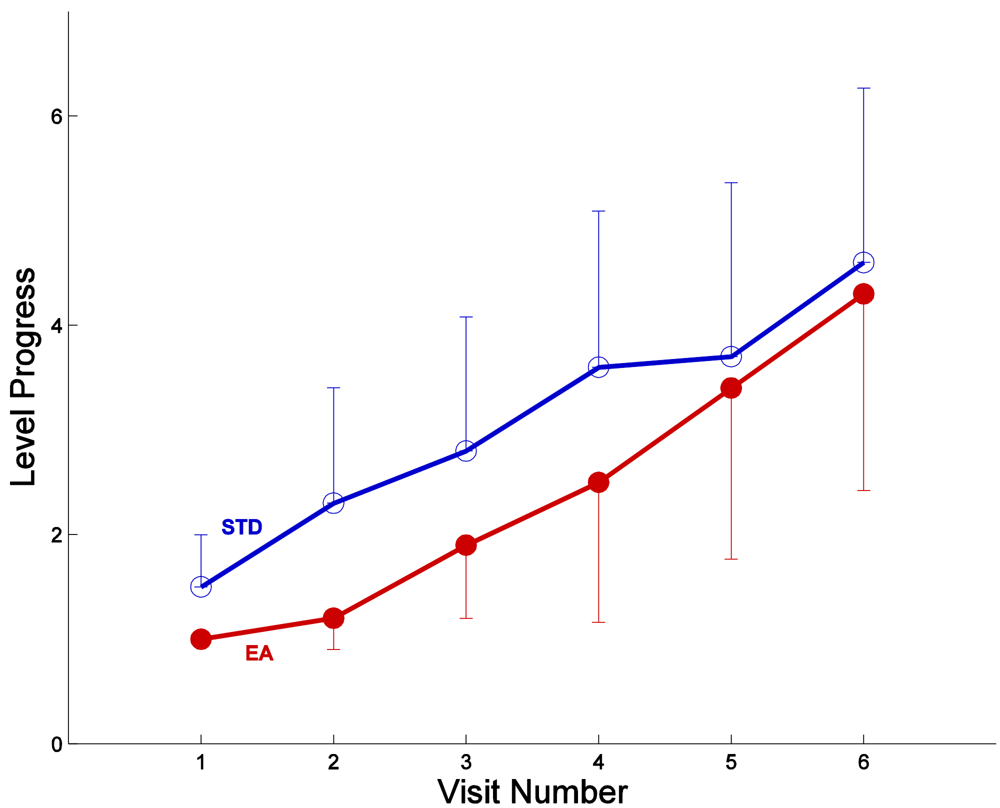

Figure 19- Progression through difficulty levels. Each point represents the average of the highest level for each visit to the lab. EA treatment (red) and standard treatment (blue)

Perceived value and enjoyment of the overall experience was evident in the IMI questionnaire results. The highest scores were associated with questions such as, "I would be willing to do this again because it had some value to me." Generally, all results were more in agreement with the positive questions and more in disagreement with negative questions (Figure 20). The lowest scores were reported in questions related to the perceived competence sub-scale, such as "I think I did pretty well at this activity, compared to others." The groups of IMI questions were averaged and then compared to the overall clinical outcome scores, but the series of 24 pair-wise correlations revealed no significant relationships higher than R^2=0.52.

6.4 Discussion

This blinded, randomized study revealed a benefit of arm recovery and functional use in the proposed self-rehabilitation system. The AMFM, WMFT FAS score, MAL Quantity and Quality scores showed significant improvements in the three-week period. While this study does not firmly establish a difference between EA and standard treatments, it does shed light on a family of future methodologies for improving motor function after stroke.

While AMFM and WMFT FAS score effect sizes were modest and could be considered not quite clinically meaningful (de NAP Shelton, Volpe, et al., 2001). We further argue that such gains might grow in longer treatment courses since in contrast to this study, typical robotic interventions include a training duration of at least six weeks or more (Lum, Burgar, et al., 2002; Stein, Krebs, et al., 2004; Volpe, Lynch, et al., 2008; Molier, Prange, et al., 2011). For example, constraint-induced movement therapy utilized six hours of daily training in two-week periods (Miltner, Bauder, et al., 1999; Taub, 2000; Wolf, Winstein, et al., 2006); others included 2 to 3 hours of training (Dromerick, Lang, et al., 2009). However, participants reported improvements in function such as increased use of the involved extremity in daily life and improved self-care independence, which was captured by , both MAL Quantity and Quality scores reaching the clinically important difference level (Uswatte, Taub, et al., 2006). Finally the level progress as presented in Figure 19, shows that participants expanded their range of motion while coordinating the movement of both arms which translated into functional recovery outside of the system.

