Sensorimotor Training in a Virtual Reality Environment: Does It Improve Functional Recovery Poststroke?

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Objective. To investigate the effectiveness of computerized virtual reality (VR) training of the hemiparetic hand of patients poststroke using a system that provides repetitive motor reeducation and skill reacquisition. *Methods.* Eight subjects in the chronic phase poststroke participated in a 3-week program using their hemiparetic hand in a series of interactive computer games for 13 days of training, weekend breaks, and pretests and posttests. Each subject trained for about 2 to 2.5 h per day. Outcome measures consisted of changes in the computerized measures of thumb and finger range of motion, thumb and finger velocity, fractionation (the ability to move fingers independently), thumb and finger strength, the Jebsen Test of Hand Function, and a Kinematic reach to grasp test. *Results.* Subjects as a group improved in fractionation of the fingers, thumb and finger range of motion, and thumb and finger speed, retaining those gains at the 1-week retention test. Transfer of these improvements was demonstrated through changes in the Jebsen Test of Hand Function and a decrease after the therapy in the overall time from hand peak velocity to the moment when an object was lifted from the table. *Conclusions.* 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.

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It is estimated that approximately 700,000 people sustain a stroke annually.[1] Because the effects of stroke are a leading cause of physical disability, there are a great variety of interventions aimed at enhancing recovery in the weakened limbs. At this time, existing physical and occupational therapy interventions are the foundation for treatment poststroke. However, studies examining these interventions have revealed inconsistent outcomes[2-4]; therefore, additional training paradigms are currently being explored. These newer training approaches are often guided by our recent understanding of the plasticity of the nervous system and the relationship of that plasticity to motor learning principles regarding frequency of use, skill development, and practice parameters. Many of these newer paradigms are taking advantage of technological advances such as the improvement in robotic design, the development of haptic interfaces, and the advent of human-machine interactions in virtual reality. These newer technologies are being investigated in an attempt to develop more effective strategies to ameliorate the physical disabilities resulting from stroke damage.[4,5]

Virtual environments are used to present complex multimodal sensory information to the user. In addition to the provision of visual-motor feedback, current haptic technology allows these virtual environments to provide force feedback that can simulate interactions with objects.[6,7] Haptic feedback refers to force and touch feedback provided to the user by the computer through specialized interfaces.[8] Force feedback gives cues on manipulated object weight, inertia, and hardness. Haptic interfaces allow users to touch, feel, and manipulate objects during virtual reality simulations and thus contribute to increased simulation realism.[7]

Virtual environments (VEs) or virtual reality (VR) (we are using the terms interchangeably) have a history of use in military training, entertainment simulations, surgical training, training in spatial awareness, and more recently as a therapeutic intervention for phobias.[6,7] Several systems exist commercially, such as MIST-VR,[9] that have shown the capacity to train complex hand motor skills. Gallagher et al.[10] showed that training on MIST-VR resulted in significantly better performance on real object cutting, compared to a group without VR training attempting the same cutting task. Apart from hand/arm motor skill training on healthy subjects, VR also showed benefits in cognitive enhancements. For example, learning atomic physics in a virtual physics laboratory proved better in knowledge retention versus conventional education approaches.[11] Such results on healthy individuals suggest that disabled individuals could realize similar benefits, whether this involves physical or cognitive training.

Although it appears reasonable that VR-based movement retraining would be an appropriate approach, to date, its use is extremely limited. When VR simulations are interfaced with movement tracking and sensing glove systems, they can provide an engaging, motivating, and adaptable environment where the motion of the limb displayed in the virtual world is a replication of the motion produced in the real world by the patient's extremity. Our hypothesis for the use of VR in rehabilitation poststroke is that it can provide an appropriate interactive, challenging, and encouraging environment where a subject can practice repetitively, execute tasks, and be guided and rewarded through systematic feedback. Furthermore, we hypothesize VR to be a tool through which new motor skills can be acquired, thereby providing a rehabilitation tool that can be used to exploit the nervous system's capacity for sensorimotor adaptation. Application of this type of system is in the early stages of development but has shown excellent promise as a tool for rehabilitative movement retraining.[12-18]

Although exercising in a computerized VR environment is in the nascent stage of exploration for retraining coordinated movement, the data suggest that this technology has the potential to change the way professionals deliver therapeutic services. Currently there are several computerized systems under development to train upper arm movement; however, none of these systems focuses on hand rehabilitation.[19,20] Utilizing the biological principles related to neuroplasticity, as well as the underlying tenets of motor learning, we have been developing a computerized VR exercise system that provides repetitive motor reeducation and skill reacquisition in the hemiparetic hand of patients poststroke. Because of the complex sensorimotor control required for grasping and manipulating objects, even mild to moderate deficits in upper extremity control can impair most activities of daily living, especially when there is a loss or diminution of hand function. This complexity of sensorimotor control as well as the wide range of recovery of manipulative abilities in the fingers and hand, makes both the measurement and rehabilitation of hand function most challenging.[21-25]

Our computerized exercise system has the capability to create a functionally-based training paradigm where the intensity of practice, the interaction with task-related objects, the attention to training, and the visual, auditory, and haptic feedback can be manipulated to drive movement reeducation and skill development. This system provides precise kinematic and kinetic data on the subjects' performance and learning history. We have recently shown the usefulness of this VR technology for rehabilitation of patients with diminished hand function[12,14,26-28]; however, there is little information on the generalizability of these training effects to the physical environment.[4] Furthermore, the underlying mechanism of transfer of the skills acquired during VR therapy to real-world movements is poorly understood.[7] It is not clear what specific kinematic aspects of the movement transfer and contribute to improvement in real-world activities, nor is it clear whether the skills developed in a VR environment are retained over a period of time.[16] There is a need to use precise, objective measures to assess and understand the recovery of hand function poststroke.[29,30] Because of the complexity of measurement of manipulative function, both group and individual analyses are beneficial and complementary and will be described in this article. Given the wide variation in individual subjects' brain lesions and functional deficits, and the relatively small number of subjects, it is important to present individual results. Nonetheless, there are some common group patterns that should not be overlooked.

The specific goals of this study were 1) to investigate the effectiveness of training in a VR environment for promoting recovery of hand function, 2) to determine whether motor skills gained in the VR environment transfer to real-world movements, and 3) to objectively analyze the individual patterns of change involved in this transfer.

METHODS

Participants

Eight subjects, 6 males and 2 females (age range, 46-81; mean [*SD*], 64 [11]) with hemiparesis resulting from a stroke, participated in this study. The subjects, recruited from local stroke support groups, were not receiving therapy at the time of this study. They were all in the chronic phase, having sustained the stroke between 1 and 4 years prior to the VR training. The subjects were independent in ambulation and most activities of daily living either through the use of their hemiparetic side or through learned compensations. They were selected for

Table 1. Subject Characteristics at Beginning of Training

									Jebsen Test of Hand Function (s)		Strength Dynamometer (kg)	
Subject	Gender	Age	Years Since Stroke	Hand Dominance	Type of Stroke	Lesion Side	Lesion Location	Lesion Size	Right	Left	Right	Left
1	F	58	1	R	Ischemic	R	Cortical	Large	55	134	10	1.6
2	M	71	2.5	R	Ischemic	R	Subcortical	Small	46	153	29	24
3	M	64	4	R	Hemorrhagic	R	Subcortical	Small	46	300	41	18
4	M	72	4	L	Ischemic	R	Both	Small	84	222	41	15
5	M	46	3	R	Ischemic	R	Cortical	Large	57	208	43	9
6	M	58	2	R	Ischemic	L	Subcortical	Small	142	81	36	43
7	F	64	1.6	R	Ischemic	R	Subcortical	Small	55	151	29	11
8	M	81	2	R	Ischemic	R	Both	Small	47	256	37	14

the study based on the criteria established by Taub et al[31]; specifically, the subjects had to be able to actively extend the wrist of the hemiparetic limb at least 20° and extend the metacarpophalangeal (MCP) joints at least 10°. Subjects with sensory deficits, visuospatial deficits, hemispatial neglect, or receptive aphasia were excluded from the study. All subjects were medically cleared by their physician prior to inclusion in the study, informed consent was received, and the subjects were compensated for their participation in the study. A neurologist examined each of the subject's clinical MRIs to establish lesion size and location (Table 1; Figure 1). The lesions were reconstructed on representative axial brain slices.[32] Subject 4 had a previous left hemisphere lesion with no residual impairments on his right side. The internal review boards of all the involved universities approved the study.

