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# Error-augmented bimanual therapy for stroke survivors

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**Abstract**.
**BACKGROUND:** Stroke recovery studies have shown the efficacy of bimanual training on upper limb functional recovery and others have shown the efficacy of feedback technology that augments error.
**OBJECTIVE:** In a double-blinded randomized controlled study (N = 26), we evaluated the short-term effects of bilateral arm training to foster functional recovery of a hemiparetic arm, with half of our subjects unknowingly also receiving error augmentation (where errors were visually and haptically enhanced by a robot).
**METHODS:** Twenty-six individuals with chronic stroke were randomly assigned to practice an equivalent amount of bimanual reaching either with or without error augmentation. Participants were instructed to coordinate both arms while reaching to two targets (one for each arm) in three 45-minute treatments per week for two weeks, with a follow-up visit after one week without treatment.
**RESULTS:** Subjects' 2-week gains in Fugl-Meyer score averaged 2.92, and we also observed improvements Wolf Motor Functional Ability Scale average 0.21, and Motor Activity Log of 0.58 for quantity and 0.63 for quality of life scores. The extra benefit of error augmentation over the three weeks became apparent in Fugl-Meyer score only after removing an outlier from consideration.
**CONCLUSIONS:** This modest advantage of error augmentation was detectable over a short interval encouraging further research in interactive self-rehabilitation systems that can enhance error motor recovery.

Keywords: Stroke, upper extremity, self-rehabilitation, robotics rehabilitation, bimanual coordination, error augmentation

## 1. Introduction

Despite the existing evidence of possible recovery long after the onset of stroke (Taub et al., 1999), regaining functional use of the upper extremity has been an ongoing challenge (McCombe Waller & Whitall, 2008). Emerging interventions including intensive repetitive practice (Wolf et al., 2008, Han et al., 2013), task-specific training (Dean & Shepherd, 1997, Lang et al., 2009), and interactive robotic technology (Lum et al., 2002, Volpe et al., 2005, Sanchez et al., 2006) all aim to restore upper extremity motor ability and function. Although many of these studies focus on isolated limb actions, patients also care about completing the functional task with proper coordination of *both* arms (Rose & 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 the affected limb (Mudie & Matyas, 2000, Whitall et al., 2000, Cauraugh & Kim, 2002, Hesse et al., 2003, McCombe Waller & Whitall, 2004). Others have stated that

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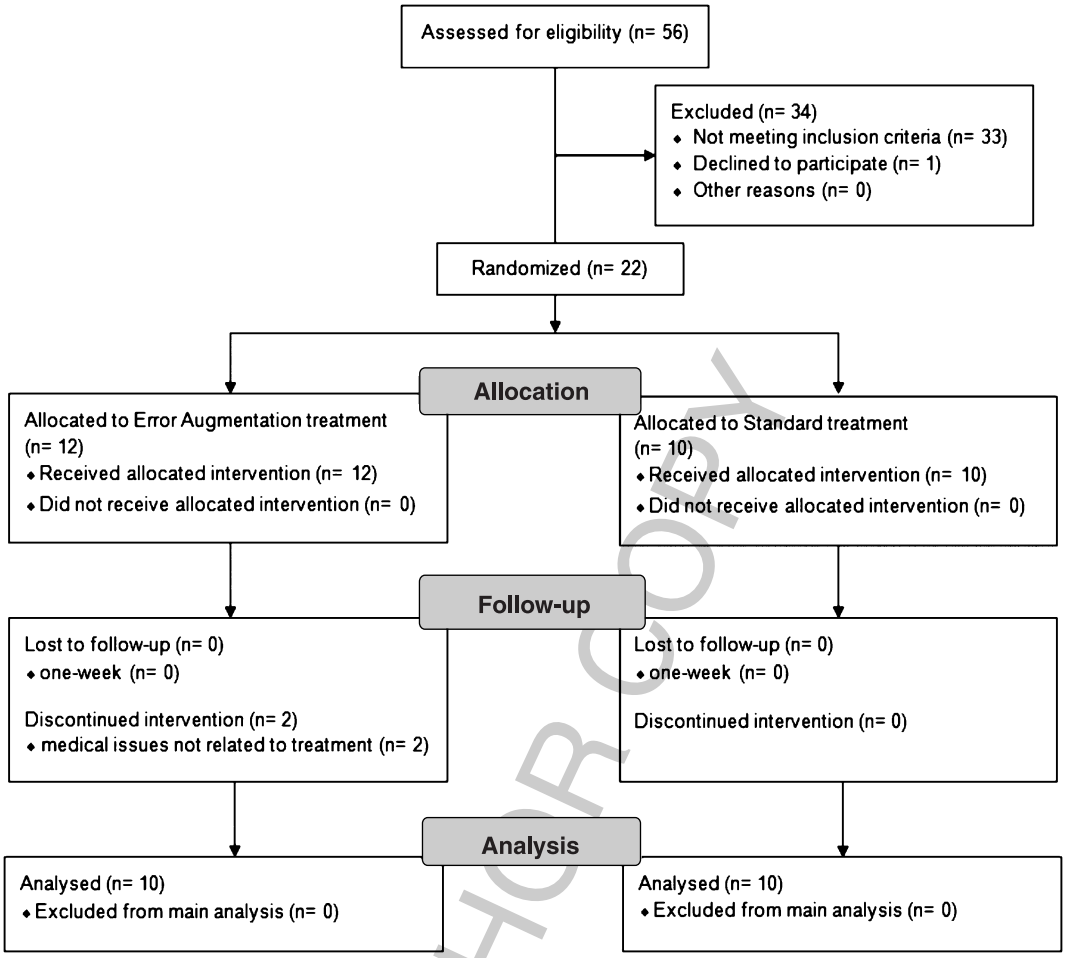


