

Clinical Trial of HEXORR II for Robotic Hand Movement Therapy After Stroke

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Abstract

Background

Impaired use of the hand in functional tasks remains difficult to overcome in many individuals after a stroke. This often leads to compensation strategies using the less-affected limb, which allows for independence in some aspects of daily activities. However, recovery of hand function remains an important therapeutic goal of many individuals, and is often resistant to conventional therapies. In prior work, we developed HEXORR I, a robotic device that allows practice of finger and thumb movements with robotic assistance. In this study, we describe modifications to the device, now called HEXORR II, and a clinical trial in individuals with chronic stroke.

Methods

Fifteen individuals with a diagnosis of chronic stroke were randomized to 12 or 24 sessions of robotic therapy. The sessions involved playing several video games using thumb and finger movement. The robot applied assistance to extension movement that was adapted based on task performance. Clinical and motion capture evaluations were performed before and after training and again at a 6 month followup.

Results

Fourteen individuals completed the protocol. Fugl-Meyer scores improved significantly over the 3 time points, indicating reductions in upper extremity impairment. Flexor hypertonia (Ashworth) also decreased significantly due to the intervention. Motion capture found increased finger range of motion and extension ability when the arm was supported by gravity. However, extension ability did not improve significantly during a reach and grasp task, and there was no change in a functional measure (Action Research Arm Test). At the followup, the high dose group had significant gains in hand displacement during a forward reach task. There were no other significant differences between groups.

Conclusions

Future work with HEXORR II should focus on integrating it with functional task practice and incorporating grip and squeezing tasks.

Trial registration: CLINICALTRIALS.GOV, NCT04536987. Registered 3 September 2020 - Retrospectively registered, <https://clinicaltrials.gov/ct2/show/record/NCT04536987>

Introduction

There are 795,000 new strokes in the U.S. each year, and there are currently 7.2 million adult Americans living with stroke.¹ The associated costs are 40.1 billion annually. After the acute and subacute recovery phases, individuals with stroke move into the chronic phase (> 6 months post) where they often need continued rehabilitation, on-going care and emotional support.² There's increasing evidence that rehabilitation in this chronic phase can impact quality of life.³ In many cases, individuals regain skills and return to independent living. However, many do not receive the appropriate amount of rehabilitation therapies needed to maximize recovery due to constraints of the current health care system related to rehabilitation services.⁴

In the upper extremity, reaching and grasping movements are often impaired and a focus of rehabilitation.^{5,6} At 3 months post stroke, hand impairments are the most commonly reported impairment after stroke.⁷ Typical impairments are hypertonia (increased passive resistance to movement), inability to activate extensors, and abnormal co-contraction of flexors.⁸ Interjoint coordination and modulation of activation patterns can also be impaired.⁹ Hand rehabilitation remains very difficult as control of many joints and muscle groups are required to produce a coordinated grasp. Movement therapies include stretching to reduce flexor hypertonia and prevent contractures, and practice of grasp and release tasks in different arm postures. However, repetitive practice of grasping tasks is difficult and frustrating for patients with moderate-severe impairments. Technologies, such as robotics, provide assistance via forces applied to the limb that may facilitate more effective practice, allowing completion of movements that would otherwise be impossible. A large body of work now exists in the area of robotic therapy. A recent meta-analysis of 45 studies including 1619 individuals with stroke, reported robotic therapy improved Activities of Daily Living (ADL) ability, function and muscle strength; however it's unclear what fraction of individuals will achieve long-term clinically meaningful gains.¹⁰

Hand therapy robots can be divided into devices designed to be worn and used as part of ADL or devices that focus on hand movement isolated from the proximal arm. Each approach has advantages and disadvantages. Wearable devices can be used during whole upper extremity tasks, such as reach and grasp tasks, and can take the form of active¹¹⁻¹⁸ or passive exoskeletons.¹⁹⁻²² However, because of space and weight constraints in wearable devices, movement kinematics and control algorithms can often be more precise and sophisticated with desktop devices that isolate finger movements, but don't allow use of the hand with objects or in conjunction with proximal arm joints.²³⁻³⁰ Many hand robots are still in the proof-of-concept prototyping phase and have not gone through clinical testing. However, the devices that have been tested clinically are showing promising results. For example, the X-Glove is a portable device with 5 linear actuators that independently extend the digits³¹. A clinical trial using the X-Glove in subacute stroke showed significant gains in clinical scales of impairment and function after 15 treatment sessions of 30 min of passive stretching followed by active-assisted, task-oriented training. Another clinical trial from this group in chronic stroke with the VAEDA glove using voice and EMG-control showed advantages in functional scales compared with control therapy without the glove.³² Amadeo (Tyromotion, Austria) is a tabletop hand robot that provides independent motion of all five fingertips along linear paths. A pilot clinical trial using Amadeo in chronic stroke showed significant gains in several clinical scales.³³ A more recent controlled clinical trial in chronic stroke showed greater gains after Amadeo training than dose-matched conventional therapy, along with normalizing some aspects of interhemispheric connectivity after robot training.³⁴ The Hand-of-Hope is an EMG-controlled exoskeleton with linkages that couple joints within each digit, decreasing the number of needed actuators. Clinical trials with this robot have shown significant impairment reductions and functional gains in chronic stroke subjects.^{35,36} The FINGER robot provides assistance to the index and middle fingers as the subject plays a video game that simulates playing a guitar. A clinical trial reported significant gains in several clinical scales, with authors noting that subjects with impaired proprioception benefited less from the training.³⁷

