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SPECIAL REPORT

UPPER LIMB REHABILITATION ROBOTICS AFTER STROKE: A PERSPECTIVE FROM THE UNIVERSITY OF PADUA, ITALY

Stefano Masiero, MD[1], Elena Carraro, MD[1], Claudio Ferraro, MD[1], Paolo Gallina, Eng PhD[3], Aldo Rossi, Eng[2], and Giulio Rosati, Eng PhD[2]

From the [1]Department of Rehabilitation Medicine, University of Padua, [2]Department of Mechanical Engineering, University of Trieste and [3]Department of Innovation in Mechanics and Management, University of Padua, Padua, Italy

Rehabilitation robotics is an emerging research field that aims to employ leading-edge robotic technology and virtual reality systems in the rehabilitation treatment of neurological patients. In post-stroke patients with upper limb impairment, clinical trials have so far shown positive results in terms of motor recovery, but poor efficacy in terms of functional outcome. Much work is needed to develop a new generation of rehabilitation robots and clinical protocols that will be more effective in helping patients to regain their abilities in activities of daily living. This paper presents some key issues in the future perspective of upper limb robotic rehabilitation after stroke.

Key words: rehabilitation, stroke, robotics.

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Correspondence address: Stefano Masiero, Department of Rehabilitation Medicine (Servizio di Riabilitazione), University of Padua, Via Giustiniani 2, IT-35128 Padova, Italy. E-mail: stef.masiero@unipd.it

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INTRODUCTION

According to the World Health Organization (WHO), by 2050 the proportion of persons over 65 years old will have increased by more than 70% in the industrialized countries and by more than 200% worldwide. This age group is particularly prone to cerebro-vascular accidents, or strokes, whose relative incidence doubles every decade after the age of 55 years (1). Stroke is a leading cause of movement disability in the USA and Europe (2). Hemiparesis/hemiplegia is the most common outcome of stroke, leading to movement deficits in the limbs contralateral to the side of the brain affected by the stroke. The main characteristics observed in hemiparetic patients are: weakness of specific muscles; abnormal muscle tone; abnormal postural adjustments; lack of mobility; incorrect timing of components within a pattern; abnormal movement synergies; loss of interjoint co-ordination, and loss of sensation (3).

The rehabilitation goal in hemiplegic subjects is to promote recovery of lost function, to allow independence and early reintegration into social and domestic life. Traditional treatments rely on the use of physiotherapy that is based partially on theories and also is heavily reliant on the therapist's training and past experience. The available scientific literature suggests that rehabilitative interventions are more effective if they ensure early, intensive multisensory stimulation (4).

REHABILITATION ROBOTICS

Among different sensorimotor exercise strategies that may be added to the rehabilitation of the post-stroke paralysed upper limb, robotic therapy seems to be a novel and realistic approach, which emerged from the idea of using robots to assist people with disabilities. The idea of automatic devices was conceived on this premise, to help therapists increase the intensity of therapies operating safely within the human's workspace and with the prospective of reducing costs during their work. In other words, robotic devices have the potential to help automate repetitive training after stroke in a controlled fashion. Mechanical devices for rehabilitation are, in fact, designed to interact with the human, guiding the upper limb through repetitive exercises based on a stereotyped pattern, and providing force feedback for sensorimotor-type rehabilitative training (5). In this regard, an appropriate concept is to consider the robot as an advanced tool under the therapist's direction. As such, the robot can handle relatively simple therapies that are characterized by a repetitive and labour-intensive nature. Clinical decisions should be managed by the rehabilitation team and, when appropriate, planned and executed on the robot, and this approach would be part of an integrated set of tools that would also include simpler non-robotic approaches (6).

Robot-aided rehabilitation after stroke has been studied primarily in motor re-learning and recovery of the upper limbs. The use of robotic devices in upper limb rehabilitation can provide high-intensity, repetitive, task-specific and interactive (passive and/or active-assisted) exercises of the impaired upper limb and an objective, reliable means of monitoring patient's progress. In fact, such mechanical devices can provide a proper force feedback to guide the patient in a sensorimotor-type rehabilitative training, can measure speed, direction, and strength of the residual voluntary activity, and can interactively evaluate patients' movements and assist them in moving the limb through a predetermined trajectory during a given motor task. In this way it is possible to monitor motor and functional progress (7). In most cases, the robot is not used in a stand-alone modality and requires at least a computer interface. In order to provide a proper multisensory feedback to the patient,

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a virtual environment (including visual and acoustic feedback) is also required (6).

