

Effects of Robotic Therapy on Motor Impairment and Recovery in Chronic Stroke

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ABSTRACT. Fasoli SE, Krebs HI, Stein J, Frontera WR, Hogan N. Effects of robotic therapy on motor impairment and recovery in chronic stroke. *Arch Phys Med Rehabil* 2003;84:477-82.

Objective: To examine whether robotic therapy can reduce motor impairment and enhance recovery of the hemiparetic arm in persons with chronic stroke.

Design: Pre-posttest design.

Setting: Rehabilitation hospital, outpatient care.

Participants: Volunteer sample of 20 persons diagnosed with a single, unilateral stroke within the past 1 to 5 years, with persistent hemiparesis.

Interventions: Robotic therapy was provided 3 times weekly for 6 weeks. Subjects able to reach robot targets were randomly assigned to sensorimotor or progressive-resistive robotic therapy groups. Robotic therapy consisted of goal-directed, planar reaching tasks to exercise the hemiparetic shoulder and elbow.

Main Outcome Measures: The Modified Ashworth Scale, Fugl-Meyer test of upper-extremity function, Motor Status Scale (MSS) score, and Medical Research Council motor power score.

Results: Evaluations by a single blinded therapist revealed statistically significant gains from admission to discharge ($P < .05$) on the Fugl-Meyer test, MSS score, and motor power score. Secondary analyses revealed group differences: the progressive-resistive therapy group experienced nonspecific improvements on wrist and hand MSS scores that were not observed in the sensorimotor group.

Conclusions: Robotic therapy may complement other treatment approaches by reducing motor impairment in persons with moderate to severe chronic impairments.

Key Words: Cerebrovascular accident; Hemiplegia; Recovery of function; Rehabilitation.

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THE DELIVERY OF REHABILITATION services has been guided by the traditional view that significant improvements in motor recovery only occur within the first year after stroke.¹ However, recent studies²⁻⁴ have shown that intensive therapeutic interventions, such as constraint-induced movement therapy (CIMT), can contribute to significantly reduced motor impairment and improved functional use of the affected arm in persons more than 1 year poststroke. Intensive use of the hemiparetic limb has been associated with cortical reorganization in primates^{5,6} and in persons with stroke-related movement disorders.^{7,8} Although research of CIMT suggests that motor function and cortical reorganization can be enhanced, only persons with high-level motor impairments (eg, some degree of active movement in the wrist and hand) have benefited thus far. It has been estimated that up to 48% of persons with stroke exhibit persistent hemiparesis that can significantly interfere with functional abilities long after stroke onset.⁹ Studies are needed to examine whether other intensive rehabilitation methods (eg, robot-assisted therapy) can produce changes in motor function and cortical reorganization in persons with moderate to severe residual motor impairments after stroke.

Recent technologic advances have made it possible to use robotic devices to provide safe and intensive rehabilitation to persons with mild to severe motor impairments after neurologic injury. Previous randomized controlled studies have shown the benefits of robot-assisted sensorimotor therapy on the upper-limb movement of persons in the acute phase of recovery after stroke.¹⁰⁻¹³ In these studies, patients receiving standard interdisciplinary inpatient rehabilitation were randomly assigned to either an experimental (robotic therapy) or control group. Inclusion criteria were that patients had been admitted to the rehabilitation hospital within 3 weeks of their first stroke, presented with moderate to severe hemiparesis in the affected limb, and were able to follow simple instructions. Patients in the experimental group received robot-assisted therapy to exercise the hemiparetic shoulder and elbow during planar reaching tasks, 4 to 5 hours weekly for 4 weeks. As they attempted to move the robot's handle toward a designated target, a video screen in front of them provided visual feedback of the target location and movement of the robot handle. If the person was unable to reach targets independently, the robot guided the hand to the target in much the same way as a therapist provides hand-over-hand assistance during conventional therapy. Patients assigned to the control group received less exposure to the robot (1-2h/wk) over 4 weeks. Patients in this group did not receive robot assistance when unable to move their arm toward targets, but could assist the hemiparetic limb with the unaffected hand as needed. These studies revealed that patients in the robotic therapy group had significant gains in motor coordination and muscle strength of the exercised shoulder and elbow that were not seen in the control group. Furthermore, Volpe et al¹² reported that these improvements were sustained over the 3-year period after inpatient hospital discharge. This finding indicates a potential long-term benefit of early robot-assisted sensorimotor therapy.