Fig. 1. Participant recruitment flow diagram, based on followed the CONSORT protocols.



bimanual training engages additional cortical areas of the brain (Sadato et al., 1997, Donchin et al., 1998). An advantage of bimanual therapy is the possibility for additional "solo" training to occur after the one-on-one therapy has been exhausted. 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 that the effectiveness of bimanual training has not been fully understood so it can be incorporated more regularly in therapy practice is that it is a broad topic with many considerations. In fact, there are many opportunities for different modes of operation 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 compared to reaching in a mirror mode (Abdollahi et al., 2013). Our group has also investigated one potential advantage of simple simultaneous bimanual motion over practicing sequentially, where 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 the 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 & Mussa-Ivaldi, 2004). In simple terms, if one perceives a 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 (Kawato, 1990, Desmurget et al., 1997), which leverages the natural adaptive nature of the nervous system (Patton et al., 2006c).

While the mechanisms for these improvements are not yet known, our group has employed the principle of error augmentation in collaborative therapist-patient-machine trio (Abdollahi et al., 2014). In this blinded randomized controlled study, the therapist used a tracking device to provide a movement cue to hemiparetic patients following stroke. An interactive robot system visually and haptically magnified their errors in real time, without the patient's knowledge. Error augmentation demonstrated significant advantages over the sham group without error augmentation. An obvious question arising from this is, whether variations on this approach might also be effective.

Here, we seek to determine whether similar results might be possible if the tracking cues come from the patient's own contralateral, less-affected arm, allowing for self-rehabilitation with error augmentation. Hence, we investigate benefit of a self-telerehabilitation variation of this approach, again testing the effect of error augmentation. Specifically, we hypothesized that patients would receive added benefits from error augmentation. The study was structured so that a comparison could be made with our prior study that included the therapist.

## 2. Methods

### 2.1. Participants

Twenty-six adults with chronic stroke agreed to participate in this double-blind randomized controlled study (8 Female, age range 26–77, mean age 53.86). Study participants were recruited from a registry of post-stroke individuals or who responded to local flyer postings. Both the Northwestern University and University of Illinois at Chicago Institutional Review Boards approved this study. All participants provided informed consent according to the Declaration of Helsinki prior to commencing the study. We followed the *CONSORT* clinical trial guidelines for our recruitment, and this project was registered on *clinicaltrials.gov* (ID# NCT01574495). Twenty-eight individuals began the study, with twenty-six individuals completing all phases of the study. Two participants dropped out due to medical reasons unrelated to the study and were excluded from analysis