Instruments

Computerized virtual reality exercise system. The system developed by our group uses two instrumented gloves, an 18-sensor CyberGlove from Immersion Co. (San Jose, CA) and the Rutgers Master II-ND (RMII) force feedback prototype glove developed in the Human-Machine Interface Laboratory at Rutgers University.[33] Range of motion, speed of movement, and fractionation (a measure of independent finger motion) exercises were done using the CyberGlove, whereas the strengthening exercise used the Rutgers Master II glove. The two gloves are connected to electronic control boxes, which in turn are wired to the serial port of a host PC running the VR simulation, through a multiplexing box. The RMII glove has a dedicated electropneumatic control interface, which receives compressed air from a small compressor. This controller sets the air pressure in the glove's small pneumatic actuators to provide force feedback to the patient's fingers (resisting flexion or assisting extension). The weight of the RMII glove is 80 g plus the weight of the air tubes from the glove to the control box. The weight of the CyberGlove is 85 g. Because of the light weight and the flexibility of both the CyberGlove and the RMII glove, using them on a hemiparetic hand is not a problem. The subject sits in front of the computer monitor and interacts with the virtual world wearing one of the two instrumented gloves. Detailed technical descriptions and initial data from several stages in the development of our computerized VR exercise system may be found in Jack et al.,[14] Boian et al.,[28] and Adamovich et al.[26]

Four hand exercise simulations were developed using the commercially available WorldTool Kit (Sense8, Palo Alto, CA) graphics library (Figure 2, left column). The exercises, in the form of simple video games, provide frequent feedback about the success of the action as well as the quality of the performance. Each game was designed to exercise one parameter of finger movement. As seen in Figure 2 in the top part of each exercise screen, the simulation software provides visual and numerical real-time feedback about each finger performance compared to the goal. This engaging format is augmented by congratulatory sound feedback as well as summary of the subject's performance during a block of trials, once that block of trials is completed. Target goals for flexion, extension, velocity, and force were set for each game based on baseline measures. A preset algorithm automatically increased these target goals as the patients improved. When using these gloves and interacting with the VR games, the amount of movement of the virtual hand is a representation of the movement of the hand in real space.

The top row (A) of Figure 2 shows the range of motion exercise simulation (left panel) and a representative example of the resulting finger angles of the middle finger during one trial (right panel). For the range of motion exercise, the subjects had to first open their hand and then flex their fingers to uncover a variety of visually pleasing scenes. The screen is divided into

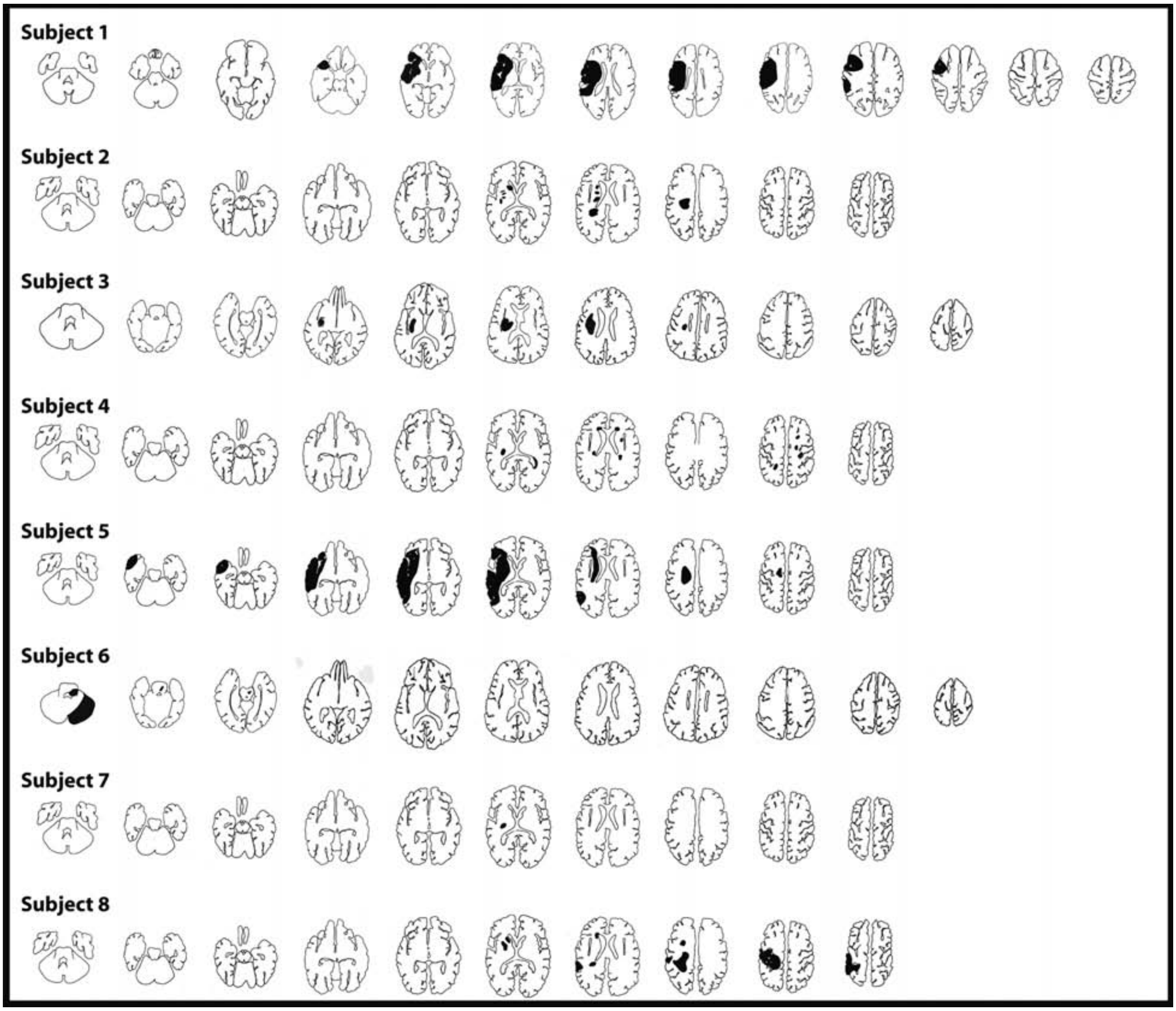
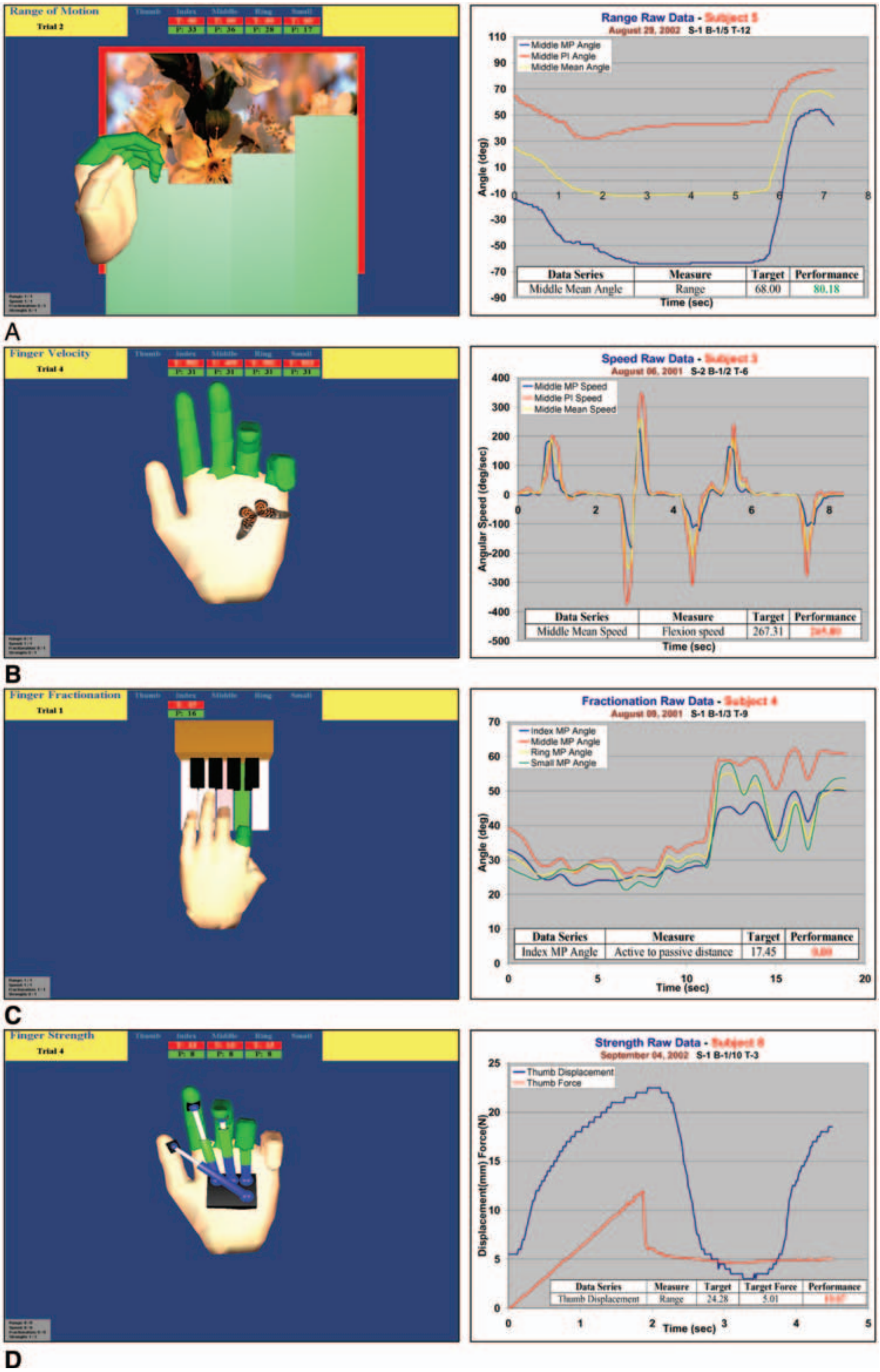


