

Integrated arm and hand training using adaptive robotics and virtual reality simulations

A S Merians¹, G G Fluet¹, Q Qiu², S Saleh², I Lafond², S V Adamovich^{1,2}

¹Department of Rehabilitation and Movement Science, University of Medicine and Dentistry of New Jersey,
65 Bergen Street, Newark, NJ, USA

^{2,3}Department of Biomedical Engineering, New Jersey Institute of Technology,
University Heights, Newark, NJ, USA

¹*merians@umdnj.edu*, ²*fluetge@umdnj.edu*, ³*qq4@njit.edu*, ⁴*shs25@njit.edu*,
⁵*ial6283@njit.edu*, ⁶*adamovich@njit.edu*

ABSTRACT

Virtual Reality simulations interfaced with robotic arm devices are being used for training the upper extremity of people post-stroke. The benefit has been hypothesized to be the ability to provide repetitive task practice, directed visual and auditory feedback, learning algorithms and graded resistive and assistive forces. All of these elements can be manipulated to provide individualized motor learning paradigms. We have developed a unique exercise system, interfaced with complex virtual reality gaming simulations that can train both the upper arm and the hand of people in the chronic phase post-stroke. After two weeks of intensive training, eleven subjects, were able to more effectively control the limb during hand interaction with the target as demonstrated by improved proximal stability, smoothness and efficiency of the movement path. This was in concert with improvement in the distal kinematic measures of fractionation and improved timing. These changes in kinematic measures were accompanied by robust changes in functional tests of upper extremity motor control, the Wolf Motor Function Test, the Jebsen Test of Hand Function and the 9-hole Peg Test.

1. INTRODUCTION

Robotic-assisted arm training devices integrated with strategically placed virtual targets or complex virtual reality gaming simulations are increasingly being used for the rehabilitation of upper extremity deficits post-stroke. Our hypothesis for the use of a virtual reality/robotic system for rehabilitation is that this environment can monitor the specificity and frequency of visual and auditory feedback, and can provide adaptive learning algorithms and graded assistive or resistive forces that can be objectively and systematically manipulated to create individualized motor learning paradigms. It provides an excellent medium for the delivery of repetitive task practice. It has been shown in both animals and humans that neuronal connections are continuously remodeled by experience and that intensive practice of a motor skill leads to an expansion of cortical representations (Merzenich, et al., 1996; Nudo, Milliken, Jenkins, & Merzenich, 1996; Plautz, Milliken, & Nudo, 2000). Congruent with the motor learning and neuroplasticity literature, it is believed that the acquisition of a skill follows a dose-response relationship (Kwakkel, 2006). In rehabilitation, the dose is often measured as the number of task repetitions or practice hours. A major impediment to the delivery of repetitive task practice is the labor intensive nature of these interventions. Multiple authors cite the ability of robotically facilitated training to provide highly repetitious training as a key factor for its effectiveness (Kwakkel, Kollen, & Krebs, 2008; Mehrholz, Platz, Kugler, & Pohl, 2009). The comparison between the training volume typical to robotic interventions and those of traditional UE interventions is marked. Subjects average over 500 repetitions/day in studies in the robotic rehabilitation literature (Aisen, Krebs, Hogan, McDowell, & Volpe, 1997; Aubert, et al., 2005; Dipietro, Krebs, Fasoli, Volpe, & Hogan, 2008) while an observational study of the repetitions performed in a traditional outpatient setting averaged 85 (Lang, MacDonald, & Gnip, 2007). Thus, virtual reality/robotic systems provide a rehabilitation tool that can be used to exploit the nervous systems' capacity for sensorimotor adaptation and provide plasticity-mediated therapies.