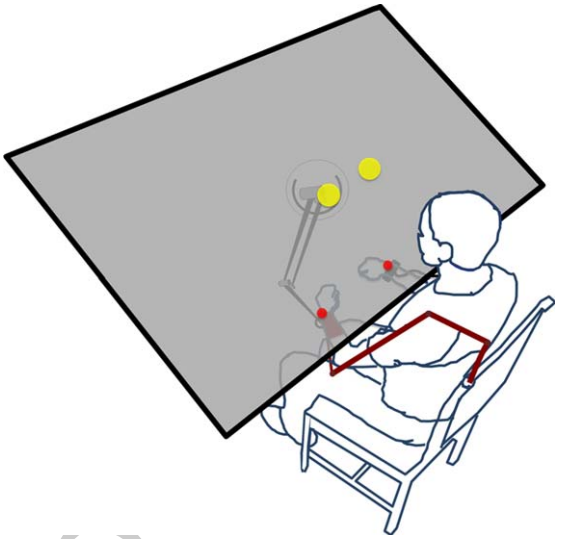

Fig. 2. Experimental setup; Robot handle is attached to participant's affected hand and a position tracker is attached to the other arm. Two red cursors each represent one of the participant's hands position, and the target pairs are shown in yellow.

(Fig. 1). Eligible participants were all adults aged 18 or over and had suffered a single hemispheric stroke at least six months prior to enrollment. Participation also required some recovery of proximal strength in the hemiparetic limb as confirmed by an upper extremity Fugl-Meyer score of 25–50. Participants were excluded if there was 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 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 if the patient had severe aphasia, affective dysfunction, or hemisensory neglect that would influence the ability to perform the experiment or provide informed consent. Participants were also excluded if they were currently receiving any other skilled upper extremity rehabilitation in a clinical setting. Table 1 displays participants' demographics and lesion characteristics.

### 2.2. Study setting

The study used a three-dimensional haptic/graphic system called the Virtual Reality Robotic and Optical Operations Machine (VRROOM) (Patton et al., 2006b). A cinema-quality digital projector

Table 1

| 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 |
| 223 | F | 78 | 51 | Left | Right | Ischemic | Subcortical |
| 224 | F | 51 | 56 | Left | Right | Hemorrhagic | Subcortical |
| 225 | M | 64 | 71 | Left | Left | Ischemic | Subcortical, Brain Stem |
| 226 | M | 46 | 11 | Left | Left | Ischemic | Cortical |
| 227 | F | 54 | 23 | Left | Left | Ischemic | Subcortical |
| 228 | M | 65 | 20 | Left | Right | Ischemic | Cortical |

F, female; M, male.



(Christie Mirage 3000 DLP) displays stereo images that span a five-foot-wide $1280 \times 1024$ pixel display, resulting in a $110^\circ$ wide viewing angle in a see-through augmented reality display. In this study, vision of the arms was occluded so that only the moving cursors (representing wrist locations) and targets were shown. Infra-red emitters synchronized separate left and right eye images through StereoGraphics liquid crystal shutter glasses. Two Ascension Flock of Birds sensors were used, one to track head motion for appropriate display of visual perspective, and another 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 (Fig. 2). A Wilmington Robotic Exoskeleton (WREX) provided anti-gravity arm support (Rahman et al., 2000).

### 2.3. Experimental protocol

A computer-generated list allocated each participant to one of the two groups, matching them on baseline Fugl-Meyer scores collected during the initial screenings. We tested visual and haptic error augmentation (EA) using two experimental groups (*EA* and *non-EA*) treatment. Each had the same amount of practice in two weeks of training with three, 45-minute sessions per week (six sessions total). The robot was also attached to the non-EA group, exerting zero force, to provide a sham that blinded participants to what treatment they were receiving. After a week of rest, each participant went through a follow-up evaluation.

For all participants, each session began with five minutes to position the participant in the apparatus, then six 5-minute blocks of training with two-minutes of rest between each block (Fig. 3). The blocks alternated, and were either bimanual targeted-reaching or free bimanual practice. Targeted reaching blocks involved attempts to reach from a location above the centers of the thighs out both to one of 4 target sets, and then stop for at least a half-second. The system allowed 3 seconds to make this motion, at which point the system cued a return to the starting point and