Figure 1. Reconstruction of lesion location for each of the 8 subjects. Note that the left half of the axial sections on the figure represents the right hemisphere.

4 vertical bands, and each band moves in relationship to the degree of flexion of a corresponding finger. In this trial, the target was set for 68° (mean excursion in the MCP and PIP [proximal interphalangeal] joints), and the subject achieved 80° of motion. For thumb range of motion, we trained the rotational motion at the MCP joint. For the speed exercise (Figure 2B), subjects had to quickly flex their fingers, and a butterfly flew away when the subjects exceeded their target finger speed goal. This example shows that the subject achieved a maximum finger flexion speed of 265 deg/s but did not achieve the target goal. For thumb velocity, we trained the rotational motion at the MCP joint. For the fractionation exercise (Figure 2C), which trained the ability to move each finger independently, the patient played a virtual piano keyboard, one finger at a time. The fractionation score was calculated during the flexion phase of the movement as the maximum difference between MCP angles of the active finger and the most flexed inactive finger. The right panel of Figure 2C reflects the finger joint angles for one trial. Subject 4 was trying to flex his index finger, which is shown in red. Figure 2C shows that the ring and small fingers flexed almost to the same degree and all the fingers moved in a similar way. For the strengthening exercise, using the RMII glove (Figure 2D), the patient exercised the thumb, index, middle, and ring fingers by pushing down against a constant force produced by the pistons of the glove. Each trial started with the RMII glove passively extending the subject's fingers. The strengthening score was calculated per trial as finger force times total displacement during flexion and is labeled as mechanical work in the subsequent analyses. The thumb displacement against a predetermined force is shown in the right panel of Figure 2D. The graph indicates that the thumb was able to move 24.5 mm against a force of 5 N. To quantify the progress



Data Series	Measure	Target	Performance
Middle Mean Angle	Range	68.00	80.18

Data Series	Measure	Target	Performance
Middle Mean Speed	Flexion speed	267.31	[illegible]

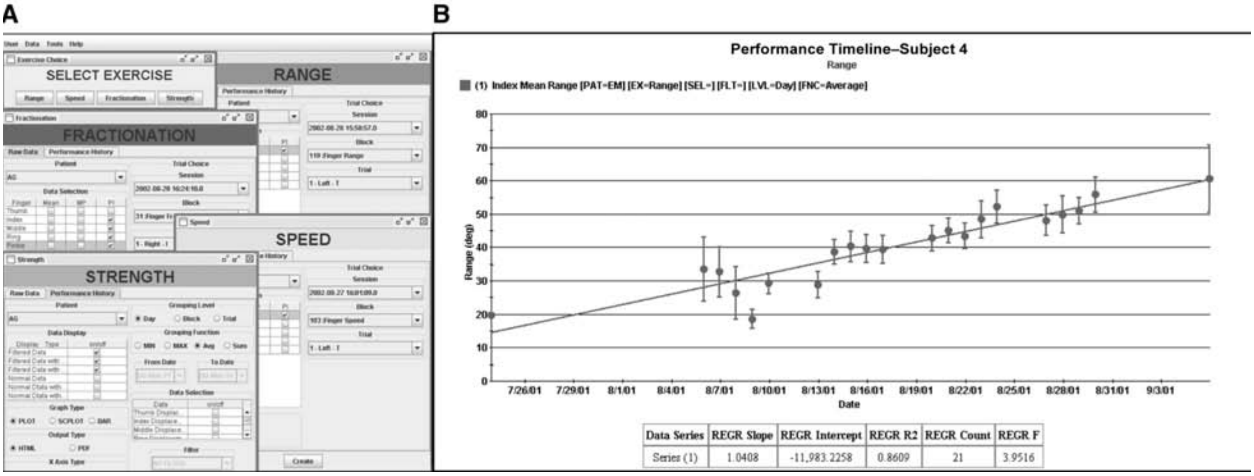
Data Series	Measure	Target	Performance
Index MP Angle	Active to passive distance	17.45	[illegible]

Data Series	Measure	Target	Target Force	Performance
Thumb Displacement	Range	24.28	5.01	[illegible]

Figure 2. Screen snapshots of the hand exercise simulations for each parameter of hand function (left) and a representative example of the kinematic data available from one trial of the training session (right). Panel A, Range of motion simulation and middle finger metacarpophalangeal (red), proximal interphalangeal (blue) angles, and mean of the 2 angles (yellow) during one trial. Panel B, Velocity simulation and angular velocity profiles of middle finger flexion (MP, PI, mean of the 2 angles) during one trial. Panel C, Fractionation simulation and angular displacements during one trial. Panel D, Strengthening simulation and thumb displacement (blue) and thumb force (yellow) during one trial. MP = metacarpophalangeal; PI = proximal interphalangeal. © Rutgers University CAIP Center. Reprinted by permission.