Most of these robotic therapies have focused on training the proximal, rather than distal effectors of the upper extremity. This is in keeping with the prevailing clinical paradigm to develop proximal control and mobility of the shoulder prior to initiating training of the hand (Lennon, Ashburn, & Baxter, 2006). However,

stroke patients report that hand function is the most disabling upper extremity motor deficit. In our past work, we trained the hand alone, with gaming simulations that used relatively simple activities, requiring only control of wrist and finger movement. Neural control mechanisms indicate that arm transport and hand-object interaction are interdependent (Levin, Michaelsen, Cirstea, & Roby-Brami, 2002; Michaelsen, Jacobs, Roby-Brami, & Levin, 2004) suggesting that training on complex tasks that require coordinated effort of both the upper arm and hand may be a more effective method for optimizing recovery of real world hand function (Michaelsen, Luta, Roby-Brami, & Levin, 2001). We have now refined and optimized our system to exercise the hand and the arm together using more complex gaming simulations requiring simultaneous control of integrated shoulder, elbow, forearm, wrist and finger movements. In this paper we report on a study that used multi-faceted interactive gaming simulations and adaptive robots to test the assumption that training the entire upper extremity as a unit will improve hemiparetic hand function of patients post-stroke.

2. METHODS

2.1 Hardware

All simulations in this study utilized CyberGlove[©] (Immersion) instrumented gloves for hand tracking. A CyberGrasp[©] (Immersion), a lightweight, force-reflecting exoskeleton that fits over the CyberGlove was used to facilitate individual finger movement in patients with more pronounced deficits (Fig 1). Two of the four simulations use the Flock of Birds (Ascension Technologies) motion sensors for arm tracking and the other two use the Haptic Master robot (Moog FCS Corporation) (Fig 2). Please see (S. V. Adamovich, Fluet, Mathai, et al., 2009; S. V. Adamovich, Fluet, Merians, Mathai, & Qiu, 2009) for full descriptions of the hardware.

2.2 System

Four gaming simulations were developed. They were programmed using either C++/OpenGL or the Virtools software package with the VRPack plug-in (Dassault Systemes). One game was adapted from an existing Pong game in which we transferred the game control from the computer mouse to the CyberGlove and Haptic Master. We used the Haptic Master's Application Programming Interface (API) to program the robot to produce haptic objects, including walls, blocks, cylinders, toruses and spheres as well as haptic effects, such as springs, dampers and global forces. All four simulations integrate components of upper arm movement with wrist and hand movement. In the Plasma Pong game (Fig. 3a), the pong paddle is moved vertically using shoulder flexion/extension while the moving ball is engaged using rapid finger extension. The Hummingbird Hunt simulation depicts a hummingbird as it moves through an environment filled with trees, flowers and a river (Fig.3b) providing practice in the composite movement of arm transport, hand-shaping and grasp. A pincer grip is used to catch and release the bird while it is perched on different objects located on different levels and sections of the workspace. The Hammer Task (Fig. 3c) trains three-dimensional reaching coordinated with repetitive finger flexion/ extension. The subjects reach toward a virtual wooden cylinder, stabilize their upper arm and then use either finger extension or flexion to hammer the cylinders into the floor. The Virtual Piano simulation consists of a complete virtual piano (Fig. 3d) that plays the appropriate notes as they are pressed by the virtual fingers. Please see (Merians, Tunik, & Adamovich, 2009) for full description of the simulations.

2.3 Subjects

Eleven subjects (7 male, 4 female) with a mean (SD) age of 58 (14) years, and a mean (SD) time post stroke of 6 (5) years, participated. Although all subjects met the inclusion criteria of 20° of wrist extension and 10° of finger extension of the hemiplegic hand (Wolf, et al., 2006) there were a range of impairments as shown by the Chedoke McMaster Impairment Inventory stages. The Chedoke McMaster Hand Impairment Inventory stage range was 3-6 and the Chedoke McMaster Arm Impairment Inventory stage range was 4-7. Both universities approved the protocol. Subjects trained eight days, on all four simulations during 2-3 hour sessions. Training was divided equally between the four simulations. Because of the intensity of the training and the possible fatigue effect on the hemiplegic shoulder, total training time started on day one at two hours and increased in fifteen minute increments to three hours during Week 1. Training time started and remained at three hours during Week 2.

