Robotics in the Rehabilitation Treatment of Patients with Stroke

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Current Atherosclerosis Reports 2002, **4:**270–276
Current Science Inc. ISSN 1523–3804

Stroke is the leading cause of permanent disability despite continued advances in prevention and novel interventional treatments. Post-stroke neuro-rehabilitation programs teach compensatory strategies that alter the degree of permanent disability. Robotic devices are new tools for therapists to deliver enhanced sensorimotor training and concentrate on impairment reduction. Results from several groups have registered success in reducing impairment and increasing motor power with task-specific exercise delivered by the robotic devices. Enhancing the rehabilitation experience with task-specific repetitive exercise marks a different approach to the patient with stroke. The clinical challenge will be to streamline, adapt, and expand the robot protocols to accommodate healthcare economies, to determine which patients sustain the greatest benefit, and to explore the relationship between impairment reduction and disability level. With these new tools, therapists will measure aspects of outcome objectively and contribute to the emerging scientific basis of neuro-rehabilitation.

Introduction

The treatment of acute stroke has registered limited success as investigators learn about the crucial requirements of appropriately timed intervention and increase the understanding of brain-hemodynamic relationships. Established stroke prevention strategies that control blood pressure, treat atrial fibrillation, and that encourage the cessation of smoking, attention to weight control, and modest exercise regimens have been effective. Although lipid levels are not a surrogate marker for stroke, emerging evidence suggests that statin therapy is associated with a reduced incidence of stroke (another of the possible benefits statins may have for the cerebrovasculature) [1,2]. Time will tell whether the addition of this new potential protection will alter the current trend upward in the incidence of stroke [3]. The combined effects of increasing life expectancy, the "Baby Boom" generation growing older, and improved medical treatment of the complications caused by acute stroke are likely to swell the ranks of the over 4 million survivors of stroke alive today. Because over 90% of the survivors of stroke have significant physical, cognitive, and psychologic impairments, the combination of which results in disability, there is an established need for new therapeutic approaches.

The Rationale for Refocusing Treatments on Impairment Reduction

The modernization of post-stroke treatment programs for motor recovery is based on new information from clinical and basic studies that favor task-specific repetitive exercise that is reproducibly administered. Robotic devices are obvious tools to deliver this enhanced sensorimotor experience, although the therapist must continue to attend to both impairment and disability reduction. Relearning ordinary activities of daily life (disability reduction) makes common sense and coincides with the patient's main concern. Healthcare economies have shortened the length of stay in treatment facilities, and the rush to discharge the patient from the rehabilitation hospital more quickly has prompted a shift toward encouraging functional improvement by learning compensatory techniques. However, unbalanced attention to disability reduction may occur at the expense of impairment reduction. For example, clinical results suggest that the hasty compensation for a disability engenders a pattern of disuse in the impaired limbs that extinguishes temporarily that aspect of recovery and mutes the potential for future impairment change, if not recovery, measured in terms of disability reduction [4–6].

Candidate Mechanisms for Recovery Depend on Environmental Experience: The Return of "Use It or Lose It"

The fundamental molecular and cellular events that underlie recovery after stroke are unknown. Potential candidate mechanisms include recovery of undamaged brain from functional inactivation caused by the damage, activation of undamaged regions of brain in the hemisphere opposite the damaged brain, and reorganization of the synaptic connections upstream and downstream from the injury. Recent information from the clinic and the laboratory suggest that some recovery of function depends on the post-injury experience, the notion that plasticity or reorganization potential is enhanced by activity in the environment. For example, several groups have described results from functional imaging of the brain in patients recovered from stroke [7–9]. There was increased blood flow in areas around the lesion in supplemental and premotor cortex, and in ipsilateral motor cortex (ipsilesional). In patients recovering from stroke, other work has tested the effect of enhanced treatment for the paralyzed arm using sequential positron emission tomography images performed while the patients had their effected limb passively moved [10•]. Increased regional activation was also observed in a functional magnetic resonance imaging task in patients recovering from stroke [11•].

Work from animal recovery models also supports the idea that training enhances recovery after damage to the central nervous system. Animals with focal cortical injury exposed to enriched or challenging sensorimotor environments registered greater anatomic responses. Other experiments in animals in which highly practiced motor tasks were interrupted by specific focal brain injury demonstrated that the motor-impaired animals exposed to the early enhanced sensorimotor training had improved functional output, sometimes nearly to levels of prelesion performance, depending on the task and lesion size [12–14].