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Our long-range goal is to develop robotic technology that provides a new set of tools for the health care professionals delivering care and treatment to persons with sensory, motor, and cognitive disabilities. Our immediate focus is on the development of intensive and cost-effective robot-aided therapies for persons with motor impairments after stroke. A robot is capable of controlling and quantifying the intensity of practice and objectively measuring changes in movement kinematics and forces. Besides providing new options for treatment, this technology may further our understanding of the mechanisms that underlie the recovery of motor function after stroke, such as motor learning processes and neural reorganization. The investigation reported here complements previous research¹⁰⁻¹³ with persons in the acute phase of stroke recovery. In the present study, our primary hypothesis was that robotic therapy would significantly reduce motor impairments in persons with chronic stroke. A secondary aim, which arose from our main analysis, was to examine whether alternative forms of robotic rehabilitation (sensorimotor vs progressive-resistive) have different effects on motor impairment and recovery after stroke.

METHODS

Subjects

Based on power analyses of pilot data and a previous study,¹⁰ a conservative decision was made to include 20 subjects in the present study. Twenty community-dwelling persons with chronic stroke (16 men, 4 women) met inclusion criteria and volunteered to participate. Inclusion criteria were (1) diagnosis of a single, unilateral stroke within the past 1 to 5 years verified by brain imaging; (2) sufficient cognitive and language abilities to understand and follow instructions; and (3) stroke-related impairments in muscle strength of the affected shoulder and elbow between grades 2 and 4 on the Medical Research Council (MRC) motor power score. Subjects ranged in age from 19 to 77 years (mean \pm standard deviation [SD], 55.5 ± 17.2 y) with an average time post-stroke of 31 ± 12.1 months. Fourteen subjects had a history of right-hemisphere stroke; 6 had left-hemisphere damage. None of the subjects were engaged in conventional occupational or physical therapy programs during the experimental trials, and none had received robotic therapy before this research. All subjects gave informed consent to take part in the study. The experimental protocol was approved by the Human Studies Committee at Spaulding Rehabilitation Hospital, where the robotic therapy was provided, and by the Committee on the Use of Human Experimental Subjects of the Massachusetts Institute of Technology. Subjects were assigned to a robotic treatment group, as described later.

Measures

After subjects provided informed consent, baseline clinical evaluations to establish motor stability of the involved upper limb were administered at 2-week intervals during a 1-month observation period before robotic therapy. The same evaluation tools were used to assess the effects of robotic therapy after 3 and 6 weeks of intervention.

The Modified Ashworth Scale¹⁴ (MAS) was used to measure muscle spasticity by rating the resistance to passive stretch in 14 different muscle groups of the upper limb. The Fugl-Meyer test of upper-extremity function¹⁵ examined the presence of synergistic and isolated movement patterns and grasp. The MRC test of motor power^{16,17} measured strength in isolated muscle groups of the involved shoulder and elbow on an ordinal scale (scale range: 0, no muscle contraction; 5, normal strength). The Motor Status Scale (MSS) score¹⁸ provided a

more complete and discrete measure of upper-limb isolated movement and motor function than is possible with the Fugl-Meyer test, by grading motor abilities on a well-defined 6-point scale. The MSS score was divided into 2 scales: the first for shoulder and elbow movements (which were exercised by the robot) and the second for wrist and finger movements (which were not exercised by the robot). Reliability of these clinical evaluations has been reported.^{14,15,17,18} In addition, subjects were asked to report the amount of pain in the affected shoulder, wrist, and hand by using a Likert-type scale (range: 0, no pain; 3, pain with any motion). To ensure the consistency of testing procedures, a single, blinded therapist administered all evaluations. In addition to these clinical measures, robotic evaluations (to be used for later kinematic analyses) were administered before treatment and after 3 and 6 weeks of intervention.