Table 2. Group Means and Standard Deviations for Virtual Reality Measures and Jebsen Test of Hand Function

	Pretest	Posttest	Retention	*F* Value	*P* Value
Fractionation (deg)	5.16 (2.9)	8.1 (4.0)	7.5 (3.4)	*F*(1, 6) = 13.2	0.0009
Range of motion (deg)	22.3 (10.8)	26.7 (10.8)	28.5 (10.4)	*F*(2, 12) = 8.71	0.005
Finger range of motion (deg)	31.9 (4.3)	35.4 (6.3)	36.8 (5.7)		
Thumb range of motion (deg)	12.8 (4.9)	17.9 (5.9)	20.2 (6.5)		
Velocity (deg/s)	104.7 (54.4)	115.0 (59.8)	129.4 (62.1)	*F*(2, 12) = 7.69	0.007
Finger velocity (deg/s)	147.4 (39.1)	166.6 (32.1)	185.2 (22.3)		
Thumb velocity (deg/s)	62.1 (25.4)	63.4 (22.5)	73.7 (24.6)		
Work (N·m)	0.073 (0.02)	0.068 (0.03)	0.065 (0.02)	*F*(2, 12) = 1.67	0.23
Finger work (N·m)	0.060 (0.02)	0.052 (0.02)	0.053 (0.02)		
Thumb work (N·m)	0.086 (0.02)	0.084 (0.02)	0.077 (0.02)		
Jebsen Test of Hand Function (s)	210.0 (58.1)	178.7 (45.1)	164.6 (37.8)	*F*(2, 12) = 7.34	0.008



Data Series	REGR Slope	REGR Intercept	REGR R2	REGR Count	REGR F
Series (1)	1.0408	-11,983.2258	0.8609	21	3.9516

Figure 3. Web portal for patient database remote acces. A, Graphical user interface to access raw data. B, Performance curve graph showing patient performance data across the duration of the therapy. ©Rutgers University CAIP Center. Reprinted by permission.

in this exercise, we used the amount of work performed per trial as an indicator of finger and thumb strength.

Outcome database. The exercise system is integrated with a database that can provide the therapist or the physician with specific kinematic data for each trial or training session (Figure 2). In addition to the raw data graphs that provide precise kinematic and kinetic measures of the subjects' impairments of range of motion, speed of movement, finger fractionation, and strength for the MCP joint and the proximal interphalangeal joint of each finger/thumb (Figure 2), the database can also provide an objective view of a patient's progress and the outcome of therapy. The graphical user interface for accessing the database (Figure 3A) presents the user with a series of choices: patient, specific exercise data to be plotted, time interval over which the data will be grouped (day, block, or trial), and the 1st and last date to be shown. The clinician may choose to plot the kinematic or kinetic impairment measures described above or may choose history graphs that present the patient's performance in each trial compiled across trials, blocks, or days. Trial performances are computed after each trial is finished and stored in the database, and the performance curves provide an ongoing record of changes in finger joints over the training period (Figure 3B). These types of graphs show whether the patient is improving and can be used for documentation or to efficiently and precisely adapt the levels of difficulty of the sensorimotor tasks to be practiced.

Procedure

Training. All of the subjects participated in a 3-week program using their hemiparetic hand in a series of interactive computer games. There was a 2-week baseline period to establish that the subjects were no longer experiencing spontaneous recovery of function, confirmed by the absence of a significant change in the Jebsen Test of Hand Function, and could therefore act as their own controls. This was followed by a pretest, 13 days of training at the University of Medicine and Dentistry of New Jersey (with weekend breaks), a posttest, and a 1-week retention test. For personal reasons, 1 subject asked to be tested at 2 weeks posttraining. Subjects trained for about 2 to 2.5 h each day, completing 250 to 300 trials per day. We have previously demonstrated that for subjects in the given age range, the maximal session duration with the currently available gaming activities that does not result in substantial physical and mental fatigue is 2.5 to 3 h.[26]

Jebsen Test of Hand Function. The Jebsen Test of Hand Function (JTHF)[34] was used to investigate whether changes in hand movement gained while training in the VR environment transferred to real-world tasks. This is a timed test developed to assess hand function and finger dexterity in both the dominant and nondominant hands. It consists of 7 subtests that provide a broad sampling of functional tasks: writing, turning index cards, picking up small common objects, simulated feeding, stacking checkers, picking up large light objects, and picking up large heavy objects.[34] The test-retest reliability for each subtest of the JTHF ranges from 0.60 to 0.99. This test has been reported to be able to discriminate various degrees of disability in patients with hemiplegia.[34] Our recent studies[12,26] have confirmed that these tests appropriately distinguish between functional capabilities of the hemiparetic and nonhemiparetic hands, providing a valid discriminatory assessment tool.

Kinematic reach to grasp test. We utilized a kinematic reach to grasp test to further investigate whether any improvement in hand function gained during VR training was retained in the kinematics of nontrained real-world prehension. Finger joint flexion/extension and abduction/adduction angles were obtained via resistive bend sensors embedded in the CyberGlove. The positions of the major joints of the arm were recorded in 3D space using 4 electromagnetic sensors (MiniBird system, Ascension Technologies Inc., Milton, VT) attached with adhesive tape to the subject's arm segments at positions that were referenced to the following body landmarks: shoulder, elbow, wrist, and midpoint of the dorsum of the hand. For this study, only the finger motions and the displacement of the wrist were analyzed. Multithreaded, high-performance drivers for the MiniBird system were developed that allowed each of the 4 electromagnetic sensors to stream data to the computer at a high rate (100 Hz). The raw data were digitally low-pass filtered at 12 Hz. We analyzed the transport and grasping components during prehension of real-world household and shaped objects. Specifically, we tested whether VR training resulted in reorganization of interjoint coordination measured by increased flexibility, accuracy, precision, and/or stability of prehension. Subjects were seated in front of a table in a comfortable chair without arms, with their hips and knees in a 90° position. Their forearm rested on the table in the neutral position, with the hand positioned 10 cm away from the subject's chest, midway between midline and the subject's right shoulder. Movements of the trunk were not restricted so that the subjects were able to assist the transport of the hand with their trunk if needed. To verify that the hand therapy did not affect trunk movement, we compared pretherapy and posttherapy excursions of the shoulder sensor and found no statistically significant effects. A rectangular block (4 cm wide, 2.5 cm in height) and a circular roll of tape (5.3 cm in diameter, 2.5 cm in height) were used. These objects were chosen because they required different hand shapes and different amounts of finger abduction. The objects were placed in the midline 20 cm in the sagittal direction from the hand starting position, so that similar amounts of elbow extension and shoulder adduction would be necessary to bring the hand to the object without trunk involvement. The subjects were instructed to grasp and lift the objects and release them on to a platform. The platform was 10 cm high and located 5 cm lateral to the object. The instructions indicated that all 5 fingertips had to touch the object at the time of the grasp. The rectangular object was oriented at 45° to the midline to minimize the wrist extension that is required to properly position the hand for successful grasping. The circular object was large enough for the subjects to grasp it with all 5 fingers without the fingers touching each other. Subjects practiced grasping and lifting all objects before the experiment for 5 to 10 trials.

Movement onset was defined as the point in which the wrist sensor reached 5% of the peak velocity during the initial acceleration phase. The offset was defined as the point in time at which the object was lifted. A switch embedded into the table and located under the object indicated the moment of lift. In some trials, when the subject had difficulty lifting the object, the object was translated and the switch released but the object was actually lifted at a delayed point in time. However, when this did not occur, the switch release coincided with the marked increase in the vertical component of wrist velocity. When it did occur, we determined the moment of change in the vertical component of the wrist velocity manually using interactive graphic programs. Therefore, movement offset (object lifted) was defined as the moment of change in the vertical component of the wrist movement. In all cases, we examined each trial manually using interactive graphic programs to determine whether the switch release coincided with the change in the vertical component of the movement.

Subjective assessment. We administered a pretest questionnaire to the subjects to assess their perception of their current hand function and their expectation of the therapy. Following the training, a 2nd questionnaire was used to determine the subjects' perceptions of the results of the therapy, their satisfaction with the therapy sessions, the physical and mental effort involved in the training, and an evaluation of the different exercises. The questions used in this study were not validated; however, they were selected and modified for the study from a published, validated user interface questionnaire.[35]

Data Analysis

Computerized measurements of the kinematic changes in range of motion, speed, fractionation, and strength were taken after each practice trial. All exercise data were transparently stored in the Oracle database that allowed for later retrieval and analysis of individual and group changes.

For all the group analyses, Subject (S6) with a left brain stem and cerebellar lesion was excluded, as his lesion differed so markedly from the others. For the range of motion, speed, and strength VR measures, a repeated measures ANOVA with 2 factors, Condition (pre, post, retention) × Effector (thumb, fingers), was used. A repeated measures ANOVA, with 1 factor, Condition (pre, post, retention), was used for the fractionation VR measure. The significance levels for these 4 VR comparisons were adjusted using Bonferroni corrections. A repeated measures ANOVA, with 1 factor, Condition (pre, post, retention), was used for the JTHF and the following kinematic measures of the reach to grasp test: peak tangential velocity of the hand, time to peak velocity, and time after peak velocity. For the VR measures, pretest equals the 1st 2 days of training and posttest equals the last 2 days of training. In addition, 1-way repeated measures ANOVAs were utilized for post hoc analyses on all of the above variables to compare pretest and posttest scores and to compare pretest and retention scores. For the 6-month retention, the VR and JTHF performance scores for the 1st 2 days and last 2 days of therapy, as well as for 3 retention tests, were tested for significant changes separately for each subject by utilizing Bonferroni/Dunn *t* tests with significance levels adjusted for multiple comparisons.

