ORIGINAL ARTICLE

Robotic-Assisted Rehabilitation of the Upper Limb After Acute Stroke

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ABSTRACT. Masiero S, Celia A, Rosati G, Armani M. Robotic-assisted rehabilitation of the upper limb after acute stroke. Arch Phys Med Rehabil 2007;88:142-9.

Objective: To investigate whether early therapy with a novel robotic device can reduce motor impairment and enhance functional recovery of poststroke patients with hemiparetic and hemiplegic upper limb.

Design: A single-blind randomized controlled trial, with an 8-month follow-up.

Setting: Neurologic department and rehabilitation hospital.

Participants: Thirty-five patients with acute (≤1wk of onset), unilateral, ischemic embolic, or thrombotic stroke.

Interventions: Patients of both groups received the same dose and length per day of standard poststroke multidisciplinary rehabilitation. Patients were randomly assigned to 2 groups. The experimental group (n=17) received additional early sensorimotor robotic training, 4 hours a week for 5 weeks; the control group (n=18) was exposed to the robotic device, 30 minutes a week, twice a week, but the exercises were performed with the unimpaired upper limb. Training by robot consisted of peripheral manipulation of the shoulder and elbow of the impaired limb, correlated with visual stimuli.

Main Outcome Measures: The Fugl-Meyer Assessment (FMA) of upper-extremity function (shoulder/elbow and coordination and wrist/hand subsections) to measure each trained limb segment; the Medical Research Council (MRC) score to measure the strength of muscle force during 3 actions: shoulder abduction (MRC deltoid), elbow flexion (MRC biceps), and wrist flexion (MRC wrist flexors); the FIM instrument and its motor component; and the Trunk Control Test (TCT) and Modified Ashworth Scale (MAS).

Results: Compared with the patients in the control group, the experimental group showed significant gains in motor impairment and functional recovery of the upper limb after robot therapy, as measured by the MRC deltoid ($P \leq .05$) and biceps ($P < .05$) scores, the FMA for the proximal upper arm ($P < .05$), the FIM instrument ($P < .05$), and the FIM motor score ($P < .01$); these gains were also sustained at the 3- and 8-month follow-up. The FMA and MRC wrist flexor test findings did not differ statistically either at the end of training or at the follow-up sessions. We found no significant differences in MAS and TCT in either group in any of the evaluations. No adverse effects occurred and the robotic approach was very well accepted.

Conclusions: Patients who received robotic therapy in addition to conventional therapy showed greater reductions in motor impairment and improvements in functional abilities. Robotic therapy may therefore effectively complement standard rehabilitation from the start, by providing therapeutic support for patients with poststroke plegic and paretic upper limb.

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

RECENT STUDIES HAVE SHOWN that in Europe there are 200 to 300 new stroke cases per 100,000 every year, of whom about 30% survive with important motor deficits.[1] After the acute phase, all patients require continuous medical care and rehabilitation treatment, often necessitating one-on-one manual interaction with therapists. Optimal restoration of arm and hand motor function is essential in permitting stroke patients to independently perform activities of daily living (ADLs). Several studies have been conducted to examine the effects of the rehabilitation approach on motor and functional recovery of the hemiplegic upper arm in stroke patients, especially when provided by sensorimotor stimulation exercises.[2-4] Among the various sensorimotor exercise strategies that may be added to rehabilitation of the poststroke paralyzed upper limb, robotic-aided therapy seems to represent a novel, realistic approach. Recent technologic advances have led to the development of robotic devices to provide safe, intensive rehabilitation to persons with mild to severe motor impairments after neurologic injury.[5] The use of robotic devices in rehabilitation can provide high-intensity, repetitive, task-specific, interactive treatment of the impaired upper limb and can serve as an objective and reliable means of monitoring patient progress.[6] Robotic devices can be used to manipulate the paretic arm by high-intensity, task-specific movements rather like physical therapy exercises, that is, by repetitive movements guided through a stereotyped pattern.[7,8] Feys et al[9] have shown that highly repetitive, stereotyped movements can be effective in stroke subjects if the movements are facilitated by external forces applied to the limb. Robotic devices can also (1) provide force feedback for sensorimotor-type rehabilitative training, (2) measure speed, direction, and strength of residual voluntary activity, and (3) interactively evaluate patients' movements and assist them in moving the limb through a predetermined trajectory during a given motor task. Currently available robot-assisted neurorehabilitation systems for upper-limb rehabilitation have 2 or 3 degrees of freedom. Positive results have been achieved on clinical testing of the MIT-Manus in particular. This features a 2-degree-of-freedom robot manipulator that assists shoulder and elbow movement by guiding the patient's