2.4 Measurement

2.4.1 Kinematic Measures. We have designed the simulation tasks to have both discrete and continuous movements. The secondary measures were the kinematic measures obtained from the two tasks with discrete movements. The Virtual Piano Trainer and the Hammering game are discrete tasks with a definite beginning and end, making them more amendable to kinematic analyses. For the hammer task, maximal extension of

the metacarpal-phalangeal joints(MCP), duration of the combined transport and hammering phase for each cylinder, the smoothness of the endpoint movement trajectory and the deviation of the endpoint during the hammering were measured. Hand deviation was measured as the mean distance of the hand from the target during hammering (using finger flexion and extension) and is considered a measure of proximal stability and shoulder stabilization during hand-object interaction (Qiu, Fluet, Lafond, Merians, & Adamovich, 2009). For the virtual piano, accuracy, measured by the percent of correct key presses, time to complete the task (duration), and fractionation, which is the ability to isolate the movement of each finger and is measured as the difference in MCP joint angle between the cued finger and the most flexed non-cued finger (S. Adamovich, et al., 2009). For the Hammer Task four separate repeated measures ANOVAs with factor, Measurement Time (Start and End Measures) were used to evaluate changes in arm kinematics (Duration, Hand Path Length, Smoothness and Hand Deviation). For the Piano task, three separate repeated measures ANOVAs with factor, Measurement Time (Start and End Measures) were used to evaluate changes in hand kinematics (Fractionation, Duration, Accuracy).

2.4.2 Clinical Measures. Three timed clinical tests served as clinical outcome measures: Jebsen Test of Hand Function (JTHF) (Jebsen, Taylor, Trieschmann, Trotter, & Howard, 1969), the Wolf Motor Function Test (WMFT) (Wolf, et al., 2005), and the Nine Hole Peg Test (NHPT) (Mathiowetz, Volland, Kashman, & Weber, 1985) . Both the impaired and unimpaired arm/hand were tested for each clinical test. For both the WMFT and the JTHF, a maximum of 120 seconds was recorded when the subject could not perform the subtest (Charles, Wolf, Schneider, & Gordon, 2006). Similar to other reported studies, we eliminated the writing component of the JTHF (Conforto, Cohen, dos Santos, Scaff, & Marie, 2007; Merians, Poizner, Boian, Burdea, & Adamovich, 2006). In each session, the JTHF was administered three times and the mean of the three scores was used for analysis. For the 9-Hole peg test, the worst score in the group was assigned to a subject if they could not perform the test (Daltroy, et al., 1995). Stroke subjects were tested prior to training, immediately post training and at least three months after training. Subjects were at least 6 months post-stroke and reported to be neurologically stable. To confirm the stability of their motor function and absence of confounding spontaneous recovery, for each clinical test, we conducted two baseline tests on a subset (N=7), of the eleven subjects with stroke, two weeks before and one day before the onset of training. In addition, seven age-matched, neurologically healthy subjects were tested on the JTHF, at two week intervals, three times per session. ANOVAs with repeated measures of Measurement Time (Pre-test, Post-test, Retention) were used to evaluate the changes over time in the scores for each of the three timed clinical tests (JTHF, WMFT, NHPT). Finally, preplanned post-hoc comparisons, Pre-test versus Post-test and Pre-test versus Retention were made using two separate, repeated measures ANOVAs for each of the three tests. For the clinical measures, the percent change was calculated as 100 multiplied by the difference between pre and post test scores, divided by pretest scores. For kinematic measures, the percent changes were calculated in similar fashion using start and end measures.

3. RESULTS

Kinematic analyses showed that, as a group, the subjects were able to more effectively control the limb during hand interaction with the target as demonstrated by improved proximal stability, smoothness and efficiency of the movement path. This was in concert with improvement in the distal kinematic measures of fractionation and improved timing.

There was a significant decrease in the time required to hammer each peg, ($F_{1,10} = 11.9$; $p=.006$), showing a 65% change. The hand path length improved significantly ($F_{1,10} = 14.6$; $p=.003$), showing a 64% change, and there was an 81% improvement in smoothness of the trajectory ($F_{1,10} = 5.2$; $p=.05$). The improvement in movement time and path length appears to be related to changes in proximal segment function as finger extension did not change significantly. The improvements in smoothness are indicative of a decrease in the number of sub-movements required to complete the transport phase of the motion. Several authors cite this pattern of change as consistent with improvements in neuromotor control (Ferraro, et al., 2002; Rohrer, et al., 2004). A decrease in end-point deviation is an indicator of proximal stability. As a group, the subjects improved the proximal stability of the arm ($F_{1,10} = 19.2$; $p=.001$) while the fingers were repeatedly extending during the hammering task showing a 67% change in stability. Lang cites the ability to maintain proximal segments stationary during distal task performance as an important construct in overall upper extremity functional ability. Figure 4 displays the group average daily change in the piano task for accuracy of key presses (4a), average movement duration for each note in a song (4b), and finger fractionation (4c). Two subjects needed to use haptic assistance from the CyberGrasp for this activity and were therefore eliminated from the group calculations for fractionation (ability to isolate their finger movement). As a group the other nine subjects significantly improved in fractionation ($F_{1,8} = 5.2$, $p=.05$) showing a 38% change. There was a significant improvement in the time to complete the task ($F_{1,10} = 5.4$, $p=.04$) showing a 13% change without a