Previously, our lab developed a Hand Exoskeleton Rehabilitation Robot (HEXORR I)³⁸ to retrain hand control and function. HEXORR I is a tabletop device that allows practice of finger and thumb movement integrated with video games. Compared to other hand robots, HEXORR I is unique in the use of a tone-compensation algorithm that measures the resistance to passive extension movement and applies extension assistance to counter this

resistance.³⁹ An additional novelty is the auto-adaptation algorithm that alters the shape and magnitude of the assistance profile to achieve a desired target performance level. In theory with this approach, the patient still has control of initiation, maintenance and termination of movement, but does not have to overcome the resistance from increased flexor tone during extension movement. In an initial pilot study, nine chronic stroke subjects showed significant improvements after 18 treatment sessions in range of motion, grip strength, and the hand component of the Fugl-Meyer score after HEXORR I use.⁴⁰ Since then, HEXORR II was developed, which includes several hardware design changes to improve the performance of the robot, reduce the setup time and make the training sessions more engaging by implementation of a larger repertoire of games. In this study, we describe HEXORR II and report the results of a clinical trial that tested for a dosage effect from the robotic therapy.

Methods

Study Design

All testing protocols were approved by the MedStar Health Research Institute human subjects institutional review board and all subjects provided written consent. The inclusion criteria were: 1) a diagnosis of stroke more than 6 months prior to randomization; 2) presence of voluntary hand activity indicated by a score of at least 1 on the finger mass extension/grasp release item of the Fugl-Meyer Test of Motor Function⁴¹; 3) adequate cognitive status, as determined by Mini-Mental Status Examination⁴² score > 24. Subjects were excluded if they: 1) were under the influence of antispasticity medications during the study; 2) had MCP and IP passive extension limit > 30 degrees from full extension; 3) had pain that interfered with daily activities; 4) had excessive tone in the fingers and thumb as determined by Ashworth⁴³ scores > = 3; 5) had severe sensory loss or hemispatial neglect as determined by a neurological clinical exam.

Each subject was randomized to either 12 or 24 training sessions of 1.5 hours each. In each session, the subjects received robotic therapy supervised by a technician. The subjects also completed pre-training, a post-training, and 6 month follow-up evaluation sessions involving clinical scales and biomechanical motion capture.

Hand Exoskeleton Rehabilitation Robot (HEXORR II) (2nd Generation)

HEXORR II maintains the basic functionality of the first generation device^{38,40}, but the mechanism has been completely redesigned to improve usability and performance. A single motor (Maxon RE40, GP42C 26/1, 4.4 N m peak continuous torque) aligned with the MCP of the fingers, assists synchronous movement of the 4 fingers (Fig. 1). The motor drives a chain and gear mechanism that moves 3 bars that apply forces to the palmar surfaces of the fingers in 3 locations, helping to keep the fingers in natural postures during flexion and extension movements. The bars extend into a single plane for full extension, and collapse into a small space for full flexion. The thumb is controlled by a second motor (Maxon RE32, GP32C 33/1, 3.2 N m peak continuous torque) aligned with the thumb CMC. This motor drives a mechanism that rotates two pads that are strapped to the distal and proximal phalange of the thumb. Movement is about the IP and CMC joints in a single plane that can be adjusted for comfort. The forearm is strapped onto a horizontal surface that also restricts motion of the wrist. In this newer version of the device, there was a marked reduction in the time required to position and strap the hand. Also the moving inertia and friction of the robot was reduced compared to the prior version, allowing more natural

movement trajectories and less resistance to free movement. A Matlab Simulink program (xPCtarget, Stateflow) controlled the motors and provided feedback during training.

Training Protocol

For the first session, the hand is placed in HEXORR II and 3 slow passive stretches of the fingers are performed. The movement is constant velocity and very slow (10 deg/s). We retained the motor torque applied during these stretches as the starting point for the torque vs. angle extension assistance profiles provided during training. The subjects then spent the rest of the session playing several different types of games, while assisted by the robot.

The primary therapy mode game was the Gate Game (Fig. 2), designed to train active finger and thumb extension. It required the subject to extend and flex the fingers and thumb to guide two balls through two openings in a gate that sweeps across the screen. If the digits were not opened in time to pass the balls through the gate, the digits were moved by the robot to full extension, before the next flexion movement was prompted. An adaptation algorithm was implemented where the target performance was achievement of 2 of 3 consecutive gates. If 2 of 3 gates were successfully completed, the assistance profile was kept unchanged. If the performance was below this level, the assistance was increased by 0.1 N m over the range from the peak extension angle achieved in the prior 3 trials to full extension. If the performance was perfect over 3 trials, the assistance profile was scaled down by a 10%. The experimenter could change the adaptation rate by increasing or decreasing the increments in assistance via a GUI control panel. This adaptation strategy allowed for the shape of the torque vs. angle profile to evolve as well as the overall amplitude.⁴⁰ Subjects performed 3 blocks of 30 gates in each session.