Clinical studies using enhanced therapy sessions and measured outcome or neuroimaging information, and animal recovery studies, demonstrate that task-specific repetitive exercise abets recovery of the motor impairment after brain injury.

Rigorous Outcome Studies with Appropriate Controls Trigger the Need for New Approaches

Enhancing the sensorimotor experience reproducibly in the clinic can be daunting. Several groups have taken the challenge and demonstrated, for example, that the addition of 30 minutes of a pushing exercise of the paretic upper limb over 30 sessions to a program of post-stroke rehabilitation facilitated motor recovery of that paretic limb [15]. More general attempts to enhance rehabilitation with an "eclectic… selection of treatment techniques" also led to improved motor outcome at 6 months post-stroke, but the control group had caught up with the treatment group by 1 year [16]. Other work clearly demonstrated that specific training for the upper or lower limb led to improved outcome for the treated limbs, but not for the "untreated" limbs [17].

Present State of Therapy: An Opportunity for Technologic Experiment

Current standard interdisciplinary stroke rehabilitation treatment is labor intensive, usually relying on one-on-one, manual interactions with therapists. The studies using enhanced training are no exception. The treatment protocols rely on daily interaction over periods of weeks. For stroke, because the therapy that promotes the best recovery is unknown, most therapists use a combination of traditional techniques. Patient evaluation is usually done subjectively, making it difficult to monitor treatment effects. This situation presents an opportunity to create new technologic solutions to the problems of neuro-recovery. Robotic devices that provide safe, quantifiable, and reproducible physical activity would clearly assist healthcare delivery experts.

Whether experiments with these devices produce added value are challenges that loom large. The primary challenge is whether the robotic training has efficacy. When compared with control subjects, does enhanced sensorimotor training with robotic devices produce not only decreased impairment, but also decreased disability, and are the motor improvements long lasting? Second, and for the present beyond the scope of this debate, if these efficacy tests demonstrate effectiveness, then are there cost efficiencies that obtain as a result?

Recent data gathered by several groups concentrate on the use of upper limb robotics in patients with stroke. These studies have proposed initial design standards and have demonstrated preliminary results in over 100 patients who have had robotic sensorimotor therapy added to standard rehabilitation programs. We consider these data as an example of the potential of technology-based methods, and intentionally leave to another discussion the complementary approaches of other devices meant to enhance recovery of gait (*eg*, body weight-supported treadmill trainers [18–21], functional neuromuscular stimulation for gait training [22,23], and other functional electrical stimulation strategies for the upper limb recovery [24,25]).

Robot Training: Tools for Therapists to Increase Productivity and Quality of Care

The idea we are testing is not whether robotic devices can assist the brain-injured patient at activities of daily living, but rather whether we can improve motor outcome by equipping therapists with robotic devices to enhance the sensorimotor aspect of rehabilitation. Clinical and scientific rationales exist for added sensorimotor training during the recovery period after stroke. It is important to note that there are several different approaches to applying robotic technology. One approach is exemplified by industrial robots and emphasizes controlling robot motion so that applications that do not require controlled contact (*eg*, automobile spray-painting) are most successful and widespread. We have taken an alternative approach of controlling the dynamic relation between motion and the forces of interaction between the robot and the object it manipulates [26,27]. This strategy permits the robot manipulandum to respond rapidly and smoothly to forces exerted on

Figure 1. Patient seated in front of the MIT-Manus with her shoulders strapped to the chair and moving the manipulandum. The patient's hand is strapped to a wrist carrier attached to the manipulandum. The video screen is above the training table.

it, so that it is compliant and easy to move, emphasizing a "biologically friendly" quality [26,28]. These "back-driveable" machines also tolerate rapid or uncontrolled movement, as in tremor or myoclonus [29•], with a safety factor that exceeds the industrial designed position-controlled machines. Whether one strategy is more clinically effective than another is an empirical issue. It may be that all approaches find particular groups of patients for whom their strategy is most successful.

Experimental Results on Robotic-enhanced Rehabilitation for Stroke Recovery: Burke Institute–MIT

The Burke–MIT group subjected the upper limb robotic device to a test of clinical effectiveness for the first time some 8 years ago. The detailed results from three studies on 76 patients demonstrated that robot-trained patients had improved motor function of the paralyzed upper limb as measured by converging clinical scales compared with control subjects, and that these gains were maintained in a follow-up period of 3 years [30,31••,32••,33].