Table 3. Post Hoc Tests

	Pretest versus Posttest		Pretest versus Retention	
	$F(1, 6)$	P	$F(1, 6)$	P
Fractionation (deg)	27.1	0.002	11.0	0.01
Range of motion (deg)	5.8	0.05	11.0	0.018
Velocity (deg/s)	2.4	0.17	10.5	0.017
Jebsen Test of Hand Function (s)	6.0	0.045	8.44	0.027

In the reach to grasp test, linear discriminant analysis (LDA) was performed on finger joint angles to obtain a measurement of the error of hand preshaping during the transport phase of the movement and to estimate the predictive value of this measure for the final hand shape per object type.[36,37] At each moment in time during the movement, LDA tried to predict which object the subject was grasping in that particular trial. The percentage of incorrect predictions was used as a measure of how well the hand was preshaped to the shape of the object being grasped at each given moment in time during the reaching movement.

RESULTS

Group Effects

Virtual reality measures. Statistical analyses show that as a group, subjects improved in fractionation, range of motion, and speed (see Table 2 for means, standard deviations, and ANOVA statistics). Post hoc analysis comparing pretest to posttest showed that fractionation improved significantly (see Table 3) as did range of motion. The subjects showed significant retention in 3 out of 4 parameters of hand movement gained through practice in the VR environment. Post hoc analysis revealed improved performance at the 1-week retention session compared to the pretherapy scores in fractionation of the fingers, range of motion, and speed (see Table 3).

Jebsen Test of Hand Function. The JTHF was used to determine whether the kinematic improvements gained through practice in the VR measures transferred to real-world activities. Analysis of variance of the Jebsen scores from the pretherapy, posttherapy, and 1-week retention test demonstrated significant changes in the scores (see Table 2). Post hoc analysis revealed the subjects' affected hand improved in this test (pretherapy versus posttherapy, see Table 3). Finally, scores obtained during the retention testing were significantly better than pretherapy scores. In contrast, no significant changes were

Table 4. Questions, Means, and Standard Deviations of the Subjective Measures

Pretest Questionnaire	
1 = Strongly Disagree 7 = Strongly Agree	
Questions assess the subject's perception of his or her current hand function and his or her expectation of the therapy.	
1. I feel that movement in my affected hand is very good.	2.8 (0.75)
2. I don't expect much improvement in my affected hand motion to come from participating in these studies.	3.8 (2.3)
3. I am very eager to participate in this project.	6.8 (0.4)
Posttest Questionnaire	
1 = Strongly Disagree 7 = Strongly Agree	
Questions assess the subject's perception of the results of the therapy, his or her subjective satisfaction with the therapy sessions, and the overall physical and mental effort.	
1. These exercises improved my hand motion.	5.7 (1.4)
2. I believe that continuing these exercises will improve my hand motion.	6.1 (1.2)
3. I found the computer sessions to be engaging.	5.7 (1.5)
4. I wish that these computer tasks had been part of my original therapy.	6.6 (0.53)
5. The computer tasks took too long.	3.4 (2.2)
6. It was hard to tell how well I was doing in the tasks.	2.4 (1.7)
7. I prefer doing real-world therapy tasks to the computer tasks I did in this therapy session.	2.7 (2.1)
8. My hand was very tired doing these exercises.	4.9 (1.1)
9. Performing the tasks required a lot of mental concentration.	5.3 (0.8)
10. Please put the tasks in order from 1 = least amount of physical effort to 4 = most amount of physical effort.	
Playing the piano	2.7 (1.3)
Wiping the window clean	3 (1.2)
Pushing the plunger down	2 (1.2)
Catching the butterfly	2.3 (0.8)
11. Please put the tasks in order from 1 = least amount of mental effort to 4 = most amount of mental effort.	
Playing the piano	3.3 (1.0)
Wiping the window clean	2.6 (1.1)
Pushing the plunger down	1.4 (0.8)
Catching the butterfly	2.7 (1.0)
12. Please put the tasks in order from 1 = least engaging to 4 = most engaging.	
Playing the piano	2.6 (1.1)
Wiping the window clean	2.1 (1.2)
Pushing the plunger down	2.4 (1.3)
Catching the butterfly	2.9 (1.1)

observed for the unaffected hand in the pretherapy versus posttherapy scores, $F(1, 6) = 2.73$, $P = 0.15$.

Reach to grasp test. We further studied the transfer of hand skills during the reach-to-grasp movement. Neither time to peak velocity nor peak velocity of the affected hand changed after the therapy, $F(1, 6) = 0.41$, $P = 0.54$, and $F(1, 6) = 0.94$, $P = 0.37$. This result could be expected in that these represent the transport phase of the motion and the elbow and shoulder were not trained during the VR therapy. In contrast, the overall time from hand peak velocity to the moment when the object was lifted from the table decreased significantly after the therapy, $F(1, 6) = 5.8$, $P = 0.05$. On average, the task was performed 19% faster after the intervention, illustrating transfer of their improvement in the VR exercises to a real-world task. This was achieved through increased efficiency and improved patterns of finger prehension.

Subjective measures. Table 4 presents the means and standard deviations from the subjective questionnaires for 7 subjects. The subjects were eager to participate in the project. They found the computer sessions required a lot of mental concentration, were engaging, and helped improve their hand motion. They found the exercises to be tiring but wished this form of training had been part of their original therapy. Although they found all the exercises to be equally engaging, playing the piano 1 finger at a time (fractionation exercise) required the most physical and mental effort.

Individual Effects

Figure 4 shows a representative example of the changes in fractionation (playing virtual piano 1 finger at a time) for Subject 5 over the course of training. The top panel of Figure 4 shows the joint angles for each of the