The remainder of the 90 min session was spent playing secondary video games (Fig. 3). The subject could select from 4 different PC games, which were played by moving the thumb and fingers in HEXORR II with assistance. These games included three PC commercial games and one custom designed game. All these games had scoring systems and offered easy ways to set the game difficulty and to track individual's performance. All of the games were normally controlled by mouse movement. Interface electronics (Arduino) received input of finger and thumb angles from the Matlab robot controller (RS232 communication protocol) and mouse emulator code on the Arduino controlled the PC mouse position on the computer screen through the USB port of the PC. For games that required a mouse click, a push button was controlled by the unaffected hand and provided input to one of the Arduino digital ports and integrated into the mouse control. In this way, no modification of the commercially available PC games was needed and an array of games could be integrated into the training. The most up to date assistance profile was used in this mode, but was not automatically adapted as in the Gate Game. Games included Angry Birds, Bubble Shooter, Shopping and Ping-Pong. Studies show gamification of upper limb stroke therapy increases compliance and motivation.⁴⁴⁻⁴⁶

Evaluation Sessions

Each evaluation session consisted of clinical measures and biomechanical measures. The clinical measures included the Action Research Arm Test (ARAT)⁴⁷ for grasp, grip, pinch, and gross arm movement; the Fugl-Meyer (FM) for motor impairment; the Modified Ashworth scale for hypertonia at the fingers, wrist and elbow; the Motor Activity Log (MAL)⁴⁸ to assess use of the impaired limb in ADL. For analysis, the Ashworth-flexors score was calculated by averaging across the flexor muscles and the Ashworth-extensors score was calculated by averaging across the extensor muscle groups. The MAL amount of use score was retained for statistical analysis. A Jamar dynamometer (JAMAR 5030J1 Hand Dynamometer) was used to measure grip strength at each time point.

For the biomechanical measures, subjects were seated in front of a table at a standardized position and 4 tasks were performed. The tasks were: 1) full digit flexion/extension: straightening the fingers as much as possible from a closed fist position, with the hand in a pronated position at midline and the forearm supported against gravity; 2) thumb opposition: touching the thumb to the tip of the 5th digit, to test for thumb abduction range of motion; 3) grasp a water bottle placed lateral to a standard starting point at midline and bring to mouth to drink; 4) pick up a small nut placed at midline and put it on the top of a shelf. Each task was done twice, and each trial was 40 sec. Metrics from each trial were averaged across the 2 trials of each task before statistical analysis.

The kinematics were measured using an electromagnetic tracker (MiniBirds®, Ascension Technologies). Sensors were taped to nail of the thumb, index, middle and ring fingers. Sensors are also taped to the dorsum of the hand and forearm. An additional sensor is taped to the C7 vertebrae. Using commercially available biomechanics software (MotionMonitor, Innsport Inc.), anatomical landmarks were digitized and segment coordinate frames calculated for the hand, forearm and trunk. Raw data were exported into a custom Matlab program that calculated several metrics. For the finger markers, the total flexion angle was calculated for the finger distal phalange relative to the hand segment. This represents the sum of flexion from all three joints of each digit. For the thumb, the abduction and flexion angles were both calculated. Standard Euler sequences were used for these calculations.⁴⁹ Finger extension deficit was calculated as the smallest flexion angle (largest extension angle) achieved during the trial, averaged across the 4 digits measured. Finger range of motion (ROM) was calculated as the difference between the largest and smallest flexion angle achieved, averaged across the 4 digits. Trunk ROM was determined by first calculating the farthest movement of the trunk coordinate frame relative to the starting point at the beginning of the trial, in each of 3 directions (forward, lateral and vertical). A global measure of trunk ROM was calculated by combining ROM in these 3 directions using the Euclidean norm. Hand displacement (due to proximal arm movement during the reaching tasks) was calculated similarly, except trunk movement in each direction was subtracted from hand movement first, so that the hand displacement metric was associated with arm movement only.

Data Analysis

For each outcome, a repeated measures ANOVA was used with between subjects factor of dose (12 sessions or 24 sessions) and within subjects factor of time point (pre, post, followup). Significant time point effects were followed with paired t-tests to detect changes from pre to post, and from pre to followup.

Results

Fifteen subjects were enrolled in this study and 1 subject withdrew due to non-compliance with the training schedule. The remaining 14 subjects were randomized to the 12 session dosage (7 subjects) or the 24 session dosage (7 subjects). The mean age was 62.3 (11.7) years, and the mean time since stroke was 28.7 (18.7) months. Seven males and 7 females completed the study, and the right limb was more affected in 8 subjects. At baseline, the mean Fugl-Meyer score was 34 ± 12 , and the mean ARAT score was 19 ± 17 . The two dosage groups were not significantly different at baseline in the FM, ARAT or Ashworth scores ($p > 0.14$)

Table 1 reports the statistical analysis of the clinical outcome measures. Fugl-Meyer scores increased over the 3 time points and RM-ANOVA reported a significant time factor ($p = 0.045$). At the 6 month followup, the FM had increased 2.9 points relative to baseline ($p = 0.033$). The Ashworth scores for flexors declined over the 3 timepoints and RM-ANOVA reported this was significant ($p = 0.001$). Compared to baseline, Ashworth scores for

flexors declined by 0.46 points at the 6 month followup ($p = .005$). Significant score changes are shown in Fig. 4. There were no significant changes over time for the MAL, ARAT, Ashworth-extensors or grip strength. The group and group*time factors were not significant for any of the clinical measures.