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hand in the horizontal plane, while visual, auditory, and tactile feedback is provided during goal-directed movements.[10] The MIT-Manus trial showed that patients with moderate to severe poststroke upper hemiparesis who received robotic therapy (4−5h/wk, for 4wk) in addition to their traditional therapy presented less impaired shoulder and elbow function, and greater recovery of ADL function, than did patients who received no supplementary therapy. In persons with mild to severe motor impairments after neurologic injury, the robot-assisted sensorimotor therapy produced benefits in upper-limb movement in the subacute phase of recovery after stroke[11] and these improvements were sustained over a 3-year period after inpatient hospital discharge.[12] Other robotic devices used to train poststroke patients with upper-limb impairments are the Mirror-Image Motion Enabler robots,[13] developed for unrestricted unilateral or bilateral shoulder and elbow movement; the ARM guide,[14] which assists reaching in a straight-line trajectory; the Bi-Manu-Track,[15] which enables bilateral passive and active practice of forearm and wrist movements; and, more recently, the Mechatronic System for Motor Recovery After Stroke, which manipulates the wrist, elbow and shoulder.[16] Clinical application of these devices has revealed that goal-directed robot therapy can significantly improve motor abilities of the exercised limb in patients with chronic stroke.

At Padova University, we designed and developed the Neuro-Rehabilitation-Robot (NeReBot), a novel device for the treatment of poststroke upper-limb impairment.[17,18] This robotic device, unlike the other rehabilitation robots described in the literature, is based on direct-drive wire actuation. This solution can provide many benefits compared with devices characterized by a rigid structure, that is, lower costs, reduced complexity (spatial movements can be obtained despite the limited number of degrees of freedom), and a higher degree of reliability and safety. Our device can (1) perform spatial movements (flexion and extension, pronation and supination, adduction and abduction, circular) of shoulder and elbow, (2) be easily moved to the hospital room and used for early training of the upper limb after stroke, and (3) be used to intervene on patients not only in the sitting but also in the supine position.

Our long-range goal is to develop robotic technology that provides a new set of tools for health care professionals delivering care and treatment to persons with sensory, motor, and cognitive disabilities.

The aim of this study was: (1) to evaluate whether the addition of early sensorimotor training with NeReBot (starting in the acute phase of stroke recovery) to a traditional rehabilitative program enhanced motor and functional outcomes in poststroke patients with hemiparetic and hemiplegic upper limb; and (2) to assess any side effects, and patients' tolerance or acceptance of this novel approach.

This study was approved by the ethics committee of Padova University Hospital, and informed consent was obtained from all patients.

METHODS

NeReBot Device

NeReBot is a 3-degree-of-freedom wire-based robot, designed for the treatment of poststroke upper-limb impairment. The robot frame consists of a C-shaped base fitted with casters and a square-section central column. At the top of the column, 3 aluminum arms support 3 nylon wires, which are linked at one end to 3 direct-current motors. The other end of each wire is fastened to the patient's arm by means of a rigid orthosis. The patient lies in a supine position in bed or sits in a wheelchair during rehabilitative training (figs 1A, 1B).