Over 100 patients have experienced robot training, and the motor improvements in the paralyzed upper limb conferred by robot training compared with control subjects have continued [34••,35••]. Figure 1 depicts a patient in front of the robotic device for treatment. For these studies, consecutive patients have been randomly assigned to a robot-treatment group or control group. Candidates were admitted to the rehabilitation hospital within 3 weeks of a first stroke, had sustained some upper limb weakness, were able to follow a few simple instructions, and gave informed consent to participate in the trial. A "measuring" therapist who was unaware of the patient's group assignment made all clinical measurements of impairment and disability. All patients underwent a standard interdisciplinary rehabilitation program; the robot treatment and control was added to the standard care program.

Robot training took place in a standard therapy suite. It was supervised by a research therapist, lasted 45 minutes (without set-up, which took about 10 minutes), and required that a patient perform 1024 flexion and extension movements of the arm with gravity eliminated in eight directions represented by the points of a compass. The training program occurred 5 days per week for 4 weeks. Control subjects had less time on the robot (1 hour per week), the motors were never turned on, and the patient moved the affected limb with the unaffected limb.

Table 1 depicts the interval change from rehabilitation admission to discharge in 96 patients. Essentially, the robot training doubles the motor recovery sustained by control subjects. Specifically, on the reliable measure of upper limb movement disability, the Fugl-Meyer (FM) score for shoulder and elbow measure (maximum=42), the robot-trained group demonstrated an advantage over the control group, but the difference was not significant. The robot-trained group demonstrated significant advantages on the Motor Status Score (MSS) for shoulder and elbow (maximum=40), which is an expanded measure of upper limb movement, a combined impairment and disability scale, and also on the Motor Power (MP) standard muscle testing (maximum=20), which is a standard assessment of individual muscle testing. In data not shown but published elsewhere [31••,32••], the motor improvement was confined to the exercised proximal limb (movements around the shoulder and elbow). There was no advantage conferred by robotic training on sensorimotor activity of the wrist and fingers. Motor performance of lower limb activity, especially gait, was comparable between groups.

The focused motor improvement for the movements that were trained is consistent with clinical results from other studies [17] and current notions about motor learning. If the motor recovery prompted by robot training reflects motor learning, then, not surprisingly, there should be limited ability to generalize performance gains beyond the conditions of training. Our data reflect that lack of change in the wrist and hand movements and gait are consistent with this point, but we have been expanding some of the measurement scales in order to test this point more specifically. The expanded MP scale is derived from the standardized testing of individual muscles. It is a 6-point scale (where 0 indicates no movement and 5 indicates normal power) and is reproducible among our therapists. For the proximal arm, there are 14 individual muscles that are tested, and kinematic analysis suggested that 10 of these muscles were directly trained and four muscles were not trained during the robot protocols. We studied our initial nine out-patients, seven of whom had less than 65% of the maximal motor power in the shoulder and elbow. These seven patients (mean 8 months after stroke) returned to receive robot training comparable with the protocol

Table 1. Interval changes* from admission to discharge

Group	Fugl Meyer S/E score (max=42)	Motor status S/E score (max=40)	Motor power score (max=20)
Robot-trained (n=56)	6.6 ± 1	8.6 ± 0.9	4.1 ± 0.4
Control (n=40)	4.9 ± 0.8	3.4 ± 0.5	2.2 ± 0.3
	Not significant	P<0.0001	P<0.005

*Indicates mean ± standard error.
max—maximum; S/E—shoulder/elbow.

Table 2. Initial and final score on the expanded Motor Power (MP) scale

Out-patient robot-trained (n=7)	Robot-trained MP (max=50)	Not robot-trained MP (max=20)
Admission (mean ± sem)	15.1 ± 3.6	4.6 ± 1
Discharge (mean ± sem)	23.9 ± 3.8	5.9 ± 1.5
Interval change, %	17.6	6.5
	P<0.05	Not significant

max—maximum; sem—standard error of mean.

described previously (*ie*, 3 days per week for 8 weeks). Table 2 depicts the preliminary information about the change in motor power in the trained muscles compared with the untrained muscles. There is a significant improvement for the trained muscles (P<0.05). These results suggest that even after time intervals longer than the generally accepted 3 months, specific training can alter the motor outcome.