Table 1
Summary of clinical outcome data: mean(sd)

	Pre		Post		Followup		Group	Time	Time*group
	Mean	SD	Mean	SD	Mean	SD	P value	P value	P value
Fugl-Meyer	33.9	(11.8)	34.7	(10.5)	36.8	(12.3)	0.165	0.045	0.546
ARAT	18.9	(17.4)	19.0	(15.8)	19.3	(16.1)	0.485	0.884	0.576
Motor Activity Log	1.54	(1.38)	1.63	(1.30)	1.55	(1.21)	0.169	0.912	0.454
Ashworth-flexors	1.13	(0.78)	1.07	(0.73)	0.67	(0.57)	0.591	0.001	0.125
Ashworth-extensors	0.21	(0.26)	0.22	(0.27)	0.46	(0.76)	0.253	0.226	0.690
Grip Strength (lbs)	19.2	(15.4)	24.5	(22.4)	21.5	(15.6)	0.470	0.237	0.258

Table 2 reports the results of RM-ANOVA for the kinematic variables. For Task 1, closing and opening the hand with the forearm supported against gravity, RM-ANOVA reported that finger and thumb movements showed increased range of motion ($p = .028$) and finger extension ability ($p = .006$) over the 3 time points. Relative to baseline, finger extension increased (gain = 11.9 ± 18.3 deg, $p = .030$) immediately after training and at the 6 month followup (gain = 19.0 ± 15.7 deg, $p < .001$). Finger extension gains across all 14 subjects at the followup time point are shown in Fig. 5. Range of motion increased in parallel; the increase was significant at the post timepoint (gain = 12.7 ± 21.1 deg, $p = .042$) and at the 6 month followup (gain = 17.5 ± 21.3 deg, $p = .009$). In Task 3, where the subject must reach out and grasp a water bottle, finger extension deficit did decrease from pre-training (56.6 ± 40.2 deg) over the 3 time points to the followup (40.7 ± 32.4), but this improvement in finger extension did not reach statistical significance (time factor in RM-ANOVA, $p = .057$).

Table 2
Summary of biomechanics data: mean(sd)

Task	metric	Pre		Post		Followup		Group (p)	Time (p)	Time*group (p)
1	finger extension deficit (deg)	73.1	(53.9)	61.2	(53.5)	54.1	(52.2)	0.952	0.006	0.894
1	finger ROM (deg)	97.7	(55.4)	110.4	(56.7)	115.2	(63.2)	0.718	0.028	0.544
2	thumb abduction max (deg)	39.6	(16.2)	40.6	(9.8)	42.9	(16.8)	0.413	0.689	0.608
3	finger extension deficit (deg)	56.6	(40.2)	48.6	(33.6)	40.7	(32.4)	0.804	0.057	0.345
3	finger ROM (deg)	79.1	(38.7)	79.9	(20.7)	78.9	(32.9)	0.276	0.989	0.433
3	hand displacement max (cm)	30.3	(9.0)	33.3	(15.4)	28.9	(12.8)	0.261	0.358	0.618
3	trunk displacement max (cm)	16.6	(12.5)	13.9	(6.7)	13.7	(6.5)	0.926	0.466	0.433
4	hand displacement max (cm)	24.8	(16.0)	25.0	(14.9)	29.5	(15.2)	0.497	0.037	0.004
4	trunk displacement max (cm)	14.3	(7.8)	12.6	(4.4)	12.4	(5.5)	0.472	0.501	0.303

In Task 4, picking up a nut and placing on a high shelf, max hand displacement increased over time ($p = 0.037$) and also there was a group x time interaction ($p = 0.004$). This was due to no increase in the low-dose subjects ($p = 0.539$) and a significant increase in the high-dose group ($p = 0.005$). Compared to baseline, the high-dose group increased hand displacement by 11.8 ± 0.10 cm at the followup timepoint ($p = .020$). There were no other significant group, time or interaction factors found in the RM-ANOVA of kinematic variables (Table 2).

Discussion

HEXORR II therapy produced reductions in upper extremity impairments, as measured by significant gains in the Fugl-Meyer score. The largest changes were at the 6 month time point and included a significant reduction of flexor tone, increased finger ROM, and decreased finger extension deficit with the arm supported against gravity (Task 1). The improvement in finger extension is noteworthy, as we are aware of only one prior study of hand robotics that has reported an increase in extension range that was retained 6 months after the intervention.³² However, there were no changes on a measure of upper extremity function (ARAT). This was consistent with the kinematic analysis of a reach and grasp task (Task 3), which reported no changes in finger ROM and only a non-

significant trend of decreased finger extension deficit. No dosage effects were found, with the exception of increased hand displacement during the task requiring forward reach (Task 4) in the high-dose group, and no change in the low-dose group.

We observed significant long-term reductions in hypertonia at the followup, as measured by the Modified Ashworth Scale. To our knowledge, this is a novel result not previously reported for hand robotic devices. While the passive stretching performed at the beginning of each session was limited to only a few repetitions, we applied a stretch and hold movement immediately after each active extension attempt during the Gate game. The possibility of co-contraction of flexors during this stretch would have led to eccentric contraction of flexors, which may decrease in hypertonia following neurologic injury.⁵⁰ Studies with the X-Glove have shown that a 30 min period of cyclic passive stretching can transiently improve active motor performance in stroke patients, with effects carrying over across sessions in subacute stroke.⁵¹ Improvements in subacute stroke subjects were reported in measures of impairment and function following training that included 30 min of passive cyclic stretching followed by active-assisted, task practice.³¹ Authors attributed the passive stretching to facilitating the effectiveness of the active training and preventing any increases in spasticity. There is also some evidence that orthotic-based static stretching can decrease upper extremity spasticity, although there is no evidence this alone will improve motor performance.^{52,53} Thus, our results contribute to the evidence supporting further study into the use of robotics to integrate stretching protocols into active motor retraining.