This study contradicts with our previous study that revealed a benefit to error augmentation in a therapist-guided practice paradigm. However, the benefit of EA was mostly captured after the week of no treatment, demonstrated by significant changes from post treatment to follow-up evaluations (Figure 18). Such difference might be due to the fatigue built upon practicing with EA, which would go away in the week of no treatment allowing the participants to show their movement abilities when they come back for the follow-up evaluation. Another possible explanation of this difference could be that in the previous study EA was applied relative to an external cue while in the present study EA is relative to participant's other arm. This internal relationship may cause a conflict and therefore confusion in the nervous system that resulted in the poor performance right after the end of treatment. However, as mentioned above this phenomenon vanished in course of a week and participants showed significant gains from their post treatment evaluations. Hence, our work here joins other mounting evidence supporting error augmentation benefits in recovery (Brewer, Klatky, et al., 2005; Patton, Kovic, et al., 2006), but also pointing to the time effect of this treatment type.

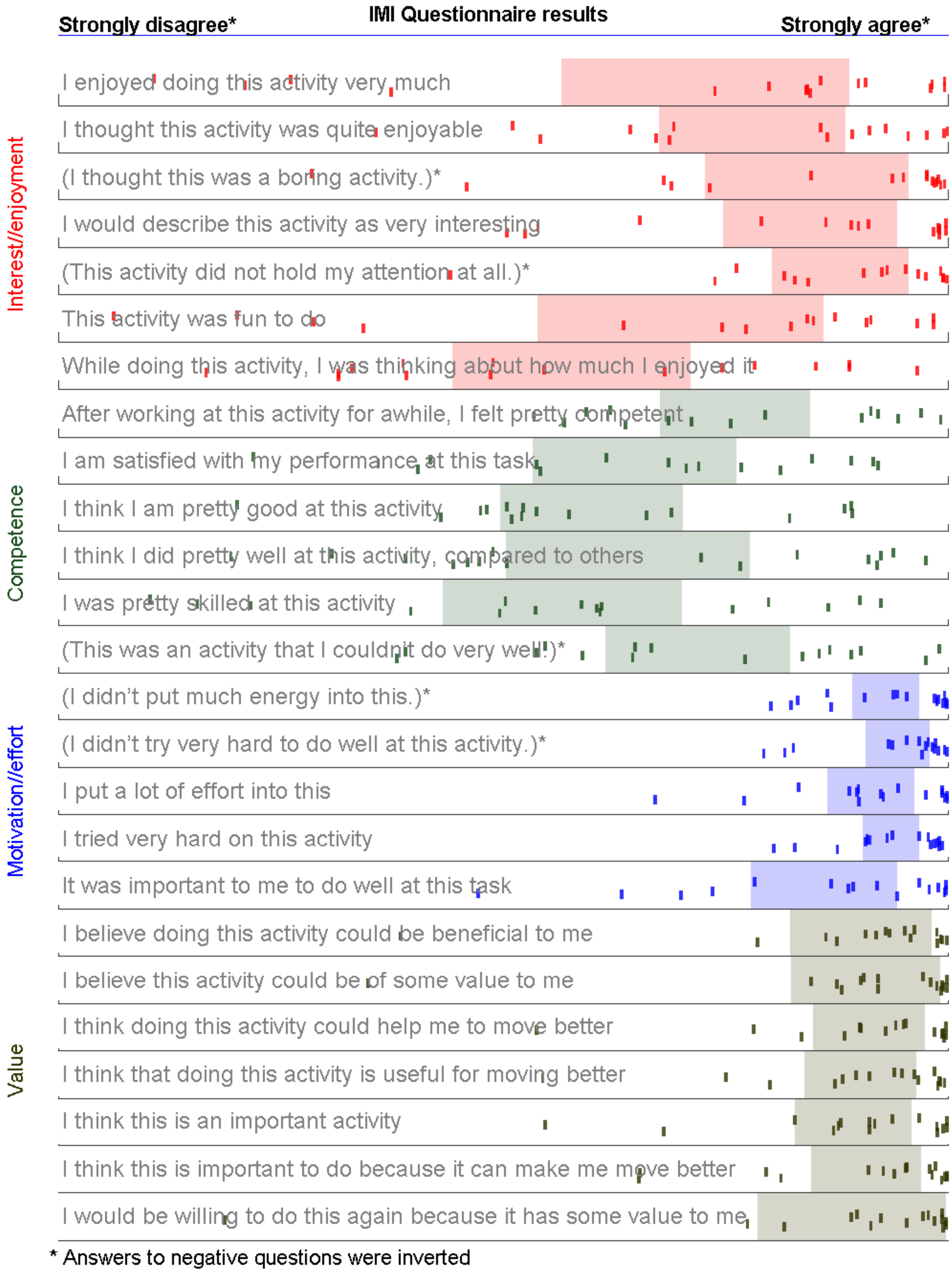

Figure 20- Intrinsic Motivation Inventory results, each tick mark shows response of a subject, different categories are shown in various colors