Intervention

Robotic therapy was delivered with the MIT-MANUS,^{19,20,a} a novel robot specifically designed and built for clinical, neurologic applications. During therapy, the subject's hemiparetic arm was placed in a customized arm support that was then attached to the end effector (ie, handle) of the robot arm. All subjects were asked to perform goal-directed, planar reaching tasks that emphasized shoulder and elbow movements. As they attempted to move the robot's handle toward designated targets, the computer screen in front of them provided visual feedback of the target location and movement of the robot handle (fig 1). Subjects received 1 hour of robotic therapy 3 times a week for 6 weeks.

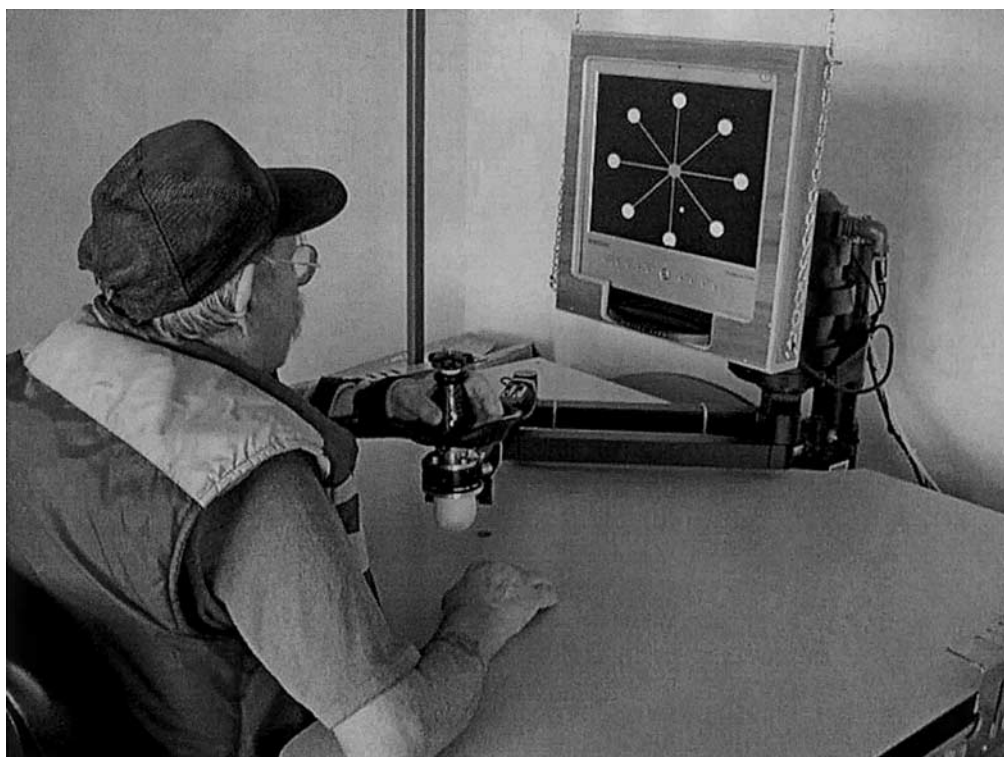
Two forms of robotic therapy (ie, sensorimotor and progressive-resistive exercise) were provided, based on the person's motor ability in the involved limb (see table 1). Subjects who were initially unable to move the robot handle to all target locations were assigned to the sensorimotor group. During this intervention, the robot provided movement assistance when the person was unable to reach the targets independently. If subjects in this group were able to independently reach all targets after 3 weeks of robotic therapy, they were randomly assigned either to continue in the sensorimotor group or to begin progressive-resistive therapy.

Subjects who were initially able to reach all targets without robot assistance were randomly assigned to the sensorimotor or to the progressive-resistive therapy group. Individuals in the progressive-resistive therapy group performed the same goal-directed, planar reaching tasks while moving against an opposing force generated by the robot. The magnitude of this opposing force was determined and modified by an adaptive algorithm that used robotic measures of the subject's muscle strength to increase or decrease the effort required to reach the targets.²¹ These measures were obtained at the end of each treatment session to determine what amount of force would be delivered by the robot during the next session. Subjects were provided with rest periods as needed throughout treatment.