One of the unique aspects of this study was the detailed biomechanical analysis that reported the kinematics of finger and arm movements under several conditions. Results support the use of HEXORR II in combination with practice of functional upper extremity tasks. The HEXORR II focuses on hand movement with the forearm and wrist immobilized and the arm supported against gravity. Hand movements in conjunction with proximal arm movements were not practiced, as is required for functional use of the upper extremity. This might explain the gains in an impairment scale (Fugl-Meyer), but no gains in a test of function that tests the ability to pick up and place objects (ARAT). There is strong evidence that control of the fingers degrades when proximal muscles must support the arm against gravity.⁵⁴⁻⁵⁶ These studies are consistent with our kinematic results, as finger extension did improve significantly when tested with the arm supported against gravity, but finger extension during reach and grasp tasks did not improve significantly. In the water bottle task, there were mean improvements in finger extension, but the time factor in the RM-ANOVA only approached significance ($p = .057$). Thus, it appears the training of distal hand control did produce gains in the training task, but did not generalize strongly to improved function in reach and grasp tasks. Two large multisite clinical trials of whole arm and hand robotic training also found similar results. The Armin was found to produce greater gains in the Fugl-Meyer scale than conventional therapy, but had no advantages in a motor function scale.⁵⁷ In the RATULS study, robotic therapy produced greater gains in the Fugl-Meyer compared to usual and customary care, but had no advantage on the ARAT.⁵⁸ In contrast, studies which combined robotic hand training with functional task practice have reported gains in functional scales. A recent study with Amadeo reported gains in the 9-hole Peg test, when subjects received the robotic training after a 3 hour session of physiotherapy that included 45 min of occupational therapy and 45 min of biomechanical training of upper and lower limbs.³⁴ Several other studies have used wearable hand robots (X-Glove³¹, VAEDA³², Hand-of-Hope^{35,36}, HandSOME⁵⁹) that enabled practice of reach, grasp and release tasks with robotic assistance to hand movement. All of these studies reporting significant gains on a variety of functional scales. Thus, functional gains with devices similar to HEXORR II that focus on distal control only, might be achieved by integrating practice of coordinated proximal and distal limb control, as is often done during

conventional therapy. Robotic and conventional therapies promote distinct patterns of motor recovery⁶⁰, and there is evidence from clinical trials that the addition of conventional task practice to robotic therapy is superior to robotic therapy alone.^{61–63}

Our results are generally consistent with prior studies of tabletop robots that train the fingers in isolation from the proximal arm. We found a 2.9 point change in the Fugl-Meyer at followup, while therapy using the FINGER robot reported gains of 1.8–3.7 at followup³⁷, and a study using the Amadeo robot reported a 5.1 Fugl-Meyer point change.³³ Our previous clinical study using HEXORR I also reported an increase in finger extension ability and significant gains in the Fugl-Meyer hand section subscore after 18 hours of training.⁴⁰ However our prior study also reported grip strength increases and significant gains in the ARAT in a subgroup of low tone subjects. Our current study did not find any changes in the ARAT or grip strength. This might be explained by fact that the prior HEXORR I training included a squeezing task that required generation of targeted isometric matching flexion forces from the fingers and thumb, followed by releasing of the grip within a certain time interval. This squeeze and release practice might have helped subjects improve in grip force and the ARAT, which involves grasping and releasing objects. We elected to drop the squeezing task from the current study to increase the number of repetitions focused on extension movement. The prior studies with the FINGER and Amadeo also reported gains in functional scales (ARAT, Box-and-Blocks, Jebsen Taylor Hand Function Test), while we did not see any improvement on functional scales in this study. One possible explanation is the low functional level of our subjects. Our mean intake Fugl-Meyer score was lower than these other two studies, and our intake ARAT scores were low (mean of 19/57 points), with 6 of our subjects having an intake ARAT of 6 points or less. In more severely impaired subjects, practice of grip or squeezing tasks might be important to include with finger extension training.

Gains were largest at the followup, with some metrics even showing no change immediately after training, but significant improvements at the 6 month time point (Fugl-Meyer, Ashworth, hand displacement). These improvements at the followup might have been due to more repetitions of hand and arm practice during the 6 month period between the end of training and the followup test. This practice during the followup period might have been more effective because of the improved finger control afforded by the training, or the subjects may have been encouraged to use the upper extremity more after noting the improvements in hand function during the training. The only significant between-group difference was an increase in hand displacement in the high dose group during a forward reaching task that appeared between post training and followup, which suggests practice of reaching tasks during this period. However, MAL scores did not indicate increased use of the more-affected arm within ADL tasks. Future studies may consider using objective methods to assess upper extremity activity as an outcome measure.⁶⁴ It is unlikely the gains during the followup period were due to encouragement or guidance from therapists, since the interaction with therapists was limited to the clinical evaluations and subjects were not given a home therapy plan during the followup period.