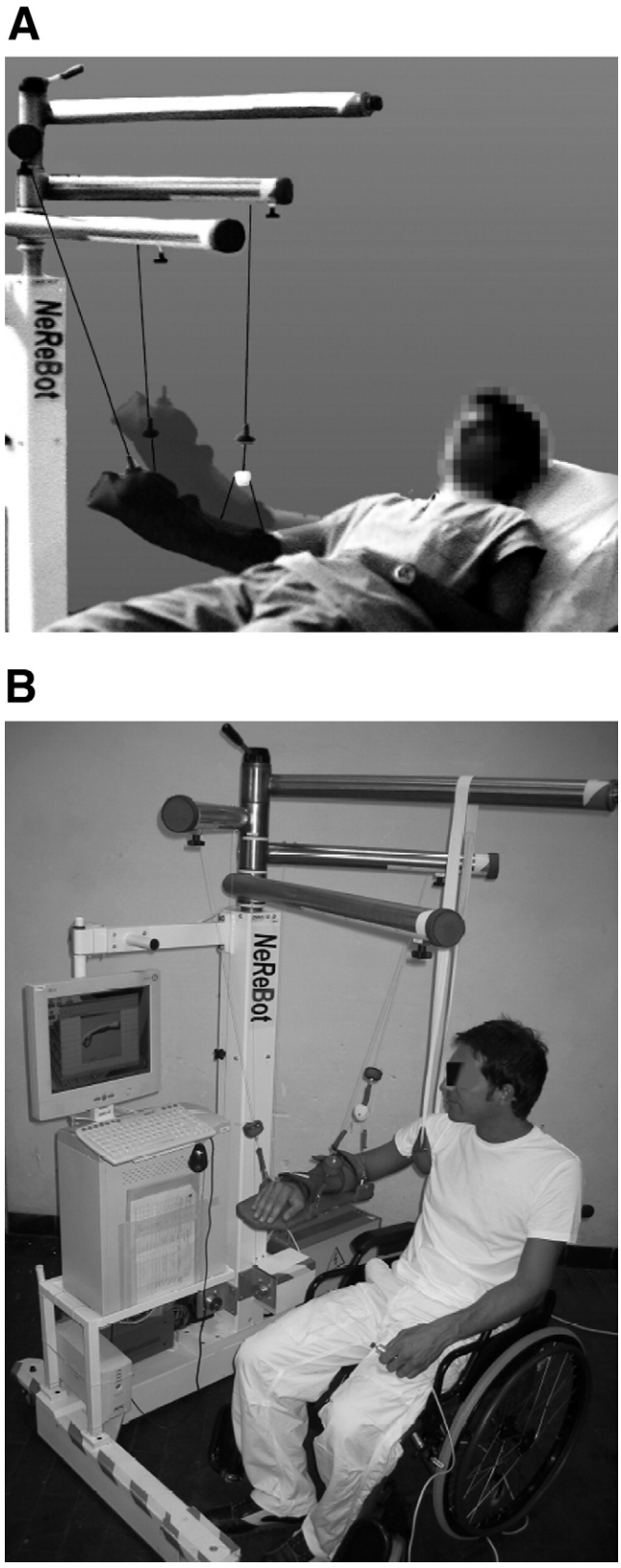

Fig 1. The patient's right forearm is fastened into the splint to receive sensorimotor stimulation with NeReBot (A) at the bedside and (B) in the sitting position.

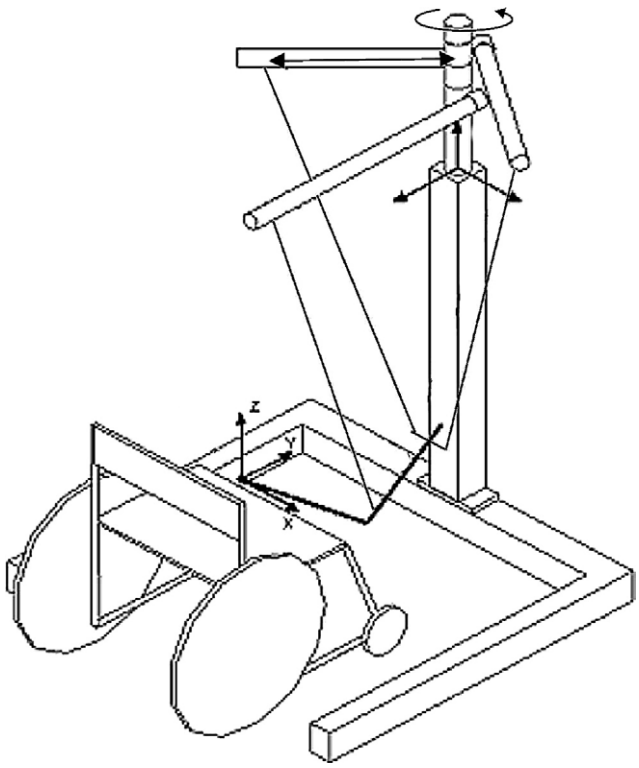

Fig 2. Diagram of the NeReBot. The angular position of each arm can be manually adjusted within a range of ±90° and the distance between each wire entry point and the main column axis can be independently set within a range of 200 to 700mm.

Wire length is controlled by individual motors. Before beginning the therapy, the operator can set the angular position of each link and the linear position of wire-entry points along the links, according to the specific needs of the patient and exercise (fig 2). The NeReBot is programmed to perform repetitive movements (flexion and extension, adduction and abduction, pronation and supination, circular) of the upper limb (shoulder and elbow), by simulating a hand-over-hand therapy with imperceptible differences in the patient's sensorimotor experience. Each exercise is recorded by manually moving the patient's forearm along a set of way points chosen by the therapist, as though the patient was being taught. Once each way point is reached, the operator stores the motor angular positions by pressing a button (learning phase). At the end of this phase, the machine control system interpolates the acquired positions (cubic-spline interpolation is used, ie, third-degree polynomial functions interpolating the way points) to obtain time-based trajectories for each motor (in other words, path planning is performed in joint space). Using these trajectories as a reference for motor position control (based on proportional integrative derivative techniques) produces very comfortable 3-dimensional motion of the patient's upper limb (therapy phase). This result is obtained by using reasonably low proportional gains in the position controllers. The control system runs on a desktop personal computer. A push button connected to a safety circuit can be operated by both therapist and patient to switch off the system's power in the event of an emergency. The control software implements both motion control and a user-friendly graphical interface, employed for setting parameters and for patient feedback. During treatment, the device provides both visual and auditory feedback to the patient. The sound is increased to signal the start and the end phase of the exercise, but it is not correlated with how the patient is performing. Visual feedback consists of a 3-dimensional image of a virtual upper limb, on which 3 arrows show the patient the forces currently applied to the limb by the wires (and hence the desired direction of motion). In this way, the patient is guided through correct execution of the exercise programmed by the physiotherapist at the start of the treatment session. This acoustic and visual feedback is also very useful in maintaining a high level of patient attention throughout the session, simulating a sort of videogame experience.