Data Analyses

Repeated-measures analyses of variance (ANOVAs) were used to compare changes in pretreatment scores among the initial baseline evaluations. Paired Student *t* tests were used to assess our research hypothesis, that the changes between admission and discharge evaluation scores would be statistically significant. Our secondary aim, to examine whether the change in clinical scores between admission and discharge differed, based on the type of robotic therapy administered (ie, sensorimotor vs progressive-resistive), was addressed by means of unpaired *t* tests. Because a slight, though nonsignificant, up-

Fig 1. Person with stroke engaged in robotic therapy using MIT-MANUS.



ward trend was noted over the 3 baseline evaluations, it was decided that the third pretreatment evaluation scores would be used as the admission scores for the *t* test analyses. StatView, version 5.0.1,^b was used for data analysis. The strength, or magnitude, of our findings was determined by calculating the effect size *r*.²² According to Cohen,²² *r* equal to .10 is a small treatment effect, *r* ≥ .30 represents a moderate effect, and *r* ≥ .50 is a large effect.

RESULTS

Baseline Evaluations

No statistically significant differences were found among any of the pretreatment clinical evaluations (see table 2), suggesting the stability of chronic motor impairments in this subject group. In this sample, it appears that any subsequent changes in motor status could be attributed to effects of the robotic therapy described above.

Effects of Robotic Therapy in Chronic Stroke

Robotic therapy led to a significant reduction of motor impairment in the hemiparetic limb. Statistically significant

and large effects of therapy were indicated by the Fugl-Meyer test ($t_{19}=3.73$, $P=.001$, $r=.65$), MSS score for shoulder and elbow ($t_{19}=2.69$, $P=.01$, $r=.53$), and the MRC test of motor power ($t_{19}=5.69$, $P<.0001$, $r=.79$). A statistically significant but moderate effect of robotic therapy was found on the MSS score for the wrist and hand ($t_{19}=2.37$, $P=.03$, $r=.48$). Overall, complaints of upper-limb pain were negligible: no pain was reported in the hemiparetic wrist and hand before or after treatment. Although subjects reported less shoulder pain at discharge compared with admission, this improvement did not reach statistical significance ($t_{19}=1.55$, $P=.07$, $r=.33$). Clinically, subjects reported greater comfort when attempting to move their hemiparetic limb, and were better able to actively coordinate shoulder and elbow movements when reaching toward visual targets during robotic therapy.

A nonsignificant and small effect of robotic therapy on muscle tone was revealed by the MAS ($t_{19}=1.25$, $P=.23$, $r=.27$).

Secondary Group Analyses

Group analyses compared the clinical change scores of persons who received sensorimotor therapy ($n=13$) with those of subjects who received at least 3 weeks of progressive-resistive

Table 1: Group Assignment

| Treatment Group | n |
|---|---|
| Sensorimotor (n=13) | |
| 1. Unable to reach all targets at baseline or at 3-week evaluations* | 8 |
| 2. Able to reach all targets at baseline evaluation, randomized to sensorimotor | 4 |
| 3. Able to reach all targets at 3-week evaluation, randomized to sensorimotor | 1 |
| Progressive resistive (n=7) | |
| 1. Able to reach all targets at baseline evaluation, randomized to resistive | 4 |
| 2. Able to reach all targets at 3-week evaluation, randomized to resistive | 3 |

* These subjects were not randomly assigned to group.