Interestingly, while the IMI did not reveal a positive experience in terms of enjoyment and competence, most participants found the nature of the intervention particularly valuable. Hence, they put a lot of effort in practice. There were no gaming elements or scores for success, and moving up through the levels was the only motivational mark for success. Nevertheless, many participants commented on how they would want to have access to such a system, and how they felt this type of practice has helped them become more aware of their affected arm capabilities. One participant, in particular, mentioned that practicing in the proposed self-therapy system enabled him to play basketball for the first time after the stroke incident.

This study provides practical clinical evidence that point to future self-rehabilitation studies that can improve arm motor recovery. The techniques associated with error augmentation may possible benefits in other strategies for rehabilitation, likely to be most effective if over longer courses of practice. In the search for optimal training methods, the evidence presented here points to possible future research that makes use of non-affected side to leverage self-training tendencies and possibly functional recovery.

6.5 Acknowledgments

We thank Felix Huang, Meghan Buell and Amit Shah, for their excellent technical and clinical assistance and advice on this project.

7 General discussion and future directions

This series of studies was dedicated to understanding the underlying mechanisms of a self-rehabilitation system for hemiparetic people after stroke. Results indicated that parallel bimanual reaching movement mode when receiving veridical feedback of arms was the least challenging mode for healthy individuals. In addition simultaneous bimanual movements proved to enhance both arms' performances when dealing with a discoordination. While error augmentation found to be most beneficial in recovery of the affected arm when combined with therapist-guided practice, when the result of the first three studies were combined to make a bimanual reaching task, equivocal results were observed in comparing error augmentation to standard treatment. Nevertheless, the self-therapy system showed significant functional benefits for the affected arm regardless of the treatment type. There are a number of unanswered questions that might represent further directions that this line of research can take, as will be described in this chapter.

7.1 Extended duration

7.1.1 Clinical study dosage

In the present thesis, both clinical studies (chapter 3 and chapter 6) were performed with minimum dosage. In the literature, the dosage varies from six hours daily training over two-week periods in constraint-induced movement therapy to others including shorter daily training hours but over 6-8 week periods. It is difficult in current service delivery models to provide the intensity of practice that appears to be needed to effect neural reorganization and functional changes poststroke. Computerized exercise systems may be a way to maximize both the patients' and the clinicians' time. The data in this study add support to the proposal to explore novel technologies for incorporation into current practice (Merians, Poizner, et al., 2006). Because error augmentation showed significant improvements during just two weeks of treatment, larger, more clinically meaningful effect sizes might be obtained with higher treatment dosages or durations.

7.1.2 Retention in the healthy population

One issue not investigated in the studies on healthy individuals is the persistence of any learning effects. Both studies described in chapters 4 and 5 were performed in a single session. While due to the reported fatigue and loss of motivation, extending the session duration is not recommended, depending on the bimanual training application, multiple training sessions may be required to leverage retention. If any of the training techniques might be ultimately used for performance enhancements, the appropriate time for follow-up tests and the durability of learning should be evaluated in that particular application.

7.2 Better understanding of Error Augmentation

It is still not clear what underlying neurological mechanisms might be the reason individuals respond to error augmentation. Nor it is clear how error augmentation translates into functional recovery. It may be that the impaired nervous system reacts to more noticeable errors or that error augmentation simply heightens motivation and/or attention by simply intensifying the signal-to-noise ratio for sensory systems. Anyhow, this intervention had greatest impact on motor ability, and had diminishing effects on functional ability. It remains to be seen whether more functionally relevant tasks in the presence of EA and leveraging the error-based adaptive tendencies of the nervous system can lead to continued gains in functional scores.

7.3 Improving the virtual environment

Although the IMI revealed a positive experience overall, some participants did not find the repetitive nature of the intervention particularly engaging. Making the virtual environment more entertaining by adding more gaming elements, interaction possibilities, scores and audio for success may result in better performances. However, it remains to be seen whether more creative elements can be used to enhance the involvement of the participants' attention to optimize clinical outcomes, or whether such elements might serve as a distraction from rigorous deliberate practice (Ericsson, Krampe, et al., 1993).