Participants

Thirty-five hemiparetic and hemiplegic patients (21 men, 14 women), consecutively admitted to the Stroke Unit of Padova Hospital after first, single, unilateral, ischemic stroke, were randomized to an experimental group (17 patients) or control group (18 patients).

We based the diagnosis of stroke on World Health Organization criteria,[19] and the following exclusion criteria were adopted for the study: (1) neurologic or cardiovascular instability contraindicating exercise (eg, uncontrolled hypertension), (2) early severe spasticity, (3) multiple cerebrovascular lesions, and (4) severe neuropsychologic impairment (global aphasia, severe attention deficit or neglect), because the patient needed to be able to follow instructions.

Outcome Measures

At baseline, we documented patient characteristics such as age, sex, side of paresis, type and onset of stroke, and associated medical conditions (arterial hypertension, hyperlipoproteinemia, diabetes, depression, obesity). We evaluated the outcome parameters before and after robot therapy, and during follow-up at 3 and 8 months after the onset of stroke.

We performed a standard assessment procedure on all the recruited patients using scales of demonstrated reliability, validity, and sensitivity to change during poststroke recovery. It included: the Medical Research Council (MRC) score, the upper-limb subsection of the Fugl-Meyer Assessment (FMA), the FIM instrument and its motor component, the Trunk Control Test (TCT), and the Modified Ashworth Scale (MAS).

The MRC is an ordinal scale for measuring strength of muscle force (range, 0 [no muscle contraction] to 5 [normal strength] for each muscle) in isolated or group muscle groups.[20] We used this scale to rate the strength of the paretic arm during 3 actions: shoulder abduction (MRC deltoid), elbow flexion (MRC biceps), and wrist flexion (MRC wrist flexors).

The FMA measures motor impairment.[21,22] The test includes items related to movements of the shoulder, elbow, forearm (proximal arm), and wrist and hand (distal arm). The total scores range between 0 and 66. We considered the shoulder/elbow and coordination subsections (42/66 items) and the wrist/hand subsection (24/66 items).

The FIM instrument uses an ordinal scale that assesses severity of motor and neuropsychologic disability, and amount of treatment needed for each patient admitted to a rehabilitation facility.[23-25] The FIM instrument is composed of 18 items divided into 6 levels (minimum score, 18; maximum score, 126 [equivalent to total functional independence]) that can be subdivided into a 13-item motor subscale (including self-care, sphincter control, mobility, locomotion) and a 5-item cognitive subscale (including communication and social cognition). The scoring ranges for the motor and cognitive subscales are 13 to 91 and 5 to 35, respectively. Each item envisages 7 levels of

performance independence (7 is total independence, 1 is total dependence or unassessable).

The TCT is a measurement scale evaluating control of trunk movements and stability. It assesses whether the patient can turn his body on the bed plane, maintain the sitting position and vary posture, yielding a score from 0 to 100.[26]

The MAS measures the muscle spasticity rate (score, 0−5); we used MAS to assess shoulder, elbow, wrist, and finger spasticity.[27]

We chose the TCT and MAS scale to check that the 2 groups were comparable at baseline.

In addition, we asked subjects to report the amount of pain they experienced in the affected shoulder; other complications, such as the development of shoulder-hand syndrome, were also recorded.

Last, at the end of robot training, we measured tolerance or acceptance of robot therapy by the visual analog scale, consisting of a 100-mm line (0, poor tolerance; 100, high tolerance). Subjects were asked to mark a point on the line describing their average degree of tolerance during robot training.

Assessments were performed for all patients involved in the study by the same blinded clinician (AC), who had previously been trained to use the scales. Physiotherapy and nursing staff had also been trained in the months prior to the survey. The clinician was not directly involved with the rehabilitative therapy (robot-assisted therapy or standard therapy) and did not know who was enrolled in the experimental or control groups.

Intervention

The patients of both groups admitted to the trial received the same dose and length per day of standard rehabilitative treatment (based on the Bobath concept) and poststroke occupational therapy by the same blinded interdisciplinary clinical team. The 17 experimental group patients received additional early sensorimotor robotic training by NeReBot, in 25 daily sessions (starting ≤1wk poststroke) divided into 2 sessions a day, 4 hours a week for 5 weeks. The control group received similar initial exposure to the robot (30min/wk twice) except that the exercises were performed with the unimpaired upper limb. The same therapist supervised the NeReBot training for all the patients; a different therapist performed standard rehabilitation.