subsequent change in accuracy ($F_{1,10} = 54$, $p=.48$), indicating that the subjects were able to do the task faster while maintaining their accuracy. This pattern of improvement is thought to be consistent with motor learning (Krakauer, 2006).

These changes in kinematic measures were accompanied by robust changes in the clinical tests. There were statistically significant effects for each clinical test. Both pre-planned post hoc comparisons (Pre-test versus Post-test and Pre-test versus Retention) for each of the three clinical tests were also significant (Table 1). As a group, the 11 subjects showed a significant improvement in the WMFT ($F_{1,10} = 12.5$, $p=.0003$) showing a 25% (SD=11) improvement from Pre-test to Post-test. There also were significant improvements in JTHF ($F_{1,10} = 10.07$, $p=.0009$) with a 28% (15) change, and a 26% (30) change in the NHPT ($F_{1,10} = 5.14$, $p=.0158$).

As a way of interpreting the robust changes in the clinical tests, it is interesting to note that the mean (SD) decrease of 17 (7) sec. in the WMFT time (Table 1) substantially exceeds the reported group change of 2 seconds needed to be regarded as a clinically important difference on the WMFT. To indicate a true change for an individual subject in the time to complete the WMFT, that is a change beyond possible measurement error, the difference in score of an individual subject has to reach 4.36 sec (Lin, et al., 2009). In this study each subject exceeded the minimum detectable change of 4.36 seconds (range 5.7 to 33.2 sec). Additionally, Wolf et al. (2006) cite the completion of an item on a clinical test of upper extremity function at post-test, which a subject was unable to complete at pre-test, as a clinically significant change. One subject was unable to complete the checker task at pre-test but was able to do it at the retention test. This same subject was also unable to complete the picking up small objects and self feeding tasks of the JTHF at pre-test but did complete them at post-test and retention. Finally, two subjects were unable to complete the NHPT at pre-testing but were able complete it at post-testing and retention.

To evaluate the functional relevance of the observed improvement in the JTHF scores, we compared the performance of the hemiparetic arm with that of the arm ipsilateral to the lesion, as well as with the scores of nine age-matched, neurologically healthy controls. The control subjects were able to complete the six activities of the JTHF in 33 (7) sec using their dominant hand and in 36 (7) sec using their non-dominant hand. The subjects with stroke required 49 (12) sec to complete the six activities using their uninvolved hand and when using their impaired hand, improved from 161 (118) sec to 116 (78) sec with training (Fig. 5). Measures for the uninvolved hand and the controls were stable across the three time frames with only the hemiparetic hand showing improved scores.

Table 1. Clinical Measurements.

Test	Pre-Test (1) (sec)	Post-Test (2) (sec)	Retention (3) (sec)	F	P	Post Hoc (1-2) F	Post Hoc (1-2) P	Post Hoc (1-3) F	Post Hoc (1-3) P
WMFT	78 (57)	61 (54)	57(42)	7.86	.003	53.6	.0001	9.89	.01
JTHF	161 (118)	116 (78)	119(61)	5.04	.017	8.94	.014	5.19	.05
NHPT	189(174)	105(94)	100(64)	5.91	.0096	6.83	.03	6.89	.03

WMFT = Wolf Motor Function Test; JTHF = Jebsen Test of Hand Function; NHPT=Nine Hole Peg Test.