Table 2: ANOVAs for Pretreatment Clinical Evaluations

| Evaluation* (possible range) | 1st Pretreatment Score (mean ± SD) | 2nd Pretreatment Score (mean ± SD) | 3rd Pretreatment Score (mean ± SD) | F _{2,18} [†] | P | r |
|----------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|--------------------------------|-----|-----|
| MAS (0–56) | 12.83±5.10 | 11.36±4.76 | 12.09±4.35 | 2.31 | .11 | .25 |
| Fugl-Meyer test (0–66) | 28.15±10.36 | 28.95±12.03 | 29.55±10.24 | 0.57 | .57 | .12 |
| MSS score: shoulder/elbow (0–40) | 24.28±5.81 | 25.01±6.13 | 25.05±6.28 | 2.08 | .14 | .24 |
| MSS score: wrist/hand (0–42) | 12.25±9.61 | 12.79±10.29 | 13.83±10.71 | 0.38 | .69 | .10 |
| MRC motor power score (0–40) | 25.40±4.65 | 26.32±4.90 | 27.20±3.96 | 1.27 | .29 | .18 |

* For all evaluations except the MAS, higher scores indicate better performance.

[†] Repeated-measures ANOVAs were performed on the change scores between the 1st and 2nd pretreatment evaluations, 2nd and 3rd pretreatment evaluations, and 1st and 3rd pretreatment evaluations. Raw scores (rather than change scores) are provided to indicate initial impairment level prior to treatment.

exercise (n=7). A statistically significant and large effect of treatment group was found for the MSS wrist and hand score ($t_{18}=3.11$, $P=.006$, $r=.59$). Subjects who received progressive-resistive therapy showed substantial improvements in wrist and hand movement that were not seen in the sensorimotor group. No significant group differences were found for the other clinical evaluation scores (see table 3) or subject age ($t_{18}=.58$, $P=.57$, $r=.13$).

DISCUSSION

These results extend previous research on robotic therapy for persons in the acute phase of stroke recovery^{10–12} to individuals with persistent, stroke-related motor impairments. Our findings suggest that intensive robotic therapy may complement other approaches, because it can significantly decrease chronic motor impairments in persons with moderate to severe upper-limb dysfunction with whom techniques such as CIMT would not be used. Although we have not yet studied the lasting effects of robotic therapy in this group, previous research¹² found that impairment reductions in persons with recent stroke were sustained up to 3 years postdischarge.

Baseline testing served as a control procedure to ensure that our subjects' motor impairments were stable before treatment and that subsequent changes in motor function could be attributed to the effects of robotic therapy. Our baseline testing procedures, similar to those used in other chronic stroke research,² also examined whether the lapse of time before therapy onset, test practice effects, and anticipation of treatment might have altered evaluation scores. The slight increase in baseline scores observed on 4 of 5 measures (see table 2) suggests that these factors should be monitored when determining baseline performance, but does not invalidate the present research findings. The lack of significant change among these baseline evaluation scores implies that these factors did not materially influence upper-limb movement in our subjects, and supports our conclusion that the observed posttreatment effect was because of robotic therapy. In addition, the relative consistency of these baseline scores suggests good test-retest reliability of our clinical measures.

The present findings add to a growing body of research^{10–13,23–25} that supports the use of focused, repetitive movement therapy to enhance motor recovery after stroke. However, the mecha-

Table 3: Change in Clinical Scores Between Admission and Discharge, by Treatment Group

| Evaluation* | Sensorimotor Group (n=13) (mean ± SD) | Progressive-Resistive Group (n=7) (mean ± SD) | t ₁₈ | P | r |
|------------------------------------|---|---|--------------------|------|-----|
| MAS | | | | | |
| Admission | 11.68±4.59 | 12.85±4.09 | | | |
| Discharge | 11.30±5.43 | 10.90±4.93 | | | |
| Change | 0.38±3.59 | 1.95±2.79 | −0.99 [†] | .33 | .23 |
| Fugl-Meyer test | | | | | |
| Admission | 29.15±11.85 | 30.29±7.06 | | | |
| Discharge | 32.30±12.96 | 34.00±9.97 | | | |
| Change | 3.15±3.63 | 3.71±4.96 | −0.29 | .77 | .07 |
| MSS score: shoulder/elbow | | | | | |
| Admission | 23.68±7.05 | 27.59±3.75 | | | |
| Discharge | 25.12±7.01 | 28.35±3.97 | | | |
| Change | 1.44±1.67 | 0.76±2.59 | 0.71 | .49 | .17 |
| MSS score: wrist/hand | | | | | |
| Admission | 13.66±10.84 | 14.16±11.33 | | | |
| Discharge | 13.81±10.81 | 16.02±11.20 | | | |
| Change | 0.15±0.98 | 1.86±1.48 | −3.11 | .006 | .59 |
| MRC motor power score [‡] | | | | | |
| Admission | 26.39±4.54 | 28.71±2.06 | | | |
| Discharge | 29.08±4.84 | 30.28±10.24 | | | |
| Change | 2.69±1.88 | 1.57±1.51 | 1.35 | .19 | .30 |