At the start of each session, the trained researcher (therapist) sought to identify the optimal path and rest positions for each patient in the robot plane, related to individual stage of recovery, in order to fully exploit the patient's residual motor skills and provide spatial stimulation. A trained research assistant provided a standardized set of instructions and was always in attendance to indicate positions and useful trajectories of movement for the upper limb and, if necessary, to intervene in emergency situations. The robot assisted and guided the patient's forearm and hand through a repetitive pattern set by the rehabilitation team based on degree of patient impairment. All treatment sessions consisted of a sequence of motor tasks followed by a short resting phase. Patients performed 5 to 7 exercise cycles lasting 3 minutes each, followed by a 1-minute resting period (total time for each session, ≈20−30min). Patients underwent robot training treatment twice a day, 5 days a week, for at least 5 weeks. The exercise protocols focused on shoulder and elbow movement patterns and included alternative flexion and extension and pronation and supination and adduction and abduction movements (≈20 repetitions per cycle). The movements were performed slowly to avoid abnormal muscle activity that might cause pain or injury of the paretic muscle. The forearm together with the wrist and hand were placed in a neutral position in the orthosis. At the start of each therapy session the clinician examined arm impairment to investigate motor function recovery and pain or other complications. Before directing each movement during therapy, the patient was instructed to remain passive while the robot moved the limb in the programmed trajectory. The patient was then instructed to voluntarily (actively) contribute to movement by pushing or pulling according to the goals' movements. During the robot therapy session, a trained research assistant verbally encouraged the patient to increase effort. In the first week the patient was usually supine (in bed) and the daily exercises included passive repetitions along simple trajectories (eg, arm elevation). Subsequently the patient sat on a chair or in a wheelchair fitted with seat belts to limit torso movements and prevent falling. The exercise package with the impaired limb was more complex at this stage (eg, it included circular motion). Motion speed was also increased according to patient improvements. Treatment was completed in the same rehabilitation center for all recruited subjects during hospitalization and no patient underwent rehabilitative treatment elsewhere during follow-up.

Statistical Analysis

We compared the baseline characteristics of the patients in the control and experimental groups by chi-square tests (nominal data) or unpaired *t* tests for independent samples (continuous data). We performed Mann-Whitney *U* tests to identify any significant differences between average gains in score on motor impairment (FMA, MRC), functional disability (FIM, FIM motor score, TCT) and MAS in the 2 groups after robot therapy, at 3 and 8 months of follow-up. Statistical significance was set at *P* less than .05. We processed the statistics using SPSS.[a]

RESULTS

Baseline Evaluations

Mean age was 63.4±12.8 years in the experimental group and 66.8±11.5 in the control group ($P=.363$); no statistically significant differences were found among the demo-

Table 1: Patients' Demographic and Clinical Characteristics Measured at Rehabilitation Admission

Characteristics	Experimental Group (n=17)	Control Group (n=18)	*P*
Sex (male/female)	10/7	11/7	NS
Dropout (male/female)	1/1	1/2	NS
Mean age ± SD (y)	63.4±11.8	68.8±10.5	NS
Disabled limb (left/right)	4/11	5/10	NS
FMA shoulder/elbow and coordination subsections*	8.0 (4.7–15.0)	6.0 (4.0–20.5)	NS
FMA wrist/hand subsection*	(0.0–4.2)	(0.0–3.5)	NS
MRC deltoid*	1.5 (0.0–2.0)	(0.0–3.0)	NS
MRC biceps*	2.0 (0.0–4.0)	(0.0–3.2)	NS
MRC wrist flexors*	2.0 (0.0–3.5)	(0.0–3.0)	NS
FIM*	57.0 (52.0–78.2)	53.0 (48.0–73.0)	NS
FIM motor*	24.9 (20.0–39.2)	18.1 (13.4–31.2)	<.05
FIM cognitive*	15.2 (7.1–17.2)	15.0 (8.2–16.9)	NS
TCT*	42.0 (21.0–61.0)	36.0 (21.0–61.0)	NS
MAS*	0.0 (0.0–1.2)	0.0 (0.0–1.0)	NS

NOTE. Statistical analysis excluded dropout patients.
Abbreviation: NS, not significant; SD, standard deviation.
*Median (upper and lower quartile).

Table 2: Average Gains in Score in the FMA Proximal and Distal Arm and MRC Score (Deltoid, Biceps, Wrist Flexors) at the End of Robot Therapy and at the 3- and 8-Month Follow-Up Assessments in the Experimental and Control Groups

Stage of Treatment	FMA Shoulder/Elbow and Coordination Subsections	FMA Wrist/Hand Subsection	MRC Deltoid	MRC Biceps	MRC Wrist Flexors
After 1.5mo (end of robot therapy)					
Experimental group	12.8±5.5	3.0±2.6	2.1±1.1	1.3±1.3	1.8±1.3
Control group	7.5±9.5	2.8±2.6	0.7±0.8	0.9±0.8	2.0±1.5
P	<.05	NS	<.05	<.05	NS
After 3mo					
Experimental group	18.8±6.4	5.8±3.1	2.7±0.8	2.1±1.3	2.3±1.5
Control group	8.9±8.3	6.1±3.1	1.3±1.0	1.3±1.3	2.5±1.1
P	<.01	NS	<.05	<.05	NS
After 8mo					
Experimental group	20.0±7.8	6.0±3.2	3.2±1.1	2.3±1.7	2.3±1.7
Control group	10.5±13.1	5.8±3.8	1.5±0.9	1.5±1.4	2.1±1.6
P	<.01	NS	<.05	NS	NS