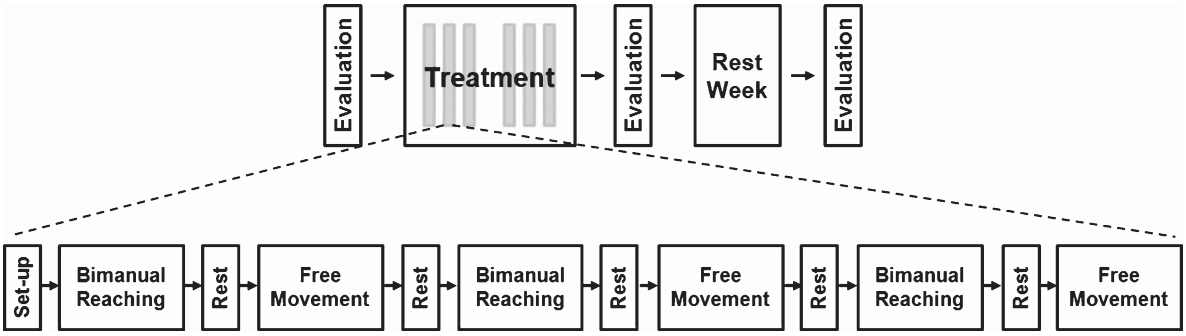


Fig. 3. Study (top), session layout (bottom).

proceeded to the next motion. The targets were spaced evenly in the reaching workspace and were also meant to probe the patient's range of motion. If subjects successfully attained more than 70% of the targets on any block, the targets were moved 20% more distant.

The free movement blocks were meant to address participants' self-tailored ideas of therapy, which included the possibility of choosing the previous standardized five-minute block for practice. This allowed the participants to partially customize their own therapy, focusing on their perceived deficits. Quantitative assessments were performed at the beginning and end of the treatment (pre- and post-) as well as one week after the post-treatment assessment (follow-up).

During all sessions, participants were seated in a chair with the hemiparetic arm supported by the WREX$^{TM}$ gravity-balanced orthosis. One cursor displayed the movement of left hand, another cursor displayed the right. The hemiparetic hand was placed in an exotendon glove that assisted with a functional hand and wrist position. Since holding an instrument handle is not necessarily the same as free-hand motion (Cothros et al., 2006), we connected the robot near the wrist joint center to allow the hand to open freely as well as allow free pronation and supination of the forearm. Both the PHANTOM$^{TM}$ robot and the position tracker were attached to the affected and non-affected forearms respectively, with the center of the devices located above the radiocarpal joint.

The error augmenting treatment involved subtle, haptic error-augmenting forces were applied by the robot during the EA treatment but not in non-EA treatment. 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, 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 a maximum of 4 Newtons.

### 2.4. Evaluation procedure

Participants were evaluated outside the VRROOM with the clinical measures immediately prior to the 2-week treatment phase and again at the end of the treatment phase. 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 et al., 2005, Wagner et al., 2008) as well as our secondary outcome measures, which included the Wolf Motor Function Test (WMFT) for functional ability (Wolf et al., 2001, Fritz et al., 2009), Motor Activity Log (MAL) for quality and quantity of arm use in activities of daily living (van der Lee et al., 1999, Uswatte et al., 2006) and the Box and Blocks assessment as an indicator of manual dexterity (Platz et al., 2005, Chen et al., 2009). Finally, to assess perception of the experience, participants completed the Intrinsic Motivation Inventory (IMI) questionnaire (McAuley et al., 1989), which consists of 25 questions in four categories (interest/enjoyment, perceived competence, motivation/effort, and perceived value).

### 2.5. Statistical analysis

To examine for treatment-related change, outcomes were analyzed using a repeated measures analysis of variance (ANOVA), with factors of time (pre, post, follow-up) and treatment type (EA vs. Non-EA). We included the one-week post treatment

evaluated to allow for any effects of fatigue to vanish as well as to determine the retention of benefits over time. Finally, Tukey *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.

## 3. Results

Our main outcome measure, upper extremity Fugl Meyer (AMFM, Fig. 4A), showed significant average gain of $2.92 \pm 4.84$ (mean change $\pm$ standard deviation) for all participants over the three weeks from pre-treatment to one-week follow-up evaluations ($F(1,24) = 9.35$, $p = 0.005$). We found no significance comparing the groups. However, one participant in our control group had an anomalously large gain of 19 points over the three weeks, which was deemed an outlier using the outlier-labeling rule (Hoaglin et al., 1986). We performed a secondary analysis removing this participant's data that resulted in a reduction in the average of this group (Fig. 4A, light blue line). The other data from this subject, did not however affect any of the secondary measures discussed below (Fig. 4 B, C and D). Importantly, when this outlier participant was removed from consideration, the EA group showed a significant advantage, with an average gain of $3.69 \pm 3.66$ ($F(1,23) = 4.72$, $p = 0.040$). Most of this improvement occurred over the final one-week period without therapy ($2.85 \pm 3.34$). It is important to mention that if we simply inspected gains from pre-treatment to the final day of treatment (rather than to the 1-week follow-up post training), we would have failed to detect a significant difference between groups, indicating that EA participants needed this final week after therapy was over to achieve their gains.