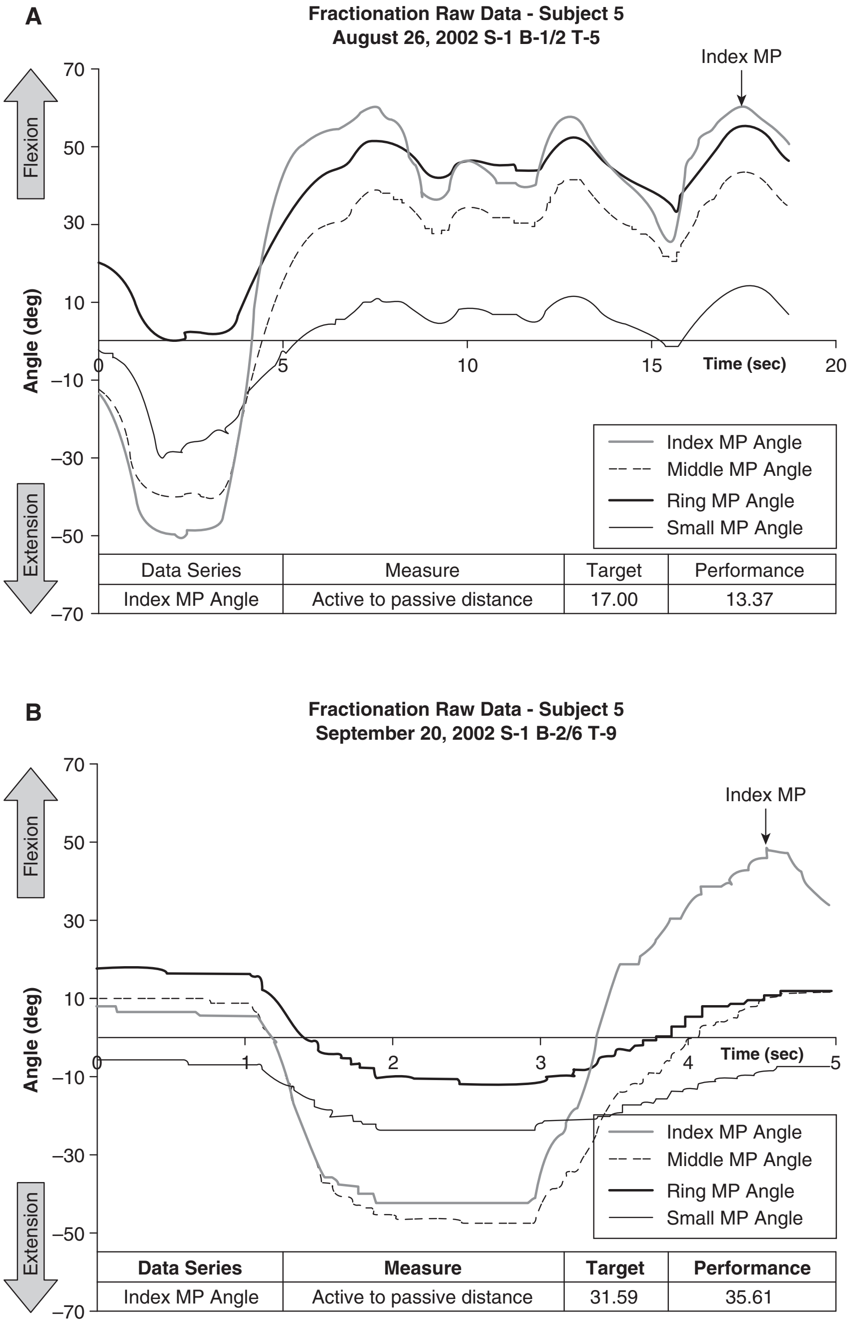
4 fingers during the piano playing game on day 1 of training. While the subject was trying to actively flex only his index finger (dark line), the ring finger flexed almost to the same degree. All the other fingers moved in a similar way, and the subject did not meet the target value. However, by the end of training (Figure 4, lower panel), the subject was able to meet the target and flex his index finger 50° while the other fingers only flexed between 5° and 15°.

The individual kinematic analyses reveal that transfer was accomplished through improvements in various subject-specific parameters of hand motion. Four of the subjects had specific finger deficits that impeded their grasping and hand function. These deficits responded to the training, with the kinematic changes for these 4 subjects shown in Figures 5 and 6. Subject 1 demonstrated abnormal timing, intermediate stops, and hesitations in finger motion and forearm orientation during reaching and grasping. The coordination between the arm displacement and orientation of the hand, and between the arm and finger motion during grasping, was severely disrupted. This subject showed several changes as a result of the training including improved arm-hand coordination and reduced movement time. Figure 5A shows the angular displacements at the finger joints (right panels) and the hand position and orientation (left panels). In the starting position, the hand was closed and the forearm in the neutral position. Relative to the initiation of arm movement, finger movement was initiated almost simultaneously in the nonhemiparetic arm (not illustrated). But in the hemiparetic arm prior to therapy, the onset of hand opening was considerably delayed relative to onset of hand displacement (thin lines). The amount of this desynchronization varied greatly between trials in the range of 0.3 to 1.7 s for the MCP1 joint (mean [*SD*], 1.1 [0.47] s), and for some of the trials, the grasping motion did not begin until the arm was very close to the object. There was a similar discoordination between the onset of arm movement and forearm pronation (Roll thin lines). The delay was in the range of 0.35 to 1.5 s (mean [*SD*], 0.81 [0.47]). By the end of training, Subject 1 was able to begin shaping her fingers earlier and decrease the variability and improve the synchronization of finger shaping, relative to the onset of arm displacement (in the range of 0 to 0.8 s for the MCP1 joint, mean [*SD*] of 0.58 [0.26]). She was also able to better coordinate forearm pronation with hand displacement, decreasing the range of the delay across trials (0 to 0.6 s, mean [*SD*] of 0.25 [0.23]). She began to lift the object earlier. Prior to training, she did not begin to lift the object until 2 s after movement onset. After training, the lift of the object (see arrow in the Zhand panel) began between 1.4 and 2 s after hand movement onset. This subject showed the largest decrease in the duration of grasping. The mean (*SD*) movement duration was 2.66 (0.54) s prior to training and 1.63 (0.45) s after training.

Subject 3 had an abnormal finger extension synergy in his right middle finger, which improved over the training. The variability of the MCP and PIP angles of the index, middle, and ring fingers is shown in Figure 5B. Prior to training (thin line), this subject had an erratic extension pattern of the PIP joint of his middle finger that resulted in elevated angular variability (thin line in PIP2) that prevented normal finger grasping. By the end of training, this subject improved in the control of that joint, significantly reducing the frequency of the erratic pattern. As seen in Figure 5B, the variability of this joint motion was considerably reduced during the grasping movement (bold line in PIP2). This in turn could well have allowed the subject to improve in the JTHF score, which he did by 28%, the largest improvement in the group.

A 3rd subject (Subject 4) had restricted motion predominately in his thumb, index, and middle fingers. He improved his range of motion in VR by 147% for the thumb and on average by 20% for the fingers. This improvement in VR exercises transferred to the reach to grasp test and is illustrated in Figure 5C. Movement amplitude in the MCP joints of the index and middle fingers (see MCP1 and MCP2 panels) increased from 8° and 10° to 25° and 19°, respectively. This increase in the active range of motion for index and middle fingers allowed the subject to replace an abnormal grasping pattern that involved opposition of the thumb and the small finger with a normal 5-finger grasp when lifting a roll of tape from the table.

The changes in finger preshaping for Subject 6 are shown in Figure 6. Although this subject had full range of motion of his fingers and wrist against a load, he had coordination problems that affected several activities of daily living including cutting with a knife and using an electric razor. This panel shows the improvement over the course of the VR training in the time needed to appropriately shape his fingers during the grasping movement. The figure shows results of linear discriminant analysis (see Methods), that is used to quantify the degree to which the hand is matched to the shape of the object to be grasped, during the reaching movement. Lower classification errors denote better preshaping. We can see that for the unaffected arm, the fast decrease in classification errors results in zero errors at about the middle of the movement. By contrast, in the hemiparetic hand prior to training, there was a delay in the appropriate shaping of the grasp, and in addition, the classification errors never reached zero. Posttherapy, the timing of the preshaping became closer to normal. Although the error levels never reached zero, they became significantly smaller. Improvement in the preshaping of his hand was accompanied by increased



Data Series	Measure	Target	Performance
Index MP Angle	Active to passive distance	17.00	13.37

Data Series	**Measure**	**Target**	**Performance**
Index MP Angle	Active to passive distance	31.59	35.61

Figure 4. The changes in the 4 metacarpophalangeal (MP) joint angles during 1 trial of the fractionation exercise for Subject 5 between day 1 (A) and day 13 (B) of virtual reality training. The downward curve shows the opening of the hand (extension), and the upward curve shows the pressing of the piano keys (flexion). The active finger is indicated by an arrow. The fractionation score was calculated during the flexion phase of the movement as the maximum difference between the MP angles of the active finger and the most flexed inactive finger. The fractionation score is an indicator of the ability to move each finger individually. ©Rutgers University CAIP Center. Reprinted by permission.

function in the affected activities of daily living, specifically in the bilateral use of a knife and fork during eating.