This study randomly assigned participants to either 12 sessions or 24 sessions. Based on RM-ANONA analysis, the group*time factors were not significant for our clinical outcomes measures (Fugl-Meyer and ARAT). A strong dosage effect has been difficult to show in interventions that rely on repetitive task practice. Lang et al. found no differences in functional gains in chronic stroke patients randomized to different levels of movement repetitions of task practice, even as the dosage ranged from 3200 to 10,808 repetitions.⁶⁵ The ICARE study in subacute stroke found no differences in functional gain between intensive task practice (28.3 hrs), conventional

occupational therapy (26.7 hrs) and usual and customary care (11.2 hrs of therapy).⁶⁶ Robotics has been touted as a means of increasing the number of movement repetitions per treatment session, however a large study of 770 stroke subjects did not find a significant difference between robotic therapy, repetitive task practice and usual care in terms of functional gains.⁵⁸ More study is needed to understand why a dosage effect is often not present in neuro-rehabilitation clinical trials of the upper extremity.

Limitations

This study has several limitations that should be noted. HEXORR II allows practice of isolated thumb movement, but the other 4 fingers are coupled together. Inability to isolate these 4 fingers may have limited the therapy's effectiveness to target weak fingers, since a weak finger can be carried along by the actions of the other 3. Another limitation was that the automatic adaptation algorithm only operated during the Gate Game, and not the secondary games, which were commercially available PC games chosen for their professional graphics and potential to entertain the subject. However, the downside of this approach is that the robot controller has no knowledge of current performance during the game, so automatic adaptation of assistance was not possible. At times, the subject would be unable to play the video game, and the experimenter would have to try and manually adjust the assistance level via a GUI menu. This trial and error process was not always successful, and detracted from the therapy. Future efforts using this approach should incorporate feedback of performance during all of the games, so the adaptation algorithm can operate during all of the training. The device currently is not portable, but getting into the device was straightforward and the potential for a home based portable device that can be used independently by patients seems possible if the overall size and footprint of the device can be reduced.

Conclusions

Overall, HEXORR II training reduced impairment levels, increased finger extension ability and decreased flexor hypertonia at the 6-month followup. The increased finger extension was achieved with the forearm supported against gravity, similar to the training task, but this did not translate to increased finger extension during a reach and grasp task. Future work with HEXORR II should focus on integrating it with functional task practice and incorporating grip and squeezing tasks. Notably, the easy setup and gaming interface make HEXORR II a potential home therapy device that could be used in conjunction with outpatient therapy, where they would receive functional upper extremity task practice.

Abbreviations

FM - Fugl-Meyer

ARAT - Action Research Arm Test

MAL – Motor Activity Log

ADL – Activities of Daily Living

ROM – range of motion

RM-ANOVA – repeated measures ANOVA

Declarations

Ethics approval and consent to participate

All testing protocols were approved by the MedStar Health Research Institute human subjects institutional review board and all subjects provided written consent.

Consent for publication

Not applicable

Availability of data and material

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JC assisted with the software development, data collection, interpretation of results and was a major contributor to writing the manuscript.

IB designed the mechanical aspects of the robotic device.

DN performed subject recruitment, data collection and assisted with interpretation of results.

TC assisted with the mechanical design, assembly of the device and data collection.

MS assisted with data collection and writing of the manuscript.

RC assisted with data collection and writing of the manuscript

PL conceived of the work, designed the clinical trial, assisted with the mechanical design of the robotic device, assisted with software development, performed data analysis, assisted with interpretation of results and was a major contributor to writing the manuscript.

All authors read and approved the final manuscript.

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Not applicable

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Figures

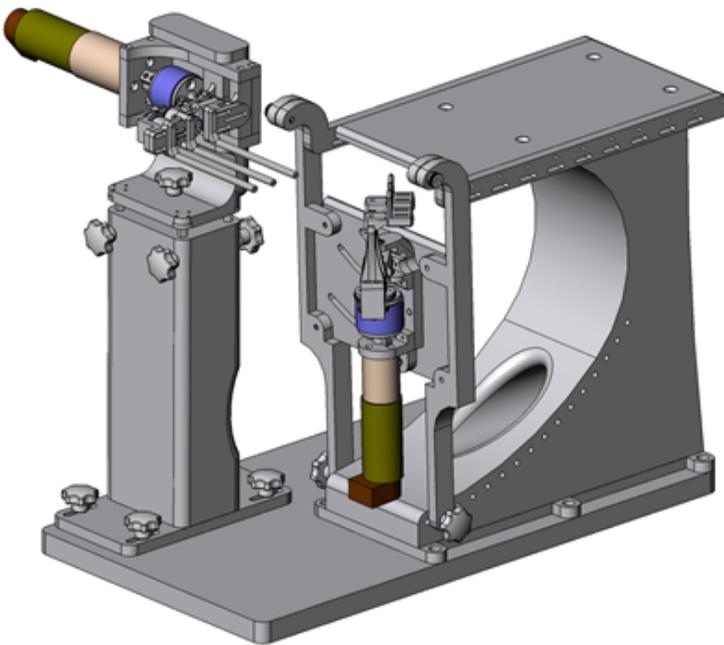
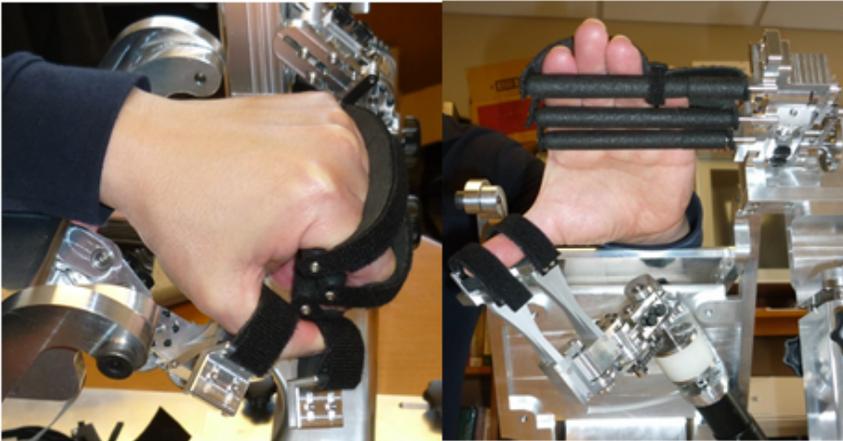