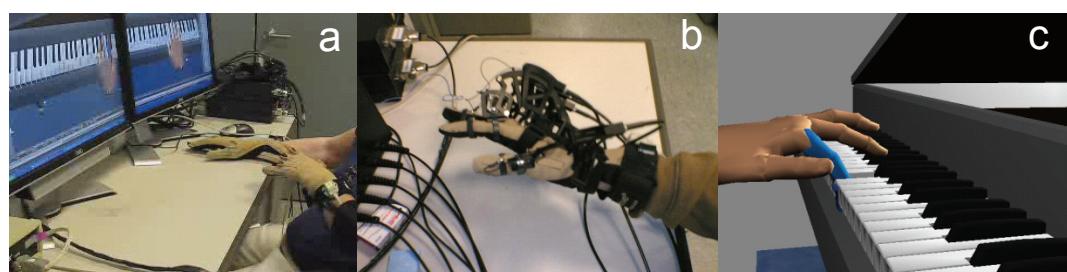


Figure 1. Virtual Piano Trainer. (a) Picture of subject wearing a CyberGlove instrumented glove using the Piano Trainer Simulation; hands shown in a first person perspective. (b) CyberGrasp haptic device worn over a CyberGlove. (c) Picture of independent finger flexion as subject moves his hand to the cued key.

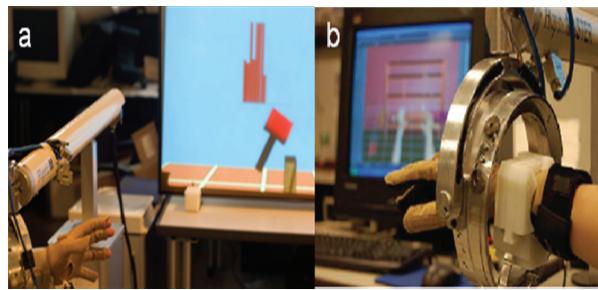


Figure 2. NJIT-RAVR System. (a) Haptic Master, a 3 degrees of freedom, admittance controlled (force controlled) robot. (b) Three more degrees of freedom (yaw, pitch and roll) can be added to the arm by using a gimbal, with force feedback available only for (roll) pronation/supination.

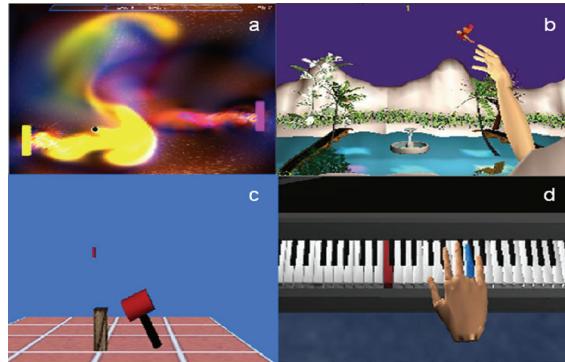


Figure 3. HAT Training Simulations. (a) Pong paddle integrates shoulder flexion/extension and finger extension. (b) Hummingbird Hunt requires composite movement of arm transport, hand-shaping and grasp. (c) Hammer Task trains reaching and repetitive finger flexion/extension. (d) The Virtual Piano simulation consists of a complete virtual piano that plays the appropriate notes as they are pressed by the virtual fingers.

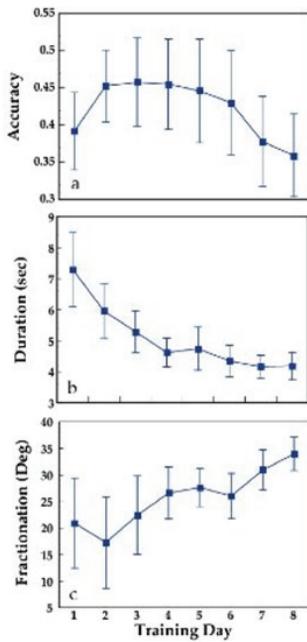


Figure 4. Virtual Piano Trainer Kinematics. (a) Describes the daily changes in the subjects as a result of practice with the Virtual Piano. (b) While maintaining the accuracy of the key presses, the subjects were able to improve the timing of the songs and (c) increase their ability to isolate individual fingers.