We found some similar results in our secondary measures. Although variable, the Wolf Functional Ability Scale (WMFT FAS) improved significantly for all participants with an average of $0.21 \pm 0.31$ points over three weeks ($F(1,24) = 11.70$, $p = 0.002$). However, we failed to detect a significant difference between the EA treatment group and the controls (Fig. 4B). Similar trends were also seen in the Motor Activity Log's (MAL) Quantity measure (Fig. 4C) indicating an increase in affected arm use, with all participants improving $0.58 \pm 0.53$ points over the three weeks ($F(1,24) = 29.80$, $p < 0.001$), but again without a significant difference between EA treatment group and controls. The EA treatment group improved more than controls over the follow-up week ($F(1,24) = 6.90$, $p = 0.015$). A similar trend was also seen in the MAL Quality measure (Fig. 4D), which measures quality of affected arm use, where all participants improved $0.63 \pm 0.55$ over three weeks ($F(1,24) = 32.89$, $p < 0.001$). However, we failed to detect a significant advantage of EA treatment over controls. We also found no significant advantage of EA treatment over controls in the remaining measures: WMFT-Time and Box and Blocks, and increases in range of motion during targeted reaching.

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 (Fig. 5). 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 $R^2 = 0.58$.

Finally, we were unable to determine whether our groups could detect whether subjects knew the error augmentation treatment was turned on or off. Both groups failed to have responses that were statistically different from chance to the exit question, "was the robot pushing during your treatment or not?" This is attributable to the treatment intensities programmed to be quite smooth and subtle.

## 4. Discussion

This blinded, randomized study revealed benefits in reaching ability and functional arm use for bimanual therapy. The AMFM, WMFT FAS score, MAL Quantity and Quality scores all showed significant improvements across this two-week intervention, measured one-week post treatment. These results establish modest but important preliminary clinical evidence of the benefits of error-augmentation, over and above repetitive practice alone. This sheds light on this error-augmentation family of rehabilitation methodologies for improving motor function.

While AMFM and WMFT FAS scores effect size were modest and not clinically meaningful (de NAP