NOTE. Values are mean ± SD.

graphic and pretreatment clinical evaluations, except for FIM motor score, which was higher in the experimental group ($P<.05$) (table 1). Of the total of 35 patients enrolled at the start of the study, 15 experimental and 15 control group patients completed the trial; 3 subjects dropped out during the intervention, and 2 died.

Effects of Robotic Therapy

NeReBot training started on average 4.8 days (range, 3−7d) after stroke, in a neurologic ward housing a stroke unit and continued in a rehabilitation center. Mean length of stay in the neurologic ward was 12±5 days and 42±30.5 days in the rehabilitation center. The total number of days in standard rehabilitation was comparable in the 2 groups: mean rehabilitation time was 52.4±28.5 days in the experimental group and 54±31 days in the control group (*P*, not significant). Patients who received both robotic therapy and standard rehabilitation showed diminished motor impairment and enhanced functional recovery in the hemiparetic and hemiplegic limb, as summarized in tables 2 and 3. At the end of robot training (>1.5mo poststroke), we found significant effects of therapy on the FMA shoulder/elbow and coordination subsections ($P<.05$), FIM ($P<.05$), FIM motor score ($P<.01$), and MRC score for the deltoid ($P<.05$) and biceps ($P<.05$), but not for the wrist flexors ($P<0.1$). At the 3- and 8-month follow-ups, statistically significant effects of robotic therapy were sustained on the FMA shoulder/elbow and coordination subsections ($P<.01$, $P<.01$), the MRC score for deltoid ($P<.05$, $P<.05$), the FIM ($P<.01$, $P<.01$), and the FIM motor score ($P<.01$, $P<.01$), respectively (figs 3A–3C). The FMA wrist/hand subsection and MRC biceps and wrist flexor evaluation at follow-up showed a positive but not significant trend (*P* range, .094−.205). A nonsignificant effect of robotic therapy on trunk control and muscle tone was instead revealed by the MAS and TCT scores, respectively, in all the assessments (*P* range, .423−.932). No differences were found between the 2 groups in terms of joint- or tendon-related pain in the shoulder, wrist, or hand, or any other complications, including shoulder-hand syndrome (2 patients each from the experimental and control groups developed shoulder-joint pain that did not influence performance of the rehabilitation program; 1 patient from the control group developed shoulder-hand syndrome). No adverse effects occurred during robot-assisted therapy in the experimental group.

The questionnaire administered to the experimental group patients at the end of robot therapy showed that this form of intervention was well accepted and tolerated (mean score, 78.7/100). Eleven experimental group patients were in favor of including NeReBot training in the poststroke rehabilitation program.

Table 3: Average Gains in Score in the FIM, FIM Motor, TCT, and MAS at the End of Robot Therapy and at the 3- and 8-Month Follow-Up Assessments in the Experimental and Control Groups

Stage of Treatment	FIM	FIM Motor	TCT	MAS
After 1.5mo (end of robot therapy)				
Experimental group	32.6±7.2	33.5±7.5	36.7±12.3	0.13±1.4
Control group	25.5±10.5	18.5±9.5	29.8±19.8	0.13±0.9
P	<.05	<.01	NS	NS
After 3mo				
Experimental group	44.2±12.1	43.2±7.9	46.3±19.1	0.25±1.4
Control group	29.7±14.5	24.6±11.8	38.7±20.5	0.50±0.5
P	<.01	<.01	NS	NS
After 8mo				
Experimental group	46.2±10.4	44.5±14.1	46.8±18.9	0.13±1.4
Control group	31.8±14.6	26.1±14.8	37.8±24.6	0.88±1.4
P	<.01	<.01	NS	NS

NOTE. Values are mean ± SD.