Figure 1

Pictures of the HEXORR II. The thumb flexion/extension plane can be adjusted by rotating the thumb actuator about 2 independent axes through the thumb CMC and locked in place.

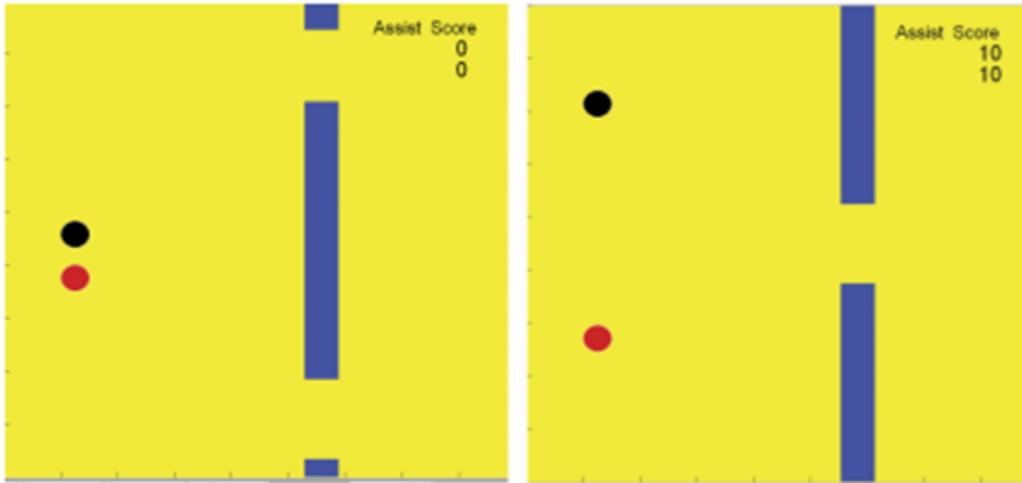


Figure 2

Graphical user interface for the Gate Game. The blue bar moves from right to left on the screen and subject moves the top ball and bottom ball with finger and thumb movement, respectively. The left shows an extension gate. The right shows a flexion gate. An automatic adaptation algorithm varied the assistance during extension movements.

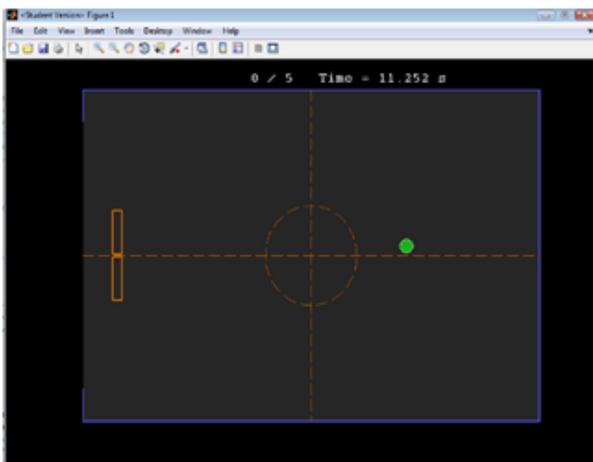
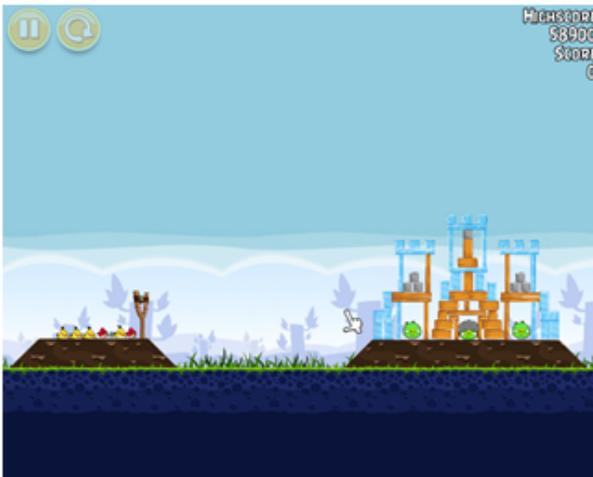


Figure 3

The secondary video games implemented were Angry Birds, Bubble Shooter, Pong and Shopping.