7.4 Improving WREX

Although helpful in assisting arm posture, the WREX gravitational assistance device may restrict movement at extremes of the reachable workspace. Participants with less impairment may benefit from less inhibited reaching without this equipment. It remains to be seen whether an alternative approach could improve results with a clinical cutoff for supplementing with such assistive devices.

7.5 Understanding the underlying neurophysiological processes of bimanual movements

While in this work, we showed the differences between parallel and mirror modes of bimanual movement, as well as simultaneous versus sequential modes of movement. Our work was purely behavioral and it lacks in providing a full understanding of the underlying neurophysiologycal processes that led to the current findings. However, the results of these studies shed light on possibility of each bimanual task requiring its own level of information processing until a competent strategy is learned. With numerous possibilities of bimanual movement modes, including the ones mentioned above, there is a need for multiple well-controlled studies to expand the understanding of such neurophysiological processes. And, it remains to be seen whether the observed error levels reflect physiological limits in sensorimotor pathways or simply a different "tolerance" for error in each feedback condition.

7.6 Testing other modes of self-therapy

We chose to build our self-therapy paradigm over the most intuitive modes found in healthy individuals. However, it is possible that this intuitiveness may not be equally intuitive for brain injured individuals. Or, the most intuitive task might not be the most appropriate mode of self-therapy and additional challenges such as the one showed in reaching to one target in a mirror mode would be more beneficial to this population. Although, the initial findings presented here in healthy subjects can help identify environments for rehabilitation or in any training situation requiring bimanual practice, it remains to be seen whether the other modes of bimanual movement would translate to a more effective neurorehabilitation method.

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APPENDIX

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

Approval Notice
Continuing Review

May 15, 2013

Farnaz Abdollahi, MS
Bioengineering
1120 SEO Bldg., M/C 152
Chicago, IL 60612
Phone: (773) 524-7571

RE: Protocol # 2010-0209
"Error Enhanced Learning and Recovery in 2 and 3 Dimensions"

Dear Dr. Abdollahi:

Please note that this research did not have Institutional Review Board (IRB) approval from midnight March 30, 2013 until May 9, 2013.

It appears that all of the subjects have been recruited and consented but testing continues in multiple sessions. Please note, "IF" you intend to recruit <u>new</u> subjects, please submit an amendment, which must be reviewed and approved by the IRB prior to new enrollment.

Your Continuing Review was reviewed and approved by Members of IRB #2 by the Expedited review process on May 9, 2013. You may now continue your research.

Please note the following information about your approved research protocol:
<u>Protocol Approval Period:</u> May 9, 2013 - May 9, 2014
<u>Approved Subject Enrollment #:</u> 80 (87 subjects enrolled; enrollment closed)
<u>Additional Determinations for Research Involving Minors:</u> These determinations have not been made for this study since it has not been approved for enrollment of minors.

Performance Sites: UIC, Northwestern University-Rehabilitation Institute of Chicago
Sponsor: Department of Education, Rehabilitation Services Administration
PAF#: - 2008-03564
Grant/Contract No: NIDRR H133E0700
Grant/Contract Title: Error Enhanced Learning and Recovery in 2 and 3 Dimensions
Research Protocol(s):

a) Error Enhanced Learning and Recovery in 2 and 3 Dimensions; Version #4; 10/12/2011

Recruitment Material(s): N/A – Closed to enrollment
Informed Consent(s): N/A – Closed to enrollment

Your research continues to meet the criteria for expedited review as defined in 45 CFR 46.110(b)(1) under the following specific categories:

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving X-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including but not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
04/30/2013	Continuing Review	Expedited	05/09/2013	Approved

Please remember to:

→ Use your **research protocol number** (2010-0209) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the enclosure,
"UIC Investigator Responsibilities, Protection of Human Research Subjects"
(http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf)

Please note that the UIC IRB has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact OPRS at (312) 996-1711 or me at (312) 355-2939. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,

Jewell Hamilton, MSW
IRB Coordinator, IRB # 2
Office for the Protection of Research Subjects

Enclosure(s): None

cc: Thomas Royston, Bioengineering, M/C 063
Robert Kenyon, Faculty Sponsor, Computer Science, M/C 152
OVCR Administration, M/C 672

VITA

NAME: Farnaz Abdollahi

EDUCATION: B.S., Biomedical Engineering, Amirkabir University of Technology, Tehran, Iran, 2005

M.S., Biomedical Engineering, University of Tehran, Tehran, Iran, 2006

PROFESSIONAL EXPERIENCE:

Assitant Direcor of Research and Operations (*May 2013 - present*)
Chicago Electrical Trauma Research Institute (Chicago, IL)

Research Assistant (*September 2008 - May 2013*)
Rehabilitation Institute of Chicago (Chicago, IL)

Doctoral Intern (*June - August 2008*)
Procter and Gamble Company (Cincinnati, OH)

Teaching Assistant (*August 2006 - May 2010*)
University of Illinois at Chicago (Chicago, IL)

Undergraduate Intern & Co-op (*June - December 2004*)
Imam Center for Scientific Research and Medical Technology (Iran)

PUBLICATIONS:

Abdollahi F, Case ED, Listenberger M, Kenyon RV, Kovic M, Bogey RA, Hedeker DR, Jovanovic BD, Patton JL. Error augmentation enhancing arm recovery in individuals with chronic hemiparetic stroke: a randomized crossover design. *J Neurorehabil Neural Repair.* In press.

Abdollahi F, Kenyon RV, Patton JL. Mirror versus parallel bimanual reaching. *J Neuroengineering and Rehabilitation*. In press.

Abdollahi F, Rozario SV, Case E, Listenberger M, Kovic M, Kenyon RV, Patton JL. Arm control recovery enhanced by error augmentation. *IEEE Int. Conf. Rehabilitation Robotics*. Zurich, Switzerland, June 29 - July 1, 2011

Abdollahi F, Setarehdan SK, Nasrabadi AM. Locating information maximization time in EEG signals recorded during mental tasks. *Proc. 5th Int. Symp. on Image and Signal Processing and Analysis*. pp. 238 - 241, Istanbul, Turkey, September, 2007

Abdollahi F, Setarehdan SK, Nasrabadi AM. A time pattern for information content of EEG signals recorded during BCI mental tasks. *7th Iranian Conference on Fuzzy Systems and 8th Conference on Intelligent Systems*. Mashhad, Iran, August 29 - 31, 2007

Abdollahi F, Nasrabadi AM. Combination of frequency bands in EEG for feature reduction in mental task classification. *Annu. Int. Conf IEEE Eng Med Biol Soc*. pp. 1146 - 1149, New York, USA, August, 2006

ABSTRACTS:

Abdollahi F, Kenyon RV, Patton JL. Simultaneous rather than sequential training is superior when learning bimanual drawing task. IEEE EMBC, Osaka, Japan, July 3 - 7, 2013

Fisher M*, **Abdollahi F***, Morehead JR, Bixby K. Effect of baseline variability in motor learning: Meta-analysis over multiple data sets. Translational and Computational Motor Control, New Orleans, USA, October 12, 2012

Abdollahi F, Kenyon RV, Patton JL. Interactive bimanual training modes: mirror vs. parallel. Society of Neuroscience, Wahington DC, USA, November 12 - 16, 2011

Abdollahi F, Rozario SV, Case E, Listenberger M, Kovic M, Kenyon RV, Patton JL. A clinical test of haptic/graphic error augmentation shows benefits over repetitive practice in stroke therapy. Society of Neuroscience, Wahington DC, USA, November 12 - 16, 2011

Abdollahi F, Kenyon RV. Speed perception and Leibowitz hypothesis. Biomedical Engineering Society, St. Louis, USA, October 1 - 4, 2008

THESES:

Abdollahi F. Locating information maximization time in EEG signals recorded during mental tasks for a use in BCI systems, for the completion of Master of Science at University of Tehran, 2006

Abdollahi F. Combination of frequency bands in EEG for feature reduction in mental task classification, For the completion of Bachelor of Science at University of Tehran, 2005

AWARDS & HONORS:

Recipient; Chancellor's graduate multi-disciplinary research fellowship, 2012 and 2013

Recipient; Graduate student presenter award, 2011 and 2012

Recipient; Graduate student council travel award, 2011

Recipient; Board of trustees' tuition and fee waiver for academic years 2006-13 at University of Illinois at Chicago

Recipient; Scholarship for outstanding GPA and academic excellence for academic years 2001-05 at Amirkabir University of Technology

PROFESSIONAL MEMBERSHIPS:

IEEE student member
EMBS student member
Biomedical Engineering Society student member
Society of Neuroscience student member
Women in Science and Engineering member
IEEE Robotics and Automation Society Student Reviewer Program
Member of Wellgates Honor Roll

PROFESSIONAL AFFILIATIONS:

IEEE International Conference on Rehabilitation Robotics scientific committee member and article reviewer

IEEE International Conference on Engineering in Medicine and Biology Conference article reviewer

IEEE BioRob Conference article reviewer