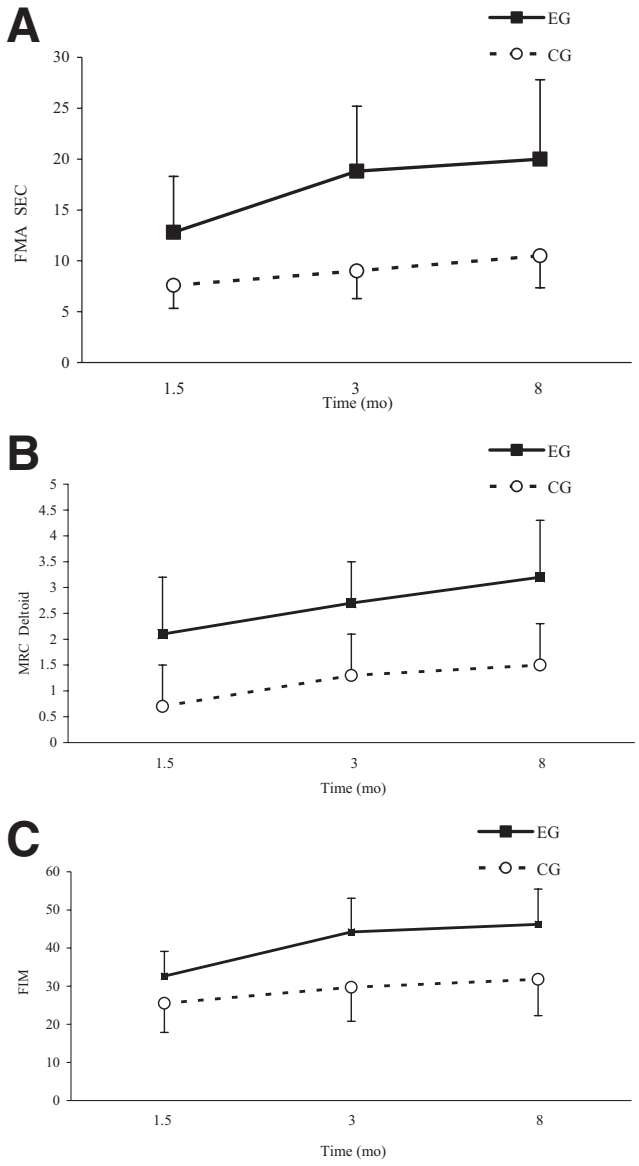

Fig 3. Average change ± standard deviation for (A) the FMA (shoulder/elbow and coordination subsections [SEC]), (B) MRC deltoid, and (C) FIM for the robot experimental (EG) and control (CG) groups at the follow-up trial.

DISCUSSION

Our findings suggest that poststroke patients exposed to early sensorimotor stimulation with NeReBot in addition to standard rehabilitation showed comparatively higher reductions in motor impairment and enhancement in paretic upper-limb function. The results are consistent with the findings of our past pilot study (conducted in a smaller number of patients with only 3mo of follow-up), which showed improved motor outcome in the exercised limb in groups of patients who had experienced robotic training by NeReBot to treat poststroke upper-limb paresis.[28] Basing comparison of the groups on clinical and neurologic variables and initial degree of impairment, we found that after early exercising with NeReBot (starting ≤1wk poststroke), at the end of robot training the experimental group patients showed significant improvements in motor and functional outcome (as measured by FMA, MRC, FIM, and FIM motor score) in the impaired upper limb. After 3 months of follow-up poststroke, the robot training group continued to show significant improvements in motor and functional recovery compared with control patients. In the 8-month period poststroke, the robot group sustained the gains recorded during the first 3 months of follow-up. This result seems to corroborate the traditional assumption that most recovery occurs within the first 3 to 6 months,[2,29] and indicates the potential long-term benefits of early robot-assisted sensorimotor therapy with NeReBot. Our results become even more meaningful considering that several investigators have reported improvements and diminished disability of the upper limb on intensification of standard physical therapy treatments in acute stroke survivors.[30,31] These results were sustained from 4 hours a week for 5 weeks of inpatient rehabilitation, with robot training starting within 1 week poststroke. The intensive movement therapies by NeReBot are capable of producing significant, sustained gains in motor function after stroke that do not end with discharge from inpatient rehabilitation. Because subjects in both groups received standard rehabilitative treatment (based on the Bobath concept) and occupational therapy by the same interdisciplinary blinded clinical team for the same dose and length of time, we can presume that intensive sensorimotor exercising with NeReBot is more effective than traditional exercising, considering that the control group did not perform this additional type of exercise. Although it is plausible that patients in the NeReBot therapy group had better outcomes simply because they received more time in therapy, other researchers have found that the type of therapy that we provided (eg, repetitive training of isolated movements, constraint-induced movement therapy, robot training) can have a greater effect on stroke-related motor impairments than can increased therapy time alone.[3,13] Indeed, our results suggest that certain characteristics of robot training contribute to enhanced recovery of upper-limb motor function. These may include task-specific practice, intensity of repetition, modalities of movements, enhanced sensory feedback, continual motivation, and others. Although we do not yet know which of these factors is most critical (these modalities were not tested separately in our work), it is apparent that robotic therapy supports further recovery. We also believe that the long-term benefits experienced by the experimental group patients were related to the type of therapy.