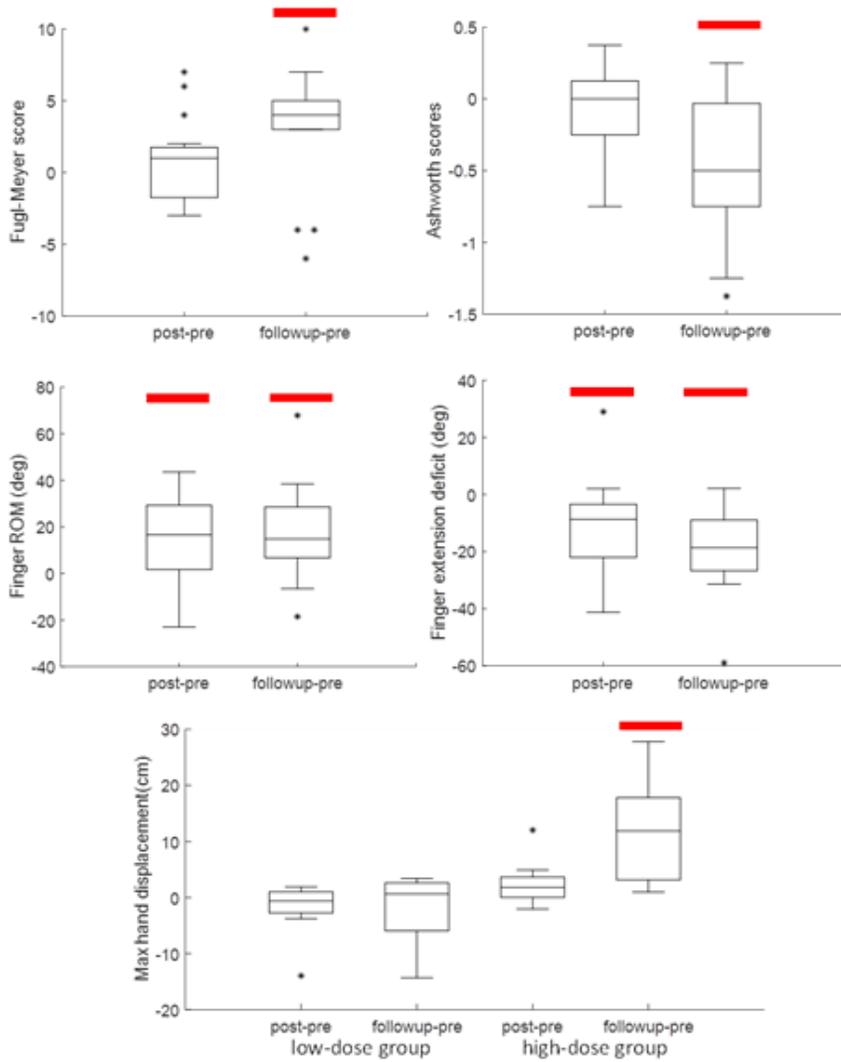


Figure 4

Boxplots of post-pre and followup-pre changes in outcome measures with a significant time factor in the RM-ANOVA. Significant changes are indicated by the red bar. Finger ROM and extension deficit are from Task 1. The max hand displacement is from Task 4 and is separated for the low-dose and high-dose group because of the significant time x group interaction in the RM-ANOVA.

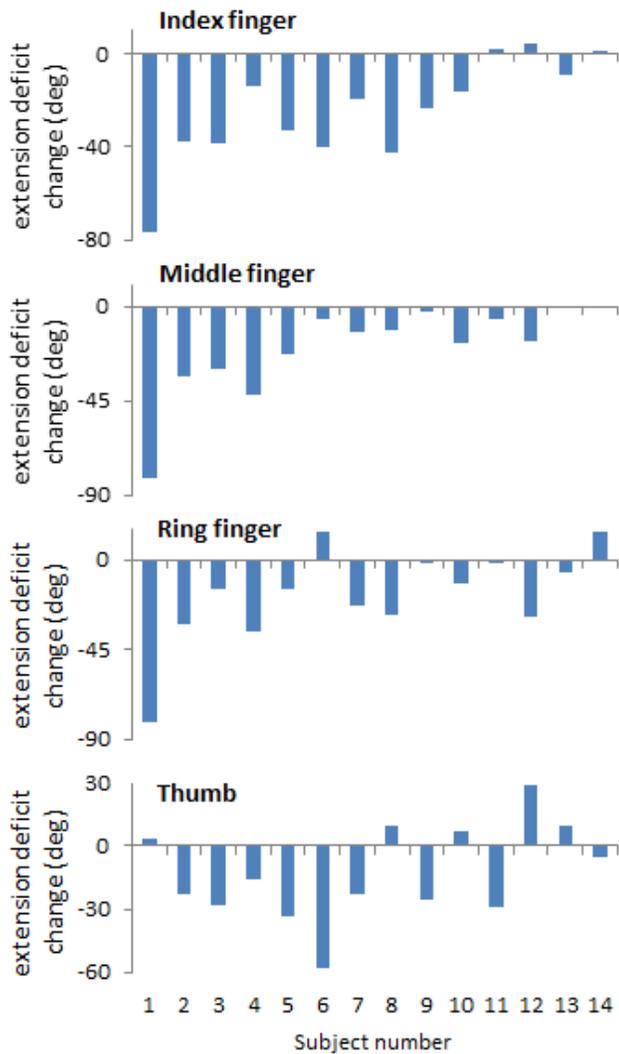


Figure 5

Decreased extension deficit at the follow-up time point compared to the pre-training time point measured during Task 1. The subjects are ordered from most positive change to least positive change when averaged across all 4 digits. Changes are strongly correlated across the Index, Middle and Ring fingers.

Supplementary Files

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