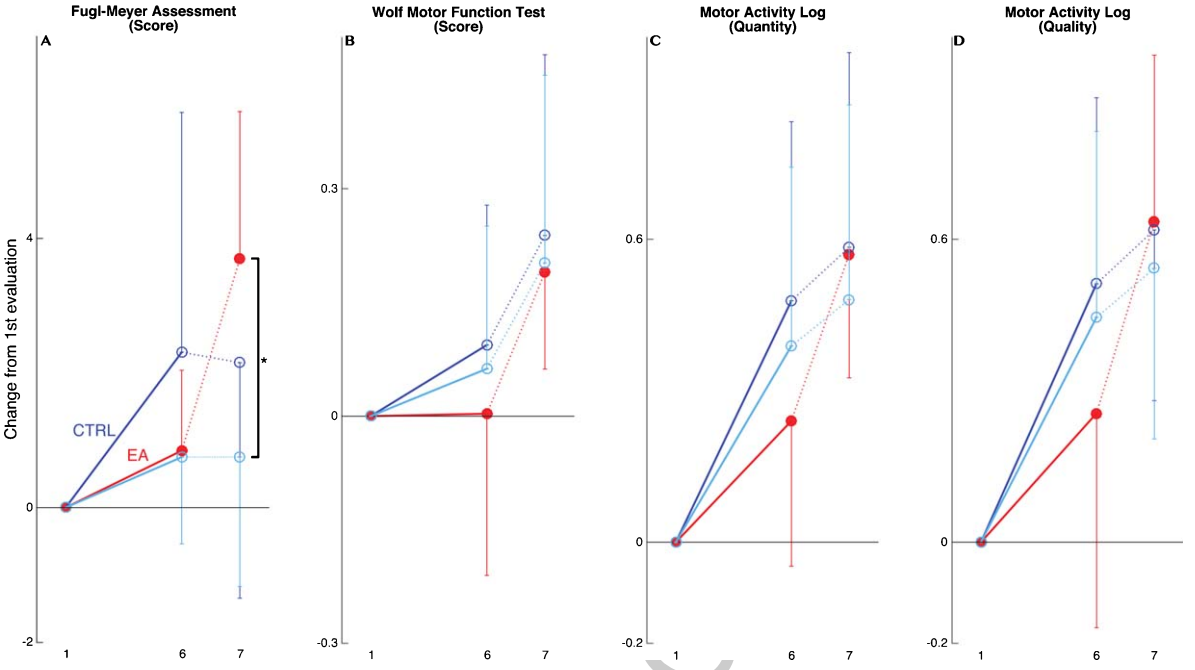


Fig. 4. Clinical score changes from the first visit, AMFM score (A), WMFT score (B), MAL quantity (C) and MAL quality (D). Solid line shows the EA treatment (red), the non-EA treatment (dark blue) and the non-EA treatment without the outlier data (light blue) and dashed lines are the periods without treatment.

Shelton et al., 2001), such gains could potentially continue to a level of clinical significance over a longer treatment course. This study did not seek to treat for a full course typically six weeks or more (Lum et al., 2002, Stein et al., 2004, Volpe et al., 2008, Molier et al., 2011). One constraint-induced movement therapy study utilized six hours of daily training in two-week periods (Miltner et al., 1999, Taub, 2000, Wolf et al., 2006); others included 2 to 3 hours of training (Dromerick et al., 2009). Nonetheless, 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 levels of clinically important change (Uswatte et al., 2006).

This study failed to find the magnitude of advantages in the EA applied in our previous study (Abdollahi et al., 2014). However, removing one outlier from the non-EA treatment group resulted in similar trends. Interestingly, this participant was only six months post stroke, and may have been exhibiting the larger improvements normally associated with sub-acute recovery. Furthermore, the benefit of EA was observed after the week without treatment (post treatment to follow-up evaluations; Fig. 4). This difference might be a result of excessive fatigue after the EA treatment, which could vanish in the week without treatment allowing the participants to show their movement abilities upon follow-up evaluation. Although subjects did not report any signs of fatigue, we know that robotic forces were present only in the EA treatment, raising the possibility for more effort required by this group. 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 the participant's other arm. This internal relationship may cause a conflict between arm controllers 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 during a week without treatment 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 et al., 2005, Patton et al., 2006a), but also points to the time effect of this treatment type.

One reason why these findings were not quite as strong as the previous study may be that self-telerehabilitation may not be as effective. The expertise, guidance, and social interaction of a