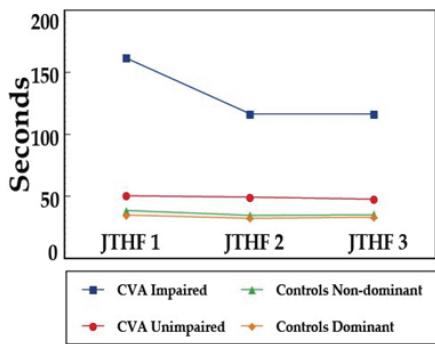


Figure 5. Changes in Jabsen Test of Hand Function Score. Describes the changes in the JTHF in the hemiparetic hand as a result of training. This is compared to the stability of the measure in the unininvolved hand and in the control subjects.

4. CONCLUSIONS

Our goal was to optimize training paradigms and enhance neuro-rehabilitation interventions. Specifically, to improve hemiparetic hand function by testing a rehabilitation paradigm that simultaneously exercised the proximal and distal components of the upper extremity using virtual reality task-based simulations interfaced with adaptive robots. Upper extremity and hand rehabilitation in particular, is a challenge in stroke rehabilitation. It remains controversial as to the most advantageous method of hand rehabilitation. It is therefore important to compare the clinical changes achieved in this study to results from other studies performed in both our lab and others. Krebs et al (2008) compared a robotically facilitated program of planar reaching tasks emphasizing proximal function to two different approaches combining robotically facilitated proximal movement integrated with manual interaction with real or simulated objects (Krebs, et al., 2008). The group training isolated proximal function made larger improvements in shoulder and elbow upper extremity Fugl -Meyer Assessment score when compared to each of the two hand and arm training groups. But those that trained the whole arm showed greater changes in the wrist/hand portion of the Fugl-Meyer. In our lab, in a former study of comparable duration, that trained the hand only, the subjects showed a 10% improvement in the time of the JTHF (Merians, et al., 2006), while in this current study that trained the arm and hand simultaneously, subjects showed a 28% change in the time needed to complete all the items on the JTHF. When we trained the hand alone, the gaming simulations were very simple activities, requiring only control of wrist and finger movement. Whereas in this study the activities required by the gaming simulations were more complex and required simultaneous control of integrated shoulder, elbow, forearm, wrist and finger movements.

Congruent with the motor learning and neuroplasticity literature, it is believed that the acquisition of a skill follows a dose-response relationship (Kwakkel, 2006). Subjects average over 500 repetitions/day in studies in the robotic rehabilitation literature (Aisen, et al., 1997; Aubert, et al., 2005; Dipietro, et al., 2008) while an observational study of the repetitions performed in a traditional outpatient setting averaged 85 (Lang, et al., 2007). The average number of repetitions during the two to three hour training sessions used in this study exceeded 2200. Each training session in this study was considerably longer than the twenty to ninety minute sessions described in the current robotic literature (Kwakkel, et al., 2008; Mehrholz, et al., 2009) and was delivered within a more concentrated time period (Daly, et al., 2005; Dipietro, et al., 2008; Fasoli, Krebs, Stein, Frontera, & Hogan, 2003; Kahn, Lum, Rymer, & Reinkensmeyer, 2006; Lum, Burgar, & Shor, 2004).

Our hypothesis for the use of a virtual reality/robotic system for rehabilitation are that in addition to providing a motivating environment for repetitive task practice, this medium can provide adaptive learning algorithms to create individualized motor learning paradigms. In this study the largest improvements demonstrated with the Virtual Piano Trainer were for finger fractionation, which is the ability to flex one finger independently of the other fingers. Fractionation is specifically reinforced with an adaptive algorithm which increases and decreases the fractionation target, based on the subjects' performance. This algorithm is described in detail elsewhere (S. Adamovich, et al., 2009). Subjects made larger improvements in fractionation than in speed or accuracy, which were not shaped with an algorithm or reinforced with feedback. These results are congruent with those of Lum et al, (Lum, et al., 2004) who found that subjects with strokes, training using the MIME system, reduced force direction errors when this construct was shaped with an algorithm.

Essential factors such as the dosage and intensity of the practice, the drive provided by specific algorithms as well as the complexity of the gaming simulations appear to have had a substantial, positive effect on our goal of improving hemiparetic hand function. In conclusion, we have designed a library of complex gaming simulations that are interfaced with robotic devices that can train the entire upper extremity of patients post-stroke. In preliminary studies, using this technology, patients with a range of sensorimotor upper extremity impairments have made robust changes in functional tests of upper extremity motor control.