These preliminary results in out-patients also point to the need for more specific outcome scales, a need generally reflected by the several investigators who have tested the effect of increased task-specific activity in post-stroke rehabilitation. Examining our composite findings with in-patients (Table 1), we were not able to discriminate an effect of robot training with the long-used and reliable FM scale for the upper extremity, but there were statistically significant improvements for the robot-trained group on the MSS and on the MP assessment. We have demonstrated that these scales are linearly related (with significant correlation, r^2 values were greater than 0.92 and P was always <0.001 [36,37]), but the FM scale lacks resolution compared with the MSS [36]. Although the MSS for the shoulder and elbow and for the wrist and fingers has been used in the past (complete evaluation forms with instructions are available upon request from the author), we needed to test directly its reliability and validity. To that end, we assembled co-investigators and therapists to learn and evaluate the MSS. Over a dozen raters from five different institutions concurrently evaluated the same patients (over 15 patients). After training on the MSS, these raters generated significant intraclass correlation coefficients and Pearson Correlation coefficients. Furthermore, the internal item consistency for the overall MSS was also significant. These results attest to the usefulness of the MSS as a sensitive, reliable, and valid scale for recording change in upper motor movements. This scale is a bridge between a measure like the MP score, which assesses individual muscle power and grades impairment, and the FM score, which measures functional movements and is closer to grading disability.

One goal is to continue to build on the clinical benchmark scores by developing objective measures. The robot can measure speed, position, and force. In preliminary observations, we have tested whether robot-measured force (in Newtons) correlates with the scores of the composite testing of muscle strength for shoulder flexion, extension, abduction, and adduction. Eighteen patients with different stroke severity and impairment level attempted to elevate and depress their arms while holding the end of the robot arm with their elbow extended. The robot was programmed to hold the position in the center of the workspace and registered the force exerted in the intended direction. For 18 patients, the mean peak force across five attempted elevation and depression movements was summed and correlated with the composite muscle strength testing with the MP score. Different therapists assessed the MP scores before and after robot testing. Figure 2 demonstrates the correlation of these measures (Y=1.1 + 1.5X, r^2=0.84; P<0.0001).

These preliminary results demonstrate the validity of the robot measures. Moreover, the potential that the robot provides for measuring precisely, repetitively, and objectively will contribute to the growing body of detailed information about change after intervention. Extracting meaningful information from the wealth of kinematic information presents formidable challenges, but at the very least some of this measurement capability represents a promise for a level of objectivity long desired in the field of neuro-rehabilitation.

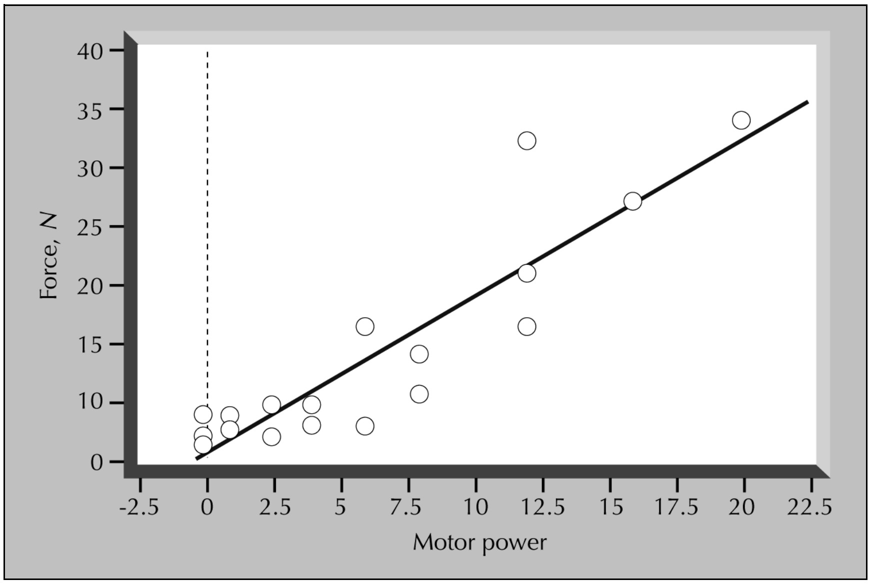

Figure 2. Relationship between a clinical benchmark measure of muscle power (Motor Power score) and the force registered by the robotic device (in Newtons). The correlation is significant ($P<0.0001$), supporting the validity of the robotic measure.