Two of the subjects (Subjects 2 and 7) showed minimal improvements on the grasping test. This occurred despite substantial progress in the VR exercises and a transfer of these improvements in the fine-motor tasks on the JTHF. Finally, 2 other subjects (5 and 8) were more involved and did not improve on any of the reach to grasp movement parameters. Subject 5 only improved significantly in one of the VR measures and did not show any evidence of transfer in either the JTHF or the reach to grasp test. He had a large lesion. Subject

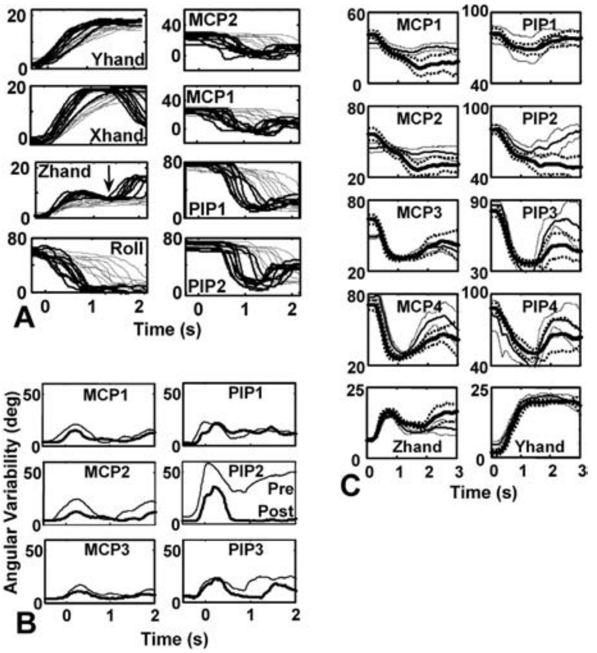


Figure 5. Time traces of finger angles and hand displacement and orientation in the reach to grasp test (see Methods) before and after training for Subject 1 (A), Subject 3 (B), and Subject 4 (C). See text for description of the specific kinematic changes. A, Hand coordinates (Xhand, Yhand, Zhand), forearm orientation (Roll), and MCP/PIP angles for index and middle fingers for 10 movement trials performed before (thin lines) and after training (bold lines). The time profiles are synchronized to the initiation of the vertical motion of the hand (Zhand). Arrow in Zhand indicates time of object lifting for one of the trials. B, Variability (standard deviation) of the MCP and PIP angles of the index, middle, and ring fingers across 10 reaching movements toward a rectangular object. Note the reduction in PIP2 variability after the therapy. C, Mean (solid line) plus/minus standard deviation (dashed lines) of angular displacements in the MCP and PIP joints of the index, middle, ring, and 5th fingers, as well as the vertical and sagittal coordinates of the hand. MCP = metacarpophalangeal; PIP = proximal interphalangeal.

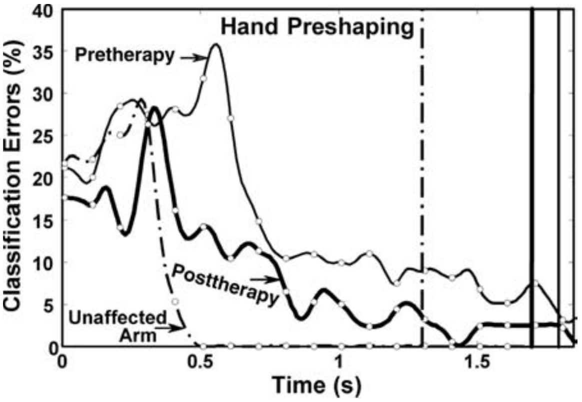


Figure 6. Linear discriminant analysis (LDA) was used to quantify the preshaping of the subject's hand to the object during reaching. Ten reaching movements to a rectangular object and 10 movements to a circular object of a similar size were synchronized and entered into the analysis. At each moment during a reaching movement, angular displacements in the metacarpophalangeal and proximal interphalangeal joints of 5 fingers, as well as finger abduction angles, were used by the LDA to classify the current movement as directed toward one of the two objects. Figure 6 shows the results of LDA for Subject 6 before and after training. Lower classification errors denote better preshaping. Vertical lines indicate time of object lifting for, from left to right, unaffected arm, affected arm posttherapy, and affected arm pretherapy. Although time to object lifting did not change significantly after the therapy, the pattern of finger coordination as reflected in the classification errors shifted substantially toward the coordination pattern of the unaffected arm.

8 did not show improvement in any of the VR measures; however, he did improve on the JTHF and showed a decrease in the duration of his movement time on the reach to grasp test. This subject could not sustain the constant effort and intensity of training demanded by the VR computer algorithms. He required frequent rest periods. This may have influenced his outcome on the VR measures.

Six-month retention. Two of the subjects from the group (Subjects 6 and 7) were retested 1 week, 2 weeks, and 6 months after the completion of their 13-day training. Figure 7 presents the changes in 4 movement parameters: range of motion of the fingers, fractionation of the fingers, speed of finger flexion, and mechanical work per trial performed by the thumb when moving against a load. The data are shown for each day of training and the 3 retention periods, R1 at 1 week, R2 at 2 weeks, and R3 at 6 months posttherapy. Each circle and cross on the graph represents the mean of 10 trials averaged across all fingers and across the MCP and PIP joints of each finger. Subject 6 (cross) was able to improve the range of motion of his fingers by 8% over the course of training (percentage increase between the 1st 2 days and the last 2 days of training, 75° to 81°, $P < 0.0001$). He also improved his speed of finger motion (by 6%, 528 deg/s to 558 deg/s, $P < 0.0002$) but did not significantly change his fractionation ability. The increase in the mechanical work of his thumb was significant (55%, 0.21 N·m/trial to 0.34 N·m/trial, $P < 0.004$). For 3 of the 4 movement parameters reported here, scores for the 6-month retention test were significantly higher than the scores for the 1st day of training. Thus, VR retention tests indicate this subject retained most of the gains acquired during the therapy. In terms of real-task changes after training, subject 6 showed a decrease in

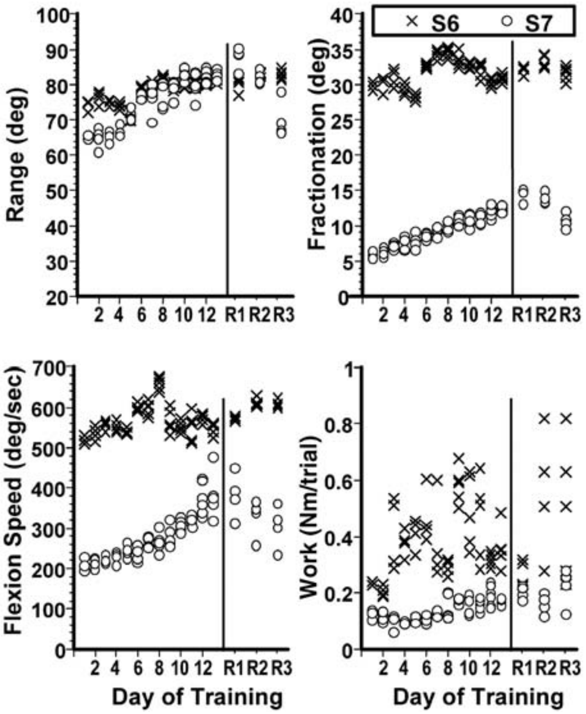


Figure 7. Changes in the performance in each of the 4 virtual reality exercises are shown for 2 Subjects 6 and 7. R1, R2, and R3 denote the results of retention tests 1 week, 2 weeks, and 6 months after the end of the therapy, respectively.

his JTHF scores (total of 7 subtests) from 142 s to 128 s, indicating a 10% improvement in time. Although he retained much of the gains in the VR activities at 6 months, this was not true of the transfer test. At the 6-month retention test, the total JTHF scores were 139 s, similar to his original baseline.

Subject 7 (white circles) showed a more substantial improvement across the VR movement parameters. Her finger range of motion significantly increased by 27% (65° to 82°, $P < 0.0001$), her fractionation by 101% (5° to 12°, $P < 0.0001$), and the speed of her finger motion by 77% (211 deg/s to 375 deg/s, $P < 0.0001$). Finally, the mechanical work of her thumb also increased significantly (by 55%, 0.11 N·m/trial to 0.18 N·m/trial, $P < 0.0005$). The retention tests indicate that for each parameter, scores for the 6-month retention test are significantly higher than scores for the 1st day of training. The results of the VR retention tests indicate that although for some measures the subject lost part of the gains acquired during the therapy, she was still significantly better on all measures after 6-month retention, when compared to the 1st day of training. In terms of her functional transfer, the JTHF scores decreased from 151 s to 141 s (total of 7 subtests), indicating a 7% improvement in time. At the 6-month retention test, her total JTHF scores decreased further to 111 s (an improvement of 22% when compared to the 1st day of training). She reported that after VR training, she continued to use her hemiparetic arm at home. This factor may have been an important contribution to her continued improvement in the transfer test.