Acknowledgements: This work was supported in part by NIH grant HD 42161 and by the National Institute on Disability and Rehabilitation Research RERC (Grant # H133E050011).

5. REFERENCES

- S V Adamovich, G G Fluet, A Mathai, , Q Qiu, J Lewis, & A S Merians (2009) Design of a complex virtual reality simulation to train finger motion for persons with hemiparesis: a proof of concept study. *J Neuroeng Rehabil*, **6**, 28.
- S V Adamovich, G G Fluet, A S Merians, A Mathai & Q Qiu (2009) Incorporating haptic effects into three-dimensional virtual environments to train the hemiparetic upper extremity. *IEEE Trans Neural Syst Rehabil Eng*, **17**, 5, 512-520.
- M L Aisen, H I Krebs, N Hogan, F McDowell & B T Volpe (1997). The effect of robot-assisted therapy and rehabilitative training on motor recovery following stroke. *Arch Neurol*, **54**, 4, 443-446.
- C Ansuini, M Santello, F Tubaldi, S Massaccesi & U Castiello. (2007) Control of hand shaping in response to object shape perturbation. *Exp Brain Res*, **180**, 1, 85-96.
- J R Charles, S LWolf, J A Schneider & A M Gordon. (2006) Efficacy of a child-friendly form of constraint-induced movement therapy in hemiplegic cerebral palsy: a randomized control trial. *Dev Med Child Neurol*, **48**, 8, 635-642.
- A B Conforto, L G Cohen, R L dos Santos, M Scaff & S K Marie (2007) Effects of somatosensory stimulation on motor function in chronic cortico-subcortical strokes. *J Neurol*, **254**, 3, 333-339.
- L H Daltroy, C B Phillips, H M Eaton, M G Larson, A J Partridge, M Logigan, et al. (1995) Objectively measuring physical ability in elderly persons: the Physical Capacity Evaluation. *Am J Public Health*, **85**, 4, 558-560.
- J J Daly, N Hogan, E M Perepezko, H I Krebs, J M Rogers, K S Goyal, et al. (2005) Response to upper-limb robotics and functional neuromuscular stimulation following stroke. *J Rehabil Res Dev*, **42**, 6, 723-736.
- L Dipietro, H I Krebs, S E Fasoli, B T Volpe, & N Hogan. (2008) Submovement changes characterize generalization of motor recovery after stroke. *Cortex*.
- S E Fasoli, H I Krebs, J Stein, W R Frontera, & N Hogan (2003) Effects of robotic therapy on motor impairment and recovery in chronic stroke. *Arch Phys Med Rehabil*, **84**, 4, 477-482.
- M Ferraro, J H Demaio, J Krol, C Trudell, K Rannekleiv, L Edelstein, et al. (2002) Assessing the motor status score: a scale for the evaluation of upper limb motor outcomes in patients after stroke. *Neurorehabil Neural Repair*, **16**, 3, 283-289.
- R H Jebsen, N Taylor, R B Trieschmann, M J Trotter, & L A Howard (1969) An objective and standardized test of hand function. *Arch Phys Med Rehabil*, **50**, 6, 311-319.
- L E Kahn, P S Lum, W Z Rymer & D J Reinkensmeyer (2006) Robot-assisted movement training for the stroke-impaired arm: Does it matter what the robot does? *J Rehabil Res Dev*, **43**, 5, 619-630.
- J W Krakauer (2006) Motor learning: its relevance to stroke recovery and neurorehabilitation. *Curr Opin Neurol*, **19**(1), 84-90.
- H I Krebs, S Mernoff, S E Fasoli, R Hughes, J Stein, & N Hogan. (2008) A comparison of functional and impairment-based robotic training in severe to moderate chronic stroke: a pilot study. *NeuroRehabilitation*, **23**, 1, 81-87.
- G Kwakkel (2006) Impact of intensity of practice after stroke: issues for consideration. *Disabil Rehabil*, **28**, 13-14, 823-830.
- G Kwakkel, B J Kollen, & H I Krebs (2008) Effects of robot-assisted therapy on upper limb recovery after stroke: a systematic review. *Neurorehabil Neural Repair*, **22**, 2, 111-121.