Improved Motor Outcome for Patients with Stroke Treated with Robot Training Replicated by the Palo Alto VA–Stanford and the RIC–UC Irvine Groups

Using an industrial robotic device, the Palo Alto–Stanford VA group has treated over two dozen patients 6 months to 2 years after stroke [38,39,40••,41••]. The results demonstrated that the robot-treated patients had significantly greater interval change in the FM score for the shoulder and the elbow activity and not for wrist and hand activity. The robot-trained patients also demonstrated significantly improved percent change in mean strength of shoulder and elbow movements compared with control subjects. Consistent with the Burke–MIT results in patients treated within weeks of stroke, these experiments suggest that recovery may be induced, because it almost certainly continues in small increments months to years after the acute stroke.

Using a different device, the RIC–UC Irvine group has trained over a dozen patients with chronic stroke (some over 5 years after stroke) on an upper extremity-reaching paradigm. Trained subjects had improved kinematics of reach, velocity, and better control of tone, and patients produced smoother movements [42]. If smoothness or the quality of movement acquired in recovery matters to outcome, and if normal movement smoothness matters, then it appears that detailed measurements obtained only by technologic instrumentation could add another clinically important dimension. A randomized study demonstrated that control patients treated with equal number of movements directed by a therapist improved to a level comparable with those trained with the assisted robotic-movement device [43••,44••].

Conclusions

A variety of robotic approaches have favorably influenced the motor outcome for the paralyzed arm in patients with stroke. Most of the current studies were prospective and randomized, with masked therapists acting to assess outcome. The improved outcome appears concentrated in the exercised limb. In addition to the modest and focal gains in impairment reduction, some groups are finding gains in disability reduction. In the follow-up studies to date, the advantage conferred by robotic training continues for at least 3 years [31••,33]. These promising results prompt further questions. The data from several groups suggest that devices will not replace therapists, but serve as potent new tools for them to treat patients more effectively. Soon after stroke, teaching the compensatory skills contributes in large part to improved function (lowered disability). With longer survival after stroke, recent data suggest that increased sensorimotor experience may still affect the motor outcome. Whether the mechanism is central nervous system plasticity or conditioning the joints, tendons, and muscles is not clear. But a therapist armed with a device to deliver specific exercise safely and reproducibly might treat chronic impairment more effectively. These results herald a variety of robotic approaches used to enhance the sensorimotor experience of patients after stroke and other chronic conditions. It would appear that more sensorimotor training leads to better motor outcome.

Acknowledgments

The authors acknowledge support from the Burke Medical Research Institute, the USPHS (NIH, HD 36827 and 37397), and the Langeloth Foundation.

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The study enrolled 56 patients (30 robot treatment [RT] and 26 control patients) 3 weeks after stroke. Controls, measuring therapist, and design were comparable with first study. There was a significant advantage in motor power improvement for RT patients compared with control patients, but no effect on disability. Clinical characteristics and motor scores on admission, location, and size of stroke were comparable between groups. Preliminary evidence indicates that those with larger lesions improve more with RT than control therapy.

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Lesion location affected accuracy. Patients with cortical plus striatal lesion had speedy but impaired accuracy on reaching movement compared with a patient with striatal lesion alone who had slow but accurate reaching movements. Emphasis on robot treatment as a tool therapists use potentially to deliver individualized training to more than one patient. Therapist's role evolves away from labor-intensive manual capacity to supervisory and decision making.

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There were 21 patients (11 robot trained [RT]), at least 6 months, but on average 2 years, post-stroke. Patients were treated in same treatment space and all were aided by either therapist or robot. Results showed the RT group improved on standard impairment scores, and strength (maximum voluntary isometric contraction) areas not treated (*ie*, hand and wrist) did not improve. Improved performance was accompanied by better activation patterns for a subject measured as the difference between pre- and post-treatment electromyelogram activations.

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There were 27 patients (13 robot trained [RT], 14 control) greater than 6 months post-stroke. Results demonstrated that MIME was safe, and there was a trend for less pain the in affected limb in the RT group (both results similar to the high-compliance MIT-Manus device).

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Fourteen patients with stroke were randomized to robot treatment and comparable training by a therapist. Results demonstrated significant improvement in movement smoothness for the robot-trained group.