* For all evaluations except the MAS, higher scores indicate better performance.

[†] Negative t values indicate that mean change was greater for the progressive-resistive group.

[‡] MRC test of motor power was only performed for shoulder and elbow movements.

nisms that contribute to observed gains in motor performance are not fully understood. The fact that we could induce an improvement in chronic motor impairments after stroke suggests a relationship between motor recovery and motor learning, insofar as it shows a punctuated time course of the response to treatment. To the extent that motor recovery is similar to motor learning, what is known about motor learning may predict the course of motor recovery. For example, motor learning studies have shown that infants develop skilled reaching behaviors in an irregular progression. Even with a constant stimulus, the learning of skilled reach in children has been characterized by a plateau of little or no change, interspersed between periods of substantial improvement in reaching smoothness and quality of grasp.²⁶⁻²⁸ Although this incremental learning progression in children is associated with cortical development,²⁷ similar processes have been reported during motor skill acquisition in neurologically intact adults. In 2 studies, Karni et al^{29,30} proposed that procedural motor learning is a slowly evolving process that results from numerous movement repetitions over a prolonged period of time. They found that extended practice elicited delayed and incremental gains in motor performance and learning. Karni's imaging data³⁰ supported the notion that the time course of skilled learning in adults may be related to the functional properties of basic neuronal mechanisms.

We do not know whether the incremental time course of learning observed in neurologically intact individuals will generalize to motor recovery poststroke. However, the territory of stroke lesion can influence the course of motor recovery: patients with small basal ganglia lesions have a different time course of recovery than patients with mixed cortical and subcortical involvement.³¹ Those with mixed cortical and subcortical lesions showed substantially greater gains in motor coordination and strength during inpatient rehabilitation than patients with lesions confined to the basal ganglia. The course of recovery differed in persons with basal ganglia lesions: this group showed significant motor improvements during the period from inpatient discharge to 3-year follow-up that far surpassed those of persons with mixed lesions.³² These findings suggest that the time course of motor recovery can vary after stroke, and that individuals who exhibit little change in motor status early in the recovery process may, in fact, improve significantly as time progresses.

These studies of normal motor learning and stroke recovery have contributed to our proposal that there are "windows of opportunity" after stroke (corresponding to the periods of change between plateaus) in which gains in motor performance may occur. The evidence that specific and repetitive movement therapy can induce further improvement in persons with chronically stable motor impairments^{2-4,23-25} implies that the receptivity to therapeutic intervention does not end after the acute phase of stroke recovery. At the time of admission to the present study, we can infer that persons with stroke were at or near a plateau in their ability to move the affected arm. Both types of robotic therapy (sensorimotor and progressive-resistive) elicited improvement on the Fugl-Meyer test, MSS score, and the MRC test motor power, suggesting that a period of substantial change can follow a plateau in motor performance after stroke. In addition, this evidence supports the premise that the time course of motor recovery does, indeed, extend beyond the first 6 to 12 months after stroke.

The results of the present research with chronically impaired subjects differ to some degree from previous MIT-MANUS studies on persons in the acute phase of stroke recovery. It appears that this difference is not related to the chronicity of motor impairment, but to the type of robotic therapy provided.