DISCUSSION

In this study, we have been investigating whether movement reeducation in a VR environment has the potential to be used to augment existing rehabilitation therapies. Our primary aim was to determine whether this technology-based therapy, using a VR system without any other simultaneous training, had the capability of driving improvement in hand function of patients in the chronic phase poststroke. As a group, the subjects improved and retained gains made in range of motion, speed, and isolated use of the fingers. These changes translated to improvements in the real-world outcome measures. We were also interested in the effect of the training on individual patients' specific impairments. Individually, several subjects improved in particular aspects of the VR high-intensity therapy and showed modifications in their particular movement impairments, suggesting a potential for this type of VR-based therapy in the rehabilitation of patients with diminished hand function.

During the past few years, VEs for motor rehabilitation have been utilized experimentally.[6,9,12,13,15,16,28] Although these have all been pilot studies, and to date the concept has not been tested in large controlled clinical trials, the studies have been showing promising results. Therefore, it is timely to consider what underlying mechanisms may be driving these improvements. It is possible that functional plasticity will likely underlie many of the effects that we are getting in VR-based rehabilitation. A recent small control study using the IREX system for poststroke training has shown brain reorganization visible in fMRI pre-post images.[38] Animal studies have demonstrated the importance of repetition in inducing synaptic reorganization. A critical variable is that the repetitive motor activity needs to involve the learning of a motor skill.[39] These studies suggest that rehabilitation paradigms should be based on the understanding that the nervous system has the potential for neural modification and that attention, repetition, intensity of practice, reward, progression of complexity, and skill acquisition are critical conditions of practice for driving this change in neural structure and function.

Research has indicated that in addition to the intensity of training for skill development, the quality and quantity of feedback and the specificity of the training are important variables to which the motor system responds.[40,41] The game-like motor tasks used in this VR rehabilitation system have been designed to train specific parameters of hand use. Page[40] suggested that specificity of training is an important component in therapy regimens and that this training specificity has been shown to induce cortical reorganization in the neural representations of the anatomic areas used during practice. An important factor contributing to the subjects' learning of the movements may be the specificity and frequency of the feedback provided by the system regarding both the knowledge of their performance (KP) and the knowledge of the results of their actions (KR). Augmented feedback in the form of either KP (feedback related to the nature of the movement pattern that was produced) or KR (feedback related to the nature of the result produced in terms of the movement goal) is known to enhance motor skill learning in normal adults,[41] in older healthy populations,[42] and in individuals poststroke.[43] Feedback provides information about the success of the action, it informs the learner about the movement errors, and it is known to motivate the learner by providing information about what has been done correctly.

Attention is another significant component related to the acquisition of motor skills. It is reasonable to assume that attention to the cognitive, perceptual, and motor requirements of a skill may play a major role in plasticity. Novel movements that we attend, to while repeating them during a skill acquisition process, may induce greater plastic changes than movements performed in a less attention-demanding environment. Computerized technology appears to be able to provide the appropriate training condition where the intensity of practice; the visual, auditory, and haptic feedback; as well as the attentional demands can all be objectively and systematically manipulated and enhanced to create the most appropriate, individualized motor learning paradigm. Confirmation may be provided by the fact that the subjects in this study found that performing these tasks required a great deal of mental concentration.

It is intriguing to consider another potential mechanism for the improvement that we have seen. Many animal and human studies have shown activation of the motor cortex during observation of actions done by others.[44] Some studies indicate that neural processing is not the same when observing real actions and when observing virtual actions.[45] However, it is important to consider whether one is just watching an action, even a realistic natural movement, or whether one attributes the observed action to oneself.

This sense of agency, the feeling of being involved in an action and of attributing that action to ourselves, appears to be related to the degree of concordance between the intent of the movement and the sensory feedback related to actual movement, in other words, to the feeling of control of the action.[46] This is thought to be a continuous mechanism; the greater the sense of agency, the greater the activation in the right posterior insula.[46] Although one feels connected to the hand model in the exercise graphics because it moves in direct relationship to the movement of one's own hand, it is clear that it is not an anthropomorphic image of one's own hand. It is therefore interesting to speculate upon the degree of agency involved in this VR-based high-intensity training, the area and extent of neuronal activation, and whether learning in a VR environment may facilitate this complex visuospatial, action/observation network.

In addition to the overall improvement in 3 parameters of VR measures and the evidence of these changes in real-world functional improvement, the precise quantification of the reach to grasp digitized finger movement allowed us to specifically investigate and analyze the complex individual kinematic deficits that were most debilitating for each subject and the subsequent modifications of those deficits. Thus, individualized kinematic data provide a glimpse into the underlying mechanisms of the transfer effects. Specific kinematic impairments such as desynchronization among the distal and proximal degrees of freedom of the arm, poor finger coordination, extremely limited range of finger motion due to spasticity, and abnormal synergistic joint movement systematically interfered with functional manipulation of the subject's fingers and hand. However, these particular deficits responded to the VR training paradigm. Improved control of the fingers during grasping was evident in changes such as an increase in finger movement consistency with less interference from abnormal synergistic movement, a decrease in movement time, and more appropriate integration between hand shaping and arm transport. For the higher functioning patients, greater insight into the variety of modifications in hand coordination changes posttraining might be shown through the use of a wider range of objects to be grasped.

In this study, we used the inclusion criteria established by Taub.[31] However, this in and of itself did not provide a homogeneous sample of subjects, in that specific movement deficits differed greatly among the patients. This might be due to the differences in lesion size and location as well as the spectrum of recovery of hand abilities. Although reflective of clinical findings in patients poststroke, this may be a limitation of the study. However, there is evidence that patients with varying levels of deficits benefit from stroke rehabilitation in variable and divergent ways.[47] Our findings are consistent with this. Although the size of the effect and specific kinematic changes varied, regardless of lesion site or level of initial impairment, 7 of the 8 subjects improved on several aspects of hand function. Although the system was able to partially accommodate for the range of the impairment differences presented by these patients, there is a need to stratify the subjects more precisely to determine the type of patient for whom VR-based therapy would be most beneficial. In the future, we will investigate more discriminating inclusion criteria, somewhat similar to the inclusion criteria for higher and lower functioning groups developed for the Excite trials.[48]

When developing the VR activities for this study, we selected exercises that involved discrete movements designed to train a single movement parameter at a time (e.g., range of motion). This allowed for a more accurate tracking of the progress during the therapy and simplified posttherapy analysis. We may assume that more functionally integrated activities could result in stronger training effects on the sensorimotor abilities of the subjects. The overall success of the fractionation exercise, the most integrated and most challenging among the VR activities, could be considered as indirect confirmation of this hypothesis. Although the subjects found all the exercises to be equally engaging, they commented that playing the piano 1 finger at a time (fractionation exercise) required the most physical and mental effort. In the future, we plan to utilize a mixture of short, discrete elemental movements combined with more integrated functional activities that would provide a higher task demand. In the present study, the subjects with more impaired hand function were not as successful. For these subjects, in future studies, we plan to provide haptic assistance and guidance during part of the training. This system was designed to train manipulative functions of the hand; however, because of the interdependence between the transport and object manipulation phases of prehension,[49] training the upper extremity as a unit may lead to improved outcomes.

CLINICAL IMPLICATIONS

New technologies have provided clinicians with exciting possibilities for innovative tools for rehabilitation. However, investigating their effectiveness for patients with neurological deficits is complex and complicated by many factors. Some of these, as we have previously discussed, are the difficulty in sampling a heterogeneous population, the length and intensity of the training sessions, and the limitations of the outcome measures, especially as they relate to meaningful functional motor changes. However, the current health delivery system provides the clinician with multiple challenges engendering a need to overcome these limitations and explore additional interventions. The data in this study add support to the proposal to explore novel technologies for incorporation into current practice. It is evident that 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. This leads one to speculate about the importance of developing lower cost, home-based therapy systems. Patients would be able to practice more frequently, for a longer period of time, and for an extended duration past their initial neurological event. They would then have the opportunity to immediately put their improvements in impairments into functional activities of daily living.

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