- C E Lang, J R MacDonald, & C Gnip (2007) Counting repetitions: an observational study of outpatient therapy for people with hemiparesis post-stroke. *J Neurol Phys Ther*, **31**, 1, 3-10.
- S Lennon, A Ashburn & D Baxter (2006). Gait outcome following outpatient physiotherapy based on the Bobath concept in people post stroke. *Disabil Rehabil*, **28**, 13-14, 873-881.
- M F Levin, S M Michaelsen, C M Cirstea, & A Roby-Brami (2002) Use of the trunk for reaching targets placed within and beyond the reach in adult hemiparesis. *Exp Brain Res*, **143**, 2, 171-180.
- K C Lin, Y W Hsieh, C Y Wu, C L Chen, Y Jang, & J S Liu (2009) Minimal detectable change and clinically important difference of the Wolf Motor Function Test in stroke patients. *Neurorehabil Neural Repair*, **23**, 5, 429-434.
- P S Lum, C G Burgar, & P C Shor (2004). Evidence for improved muscle activation patterns after retraining of reaching movements with the MIME robotic system in subjects with post-stroke hemiparesis. *IEEE Trans Neural Syst Rehabil Eng*, **12**, 2, 186-194.
- V Mathiowetz, G Volland, N Kashman, & K Weber (1985) Adult norms for the Box and Block Test of manual dexterity. *Am J Occup Ther*, **39**, 6, 386-391.
- J Mehrholz, T Platz, J Kugler, & M Pohl (2009) Electromechanical and Robot-Assisted Arm Training for Improving Arm Function and Activities of Daily Living After Stroke. *Stroke*.
- A S Merians, H Poizner, R Boian, G Burdea, & S Adamovich (2006). Sensorimotor training in a virtual reality environment: does it improve functional recovery poststroke? *Neurorehabil Neural Repair*, **20**, 2, 252-267.
- A S Merians, E Tunik & S V Adamovich (2009) Virtual reality to maximize function for hand and arm rehabilitation: exploration of neural mechanisms. *Stud Health Technol Inform*, **145**, 109-125.
- M Merzenich, B Wright, W Jenkins, C Xerri, N Byl, S Miller et al. (1996) Cortical plasticity underlying perceptual, motor, and cognitive skill development: implications for neurorehabilitation. *Cold Spring Harb Symp Quant Biol*, **61** 1-8.
- S M Michaelsen, S Jacobs, A Roby-Brami, & M F Levin (2004) Compensation for distal impairments of grasping in adults with hemiparesis. *Exp Brain Res*, **157**, 2, 162-173.
- SM Michaelsen, A Luta, A Roby-Brami & M F Levin (2001) Effect of trunk restraint on the recovery of reaching movements in hemiparetic patients. *Stroke*, **32**, 8, 1875-1883.
- R J Nudo, G W Milliken, W M Jenkins & M M Merzenich (1996) Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. *J Neurosci*, **16**, 2, 785-807.
- E J Plautz, G W Milliken & R J Nudo (2000) Effects of repetitive motor training on movement representations in adult squirrel monkeys: role of use versus learning. *Neurobiol Learn Mem*, **74**, 1, 27-55.
- Q Qiu, GG Fluet, I Lafond, A S Merians & S V Adamovich (2009) Coordination changes demonstrated by subjects with hemiparesis performing hand-arm training using the NJIT-RAVR robotically assisted virtual rehabilitation system. *Conf Proc IEEE Eng Med Biol Soc*, 1143-1146.
- B Rohrer, S Fasoli, H I Krebs, B Volpe, W R Frontera, J Stein, et al. (2004) Submovements grow larger, fewer, and more blended during stroke recovery. *Motor Control*, **8**, 4, 472-483.
- S L Wolf, P A Thompson, D M Morris, D K Rose, C J Weinstein, E Taub, et al. (2005). The EXCITE trial: attributes of the Wolf Motor Function Test in patients with subacute stroke. *Neurorehabil Neural Repair*, **19**, 3, 194-205.
- S L Wolf, C J Weinstein, J P Miller, Taub, E., Uswatte, G., Morris, D., et al. (2006). Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *Jama*, **296**, 17, 2095-2104.