Prior research of persons with acute^{10,11} and chronic²³ motor impairments after stroke found sensorimotor robotic therapy to elicit a training effect that was specific to the exercised limb segments. This specificity of training, another characteristic of motor learning,³³ contributed to our proposal that motor recovery is similar in some respects to motor learning. However, the present study indicated that the effects of robotic therapy were nonspecific, with significant and moderate improvements observed in the wrist and hand as well as the exercised shoulder and elbow. When we examined changes in motor performance based on the type of robotic therapy received (sensorimotor vs progressive-resistive), we found that these nonspecific effects of therapy were limited to persons who had received some duration of progressive-resistive exercise (either 3 or 6wk). In comparison, the gains in clinical scores of the sensorimotor therapy group replicated previous research: these individuals did not exhibit improved wrist and hand MSS scores.

The nonspecific effects of progressive-resistive therapy were not attributable to subject characteristics: in this sample, no significant differences in age or clinical scores were found between treatment groups. Furthermore, our randomization procedures caused some subjects to remain in the sensorimotor group for the duration of therapy, despite their ability to coordinate the movements needed to reach all targets. Notably, these subjects did not exhibit the same improvements in wrist and hand movement that were observed in persons who received progressive-resistive therapy.

Our findings imply that rather subtle differences in the type of robotic therapy had measurably different effects on motor recovery after stroke. Although the progressive-resistive training featured the same goal-directed movements practiced in the sensorimotor group, it emphasized strength in addition to coordination. Persons in the progressive-resistive group likely exerted greater distal cocontraction and muscle activation when attempting to move the robot handle toward designated targets against an opposing force. This exertion may have led to greater motor unit recruitment and contributed to increased frequency and synchronization of motor unit discharge throughout the hemiparetic arm.³⁴ Other researchers have reported strength training to have a generalized effect on motor function after stroke.^{35,36} Although we did not evaluate distal strength, gains in the MSS score for wrist and hand imply that distal muscle activation improved to some degree in the progressive-resistive therapy group. Further study is underway to validate these proposals and to delineate the therapeutic mechanisms underlying different types of robotic therapy.

A potential confound of the present study is its small sample size and the method by which the subjects were assigned to either the sensorimotor or progressive-resistive groups for our between-group analyses (see table 1). As a result, the sensorimotor group was comprised of subjects who could not be randomly assigned to the progressive-resistive group (because they were unable to move the robot handle to all targets), as well as randomly assigned subjects, who were able to move the robot handle. Furthermore, persons in the progressive-resistive group experienced different durations of strength training (3 or 6wk). As our sample size increases, we will be able to focus our between-group analyses on randomly assigned subjects who receive an equivalent duration of sensorimotor or progressive-resistive movement therapy.

The scope of our outcome measurements could be improved by including evaluations of wrist and hand strength, sensory abilities such as proprioception, and motor function of the hemiparetic limb. Including these measures could enhance our understanding of how well a reduction in motor impairment after robotic therapy generalizes to improved functional use of

the hemiparetic limb after stroke. The extension of robotic therapy to persons with less severe motor impairments, or to those at different time periods after stroke, could increase our knowledge of the mechanisms that may contribute to motor recovery.

CONCLUSION

The present study revealed statistically significant benefits of repetitive, goal-directed, robotic therapy in persons with chronic motor impairments caused by stroke. Evidence of a punctuated time course of the response to treatment, combined with therapy-specific effects in the sensorimotor group (improvement only in the exercised shoulder and elbow), suggest that motor recovery might be similar to motor learning in these respects. We acknowledge that the functional impact of these gains is small, and that improvements in proximal coordination and strength may not substantially enhance motor function of the hemiparetic arm.¹⁰⁻¹³ Our ability to elicit therapy-specific gains in shoulder and elbow movement has motivated our ongoing development of wrist and hand robots for rehabilitation. Future research will examine whether robotic technology that provides repetitive, goal-directed therapy for the wrist and hand will have similar effects on distal strength and coordinated movement, which, in turn, may have a more direct impact on motor function of the hemiparetic arm after stroke.

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Suppliers

- Interactive Motion Technologies Inc, 56 Highland Ave, Cambridge, MA 02139.
- SAS Institute Inc, SAS Campus Dr, Cary, NC 27513.