Robot-aided training focused on the shoulder and elbow while the wrist and hand were splinted. We examined proximal and distal components of the FMA separately to enable measurement of each trained limb segment. As a result, the robot group presented significantly greater improvements in their proximal arm FMA scores compared with the control group, but the change in distal arm FMA scores did not differ significantly between the 2 groups. In this study we performed flexion and extension, abduction and adduction, and circular exercises of the shoulder, and flexion and extension and pronation and supination of the elbow; we do not know which of these exercises is better and should be given preference, but spatial (circular or spiral) movements seem to stimulate the cortex to a greater extent in animal models.[32-34]

The maintenance of FIM scores by the experimental group at the 3- and 8-month follow-ups was unexpected. The significant improvement presented by most of our patients after robot training is particularly interesting, because gains in motor function have not always been reported to translate into significant improvement in the performance of basic self-care activities, as measured by the FIM. In fact the relationship between upper-extremity FMA and the self-care component of the FIM is

modest at best, because the FIM self-care component measures general disability and is not arm-disability specific.[35] We believe that the higher scores achieved by the experimental group on the FIM self-care subscale could be due to integration of standard rehabilitation treatment with robot therapy, which promoted higher functional recovery than in the control patients (ie, motor improvement facilitates relearning in these ADLs).

We also used TCT and MAS, respectively, to evaluate (1) whether early intensive sensorimotor stimulation can influence trunk control (even though the robot does not involve the trunk directly), or spasticity, which may worsen the disability; and (2) baseline comparability of the 2 groups. Neither the TCT nor the MAS revealed significant differences between the 2 groups at baseline and at the follow-up assessments.

The responses to the questionnaire administered at the end of robot therapy showed that this early intervention method was well accepted by the patients. The patients in the experimental group did not report experiencing any discomfort with the new treatment and were in favor of including NeReBot training in the rehabilitation program for the impaired poststroke upper limb. Last, no patient presented complications or adverse side effects related to the robot therapy, confirming the safety and reliability of our device.

In this work we have not considered stroke-lesion locus (eg, patients with small ganglia lesions vs cortical involvement) and cannot therefore assess its role in the clinical course and recovery of subjects undergoing training with NeReBot.[36,37] Likewise, we have not considered variability in length of stay, which was similar in all patients, and we assessed the results of therapy without considering financial aspects.

Our results are encouraging considering that there are many other potential advantages of robot therapy by NeReBot in these patients. First, robot-assisted movements can be performed with minimal supervision, higher intensity of therapy, 4 hours a week, and can be provided without increasing one-to-one attention from therapists. In fact once the operator has set the exercise, he can leave the patient alone with the robot and only take part in the event of an emergency. Patients' attention was kept high throughout the training session by immediate visual and acoustic feedback. Second, the robot can quantify sensorimotor input and motor outcome, reproducible practice trial delivery and controllable dose of therapy, as well as objectively measure changes in movement kinematics and forces. Third, the NeReBot enables training to start early (within the first week after stroke) because it is intrinsically safe and can be easily conducted in the hospital room, permitting rehabilitation not only in the sitting but also in the supine position. Previous robotic devices are not easy to transport and require a specific room in which to work. We feel that one of the most interesting characteristics of our NeReBot robot is the fact that it can be easily transported (or transferred) to the ward or gym for training purposes and that patients can be treated either lying down in bed or in a sitting position. These aspects, together with proven therapeutic efficacy on the upper paretic limb, mean that the device can be effectively used in rehabilitation programs.

As with other rehabilitative approaches, the specific mechanisms by which robot-aided exercise training impacts on motor deficits are not well understood. Animal models with focal cortical injury exposed to enriched or challenging sensorimotor environments showed greater anatomic responses.[38,39] Presumably, the high intensity of sensorimotor robot-aided exercises, in which the stroke patient repeatedly performs a well-defined motor task, could bring about plastic changes in the cerebral cortex.[40-42] This plasticity consists of the more robust recruitment of motoneuron pools, transfer of function from damaged areas to preserved adjacent or correlated areas, strengthening of redundant or parallel synapses, new synapse formation, increased dendritic sprouting, enhanced myelination of remaining neurons or modification of cortical and noncortical representations.[43] Basic work in animal models and clinical outcomes research suggest that activity-dependent plasticity makes an important contribution to recovery.[44-46]

The data yielded by our work are very promising, indicating that integration of robot-assisted movement into regular treatment may further enhance its effectiveness. Despite these positive results, many questions regarding robotic manipulation remain unanswered. The dose and length of training are as yet indefinite, as is the usefulness of repeating training to sustain the achieved results. Only by implementing this therapy in large numbers of patients and extending the duration of the study can we confirm these results and the long-term maintenance of benefits after robot therapy.

CONCLUSIONS

This research indicates that early sensorimotor stimulation with NeReBot may efficaciously complement standard poststroke rehabilitation by providing support for therapeutic work in patients with a plegic and paretic upper limb. The most appropriate timing, intensity, role for the therapist, and therapy duration have not yet been well defined and other studies are warranted in order to answer these questions. Moreover, a larger number of patients would enable us to better quantify the role of the therapist's intervention.

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