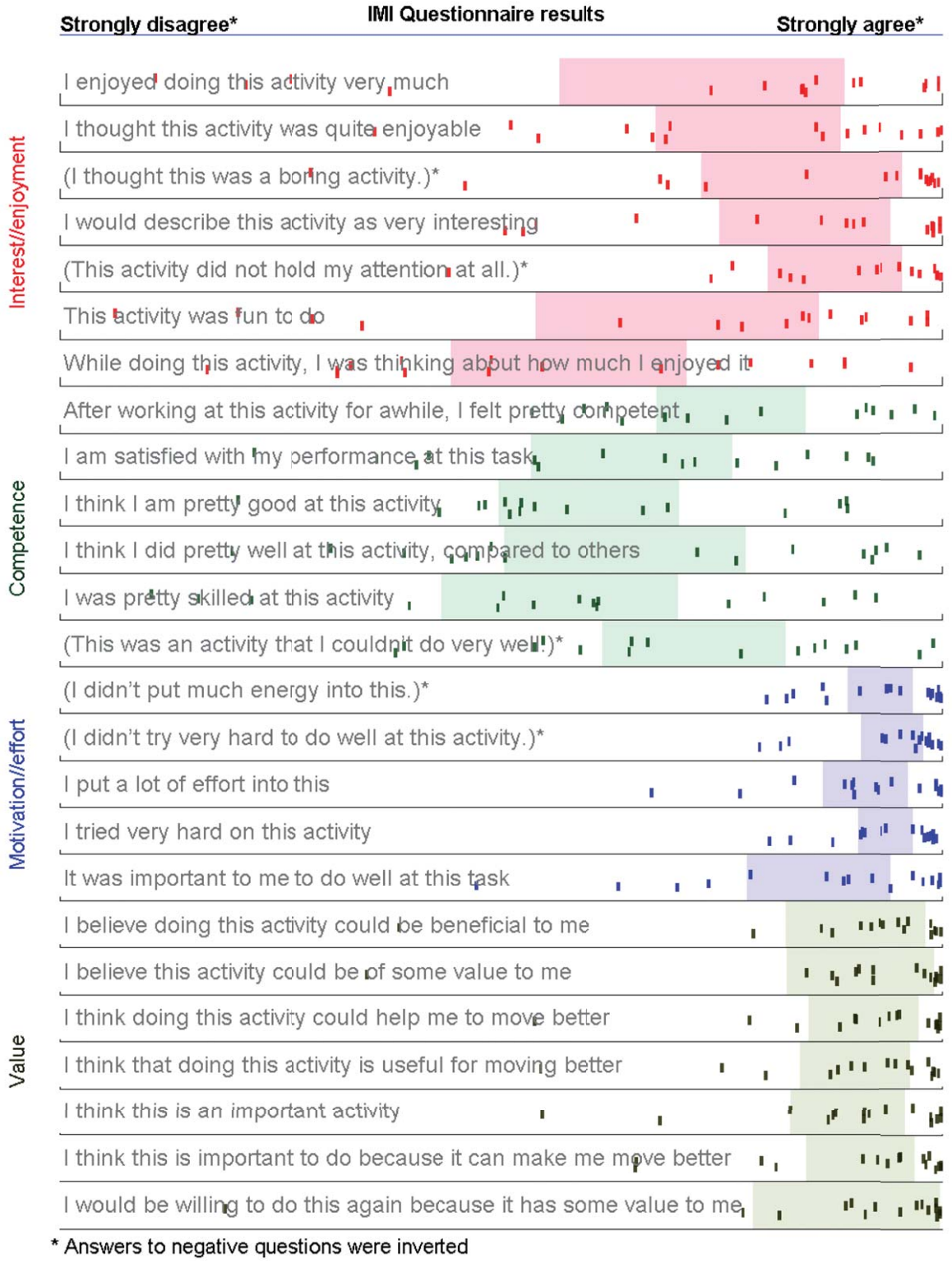


Fig. 5. Intrinsic Motivation Inventory results, each tick mark shows response of a subject, different categories are shown in various colors.

therapist is not present. A patient may not know how to focus certain aspects of their therapeutic practice and tailor their therapy to subtle needs. An extra observer monitoring and commenting may lead to enhanced performance. Patients may not always stay on task, and attention and engagement may not be as high as when not working with a therapist. It remains to be seen whether these different aspects might play decisive roles in how therapy might happen. A very practical hybrid session might be one where the patient spends time with the therapist when available, and then works with the machine in self-telerehabilitation mode for a remainder of the patient's available time.

Interestingly, while the intrinsic motivation inventory (IMI) questions revealed only a mildly positive view of the experience in terms of enjoyment and competence, most participants found the nature of the intervention particularly valuable and made substantial efforts in practice. There were no gaming elements or scores for success, but moving up through levels may have been a source of motivation. Nevertheless, many participants commented on how they would want to have access to such a system, and that they felt this type of practice has helped them become more aware of their affected arm capabilities. One participant mentioned that practicing in the proposed self-therapy system enabled him to coordinate his arms well enough to play basketball for the first time after his stroke.

This approach appears to offer several novel and beneficial aspects for therapy. First, by allowing the patient to choose their training, the system fully encourages the patient to be an active agent. There is mounting evidence that patients do not improve if technology does the work (Dobkin, 2004, Hidler et al., 2009, Marchal-Crespo & Reinkensmeyer, 2009). Importantly, these tools favorably alter the mechanics while still allowing patients the ability to make their own choices, preserving their agency in the process. Second, the system used very subtle and undetectable treatment (e.g., forces less than a pound), allowing us to keep this study blinded. We found no evidence that patients were not able to accurately report if the robot was pushing or not. Third, the system operated over the full motion range of the arm, allowing individuals to move uninhibited to the edges of their workspace if able. Finally, the system provided a stimulating augmented reality with stereo vision that challenged the patient.

This study provides practical evidence that points to future self-rehabilitation studies which can possibly improve arm motor recovery. One may envision this method as an upper-extremity version of treadmill training, where the subject is in command and can train independently after receiving some coaching from a therapist. Such methods may eventually become a form of "homework" as such technology becomes more accessible, lightweight, and inexpensive. Furthermore, the benefits associated with error augmentation may become clearer for larger dosages and longer durations of practice. In the search for optimal training methods, the evidence presented here informs the design of new clinical hardware and software for neurorehabilitation.



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## Conflict of interest

None to report.

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