SOME KEY ISSUES

In post-stroke patients with upper arm impairment robotic devices can be applied in the acute, sub-acute and chronic phase. So far, most treatment protocols have focused on robot therapy in persons with chronic impairment. However, applying this approach to patients in the sub-acute phase of stroke may lead to better results in terms of clinical outcome, mainly due to the fact that the brain has added capacity for plasticity earlier after stroke. In confirmation of this, there is evidence that by integrating stroke care to include early and appropriate rehabilitation (with traditional treatment protocols) there is a reduction in mortality of approximately 20% and a reduction in severe disability of 30% (8). Feys et al. (9) emphasized the beneficial effect of intensive therapeutic interventions for the upper limb when this approach starts precociously (i.e. in the acute phase) after stroke, which was apparent one year later. In these patients, after an intensive motor and sensory stimulation, there is an improved motor recovery. In our experience, we have adopted the same concept in the development of a rehabilitation robot: the NeReBot (Neuro-Rehabilitation-roBot), a cable-suspended device for upper limb rehabilitation of post-stroke patients, which can be used even at the bedside in the very first days after the stroke (10). The clinical results of our first trial were promising in accordance with those of Feys et al. (9). The effectiveness of this approach is also supported by a recent Cochrane review by Mehrholz et al. (11), who showed that robot-assisted training in the acute and sub-acute phases (i.e. patients within 3 months after stroke) has a greater impact on the activities of daily living (ADLs) of participants, compared with robotic therapy in the chronic phase (i.e. patients more than 3 months after stroke). However, in both sub-acute and chronic phase treatment, an important goal is to try to improve the benefits of robotic therapy, by building on the initial positive results. According to Rosati et al. (12), 2 potential ways to improve the effectiveness of robotic therapy are:

- To build robotic devices that allow more natural movements. The rationale for building robotic devices that allow more natural movements is that motor training shows specificity of learning; that is, people improve most at the movements they practice (13). If the goal is to have people improve in their ability to make functional movements, then it would seem best to have patients practice functional movements. But functional movements typically use a large number of degrees of freedom of the arm and hand, thus requiring the development of more sophisticated, multiple degrees of freedom robotic therapy devices.
- To build robotic devices that are more compliant when they assist patients in moving. Compliance has long been recognized as a desirable feature for robotic therapy, for example to promote safe human robot interactions (14). Another rationale for using compliant robotic devices is that compliance preserves the causal relationship between patient effort and resulting arm movement, even when robotic assistance is provided. If the patient has the ability to influence the way an ongoing movement occurs, this may encourage patient engagement and effort. For example, a study of patient effort when training in a non-compliant robotic gait training device found that the patient consumed less energy compared with training with the compliant arms of a human therapist (15). Robot compliance may also help stimulate the motor learning process, since it allows patients to make movement errors (that would not be permitted by a stiff controller), and errors drive the motor learning process (13, 16).

In recent years, very different robotic systems and approaches have been employed for the rehabilitation treatment of the impaired upper limb in post-stroke patients. Such robots interact with the patient in real-time and can manipulate a powerless limb just like any hand-over-hand therapy. Robots used in training can be classified and/or analysed from several points of view:

- According to the part of the upper limb function on which they focus the therapy. In this respect, there are robots designed specifically for: (*i*) unilateral or bilateral shoulder movement; (*ii*) elbow movement; (*iii*) wrist movement; and (*iv*) hand movement.
- According to their mechanical characteristics, rehabilitation robots can be classified into at least 2 main groups: exoskeleton (such as the Pnew-wrex, the Arm-In, the L-Exos, etc.) and operational machines (such as the MIT-Manus, the NeReBot, etc.). As to the exoskeletons, although they mimic exactly the kinematic chain of the arm (or limb), they present some drawbacks: since arm length varies from patient to patient, it is difficult to fit different patients in the whole range of motion of the arm. As a result, a misalignment between the patient and robot joints can occur, giving the patient an unpleasant feeling. Secondly, gear reducers are usually employed to decrease the weight of the motors. As a consequence, the robot structure is stiff, and compliance must be obtained through the control system. Such problems are not present in operational machines. On the other hand, exoskeletons can easily provide information on kinematic and dynamic parameters in patient's joint-space, allowing for not only Cartesian-space but also joint-space analysis of patient's performance. Moreover, the robot can control torques at the patient-joint level.
- According to the control strategy, robots can be programmed to deliver different behaviours. In fact, robotic systems are capable of assisting the motion of the patient in a number of different modes (17): (*i*) passive movement, in which the robotic device moves the patient's arm; (*ii*) active non-assist mode, in which the subject executes the exercise and the robot provides no help; (*iii*) active assist mode, in which the subject attempts to move and the robot provides assistance when there are some voluntary but inadequate movements; (*iv*) resistive mode when the subject is required to perform an exercise against an antagonist force provided by the robot; (*v*) bimanual exercise, in which active movement

of the unaffected arm is mirrored by simultaneous active/passive/assistive movement of the affected arm by means of the robotic device. In many cases, more than one modality is incorporated into single robot devices. Given the broad range of therapy approaches currently practised in clinics, therapists face the difficult task of selecting optimal rehabilitation interventions for hemiparetic stroke survivors. One of the most basic decisions is whether or not to provide mechanical assistance during training movements for patients who are too weak or unco-ordinated to move successfully by themselves. Active-assist exercises have been employed in many clinical practices and are consistent with a task-specific exercise. In this approach, a patient will attempt to make a volitional movement while the therapist/robot provides some form of support for the limb and mechanical assistance to complete the desired movement. Two arguments support the use of active-assist therapies (18). First, helping a patient complete an arm movement stretches muscles and soft tissue, which may be helpful in reducing spasticity and preventing contracture (19). Secondly, helping a weakened patient complete a movement through a normal range of motion introduces novel sensory-motor integration that otherwise would not be experienced. This enhanced sensory stimulation might help drive neural reorganization, and enhance movement planning. Passive training can also stimulate long-term plasticity in both sensory and motor cortices of healthy subjects (20). Thus, active-assist exercises might be expected to combine the known benefits of repetitive movement exercise (21, 22) with the benefits of stretching and enhanced sensory stimulation.

Another important issue to be investigated is the impact of intensity (or dose) in robot-assisted therapy on motor recovery after stroke. We believe that high-intensity repetitive movements constitute an important contributor to the effectiveness of robot-assisted therapy. Studies that tried to match the intensity of robotic therapy to the number of movements generated by other forms of therapy failed to show a differential effect. In other words, robotic therapy had no particular advantage at low utilization, but it also did not hinder or halt recovery (18). Pilot studies suggest that an advantage of therapy by robotic devices, compared with conventional therapies, may be an increase in repetitions during arm training (16). Robot-assistive training devices therefore allow a massed practice therapy paradigm, which is intensive, frequent and repetitive, and accords with the principles of motor learning (11).

It is clear that robotic devices are helping us to gain an insight into human motor control and learning behaviour after an injury. In fact, robots can apply controlled force-fields and at the same time record the motion/force data deriving from the patient/robot interaction. In this way, since the nervous system reorganizes internal models by experience and uses them in combination with impedance and feedback control strategies, investigators are able to shed light on the nervous system models and its interaction with the external dynamic environment. In the context of robotic therapy, several principles of motor learning need to be considered:

- The modality in which the subject performs. Brain stimuli and motor gain seem to be greater in intense, active assist repetitive movements than in non-assist or passive movements (23– 25). In the active mode, the subject's effort, i.e. devotion of attention and energy to movement generation (in subjects with arm paresis) is likely to produce a larger range of motion, with superior multi-joint co-ordination, than in non-assist mode. As such, active assist mode probably generates greater proprioceptive sensory signals to the brain than does the active non-assist or passive mode. The quantity and character of such sensory signals are known to modulate motor cortex function and excitability (26). Moreover, increased afferent feedback has been considered useful for improving motor learning (27). Though active assist mode might also generate clinical benefit via other mechanisms, such as by increasing strength or by decreasing spasticity, these findings regarding dose of active robot assistance substantiate the assertion that proprioceptive feedback and sensorimotor integration are important to the effectiveness of motor-based therapies (26–28).
- The graduation of amount and typology of feedback (visual, auditory, haptic feedback) in relation to the degree of active subject movements, or to the degree of attention of the patient or active participation. In this regard, both the virtual reality interface (29), and the use of real objects in a natural or purposeful context (30) might be useful to maximize attention to the task and enhance motor performance of individuals with hemiparesis. However, there is still a lack of knowledge of the actual relationship between sensory information and patient engagement and effort. This relationship should be investigated further to dictate the design of novel robotic systems for rehabilitation.
- The multiplanarity of the exercises, which seems to induce more motor cortex excitation (7).

ENGINEERING CHALLENGES

The idea of exploiting medical robots or automatic devices in general in the rehabilitation field is relatively new. Therefore, it is premature to advance final judgements on the grade of benefit that such a technology can bring to patients with hemiparetic and hemiplegic upper limb after stroke. Two recent systematic reviews (11, 22) about patients who received electromechanical and robot-assisted arm training after stroke showed a significant improvement in upper limb motor function, but no significant improvement was found in their ADLs. Mehrholz et al. (11) reported that only when patients are treated in their acute or sub-acute phase after stroke may they expect improvements in the ADLs through robotic training. To provide common and acknowledged design guidelines requires more trials in order to compare results from different experiences. In fact, current results still do not permit us to convey to a unique optimized robotic concept, both in terms of kinematic structure and control strategies. Nonetheless, we emphasize the importance of designing robotic devices that can truly emulate the smooth interaction between the patient and the human therapist. The NeReBot (10) was designed to fit as much as possible the major requirements necessary to deliver an effective robot-patient compliant interaction. This goal was reached thanks to a cable-driven mechanism: the patient's arm is supported and manipulated by 3 wires operated independently by 3 motors. The main advantage of this design is, among others, that the compliance is given by the kinematic structure itself (which is under-actuated) and by the choice of using unilateral actuation (*compliance by design*). Wires can move (or interact with) the patient arm along a pre-planned 3D trajectory, but, at the same time, out-of-path voluntary movements are still permitted, even while robotic assistance is provided. In this way, the patient does not have the feeling of being restrained by the robot. At the same time, inertia is reduced to the minimum, requiring no sophisticated controls to recreate the feeling of a low-inertia robot.

On the contrary, when the robot structure is intrinsically stiff and fully actuated, it is necessary to develop an appropriate controller to virtually create the robot compliance (*compliance by control*). One recently proposed example (12) of such a control system is the adaptive control with forgetting designed by Wolbrecht et al. (31), who developed a compliant robot controller for the Pnew-WREX exoskeleton, starting from the observation that kinematic error drives motor learning (13, 16). This approach is particularly notable, because the design of the robot controller is based on a model of the motor learning process, so the engineer has a target to follow (to let the patient make kinematic errors), which is directly related to the clinical target of the exercise (to make the patient learn an exercise). Further design criteria based on the same philosophy, and maybe on more complex models of the motor learning process during robot-patient interaction, could be a good starting point in defining some design guidelines for rehabilitation robots. This is one of the major challenges the rehabilitation robotics researchers must face in developing a second generation of more effective rehabilitation robots.

CONCLUSION

There is evidence that robots used to assist in repetitive movement practice following neurological injury provide a significant improvement in terms of movement recovery. Robotic paradigms may enhance motor learning and rehabilitation beyond the levels possible with conventional training techniques (32). Current primary robot usage is in adult patients with paresis or paralysis post-stroke, but in the last years some trials in patients who require chronic management of neuromotor deficits have been started. We should consider, for example, the large family of neurodegenerative diseases, in particular multiple sclerosis (33) or paediatric patients with cortical lesion (34). It is desirable that, in the future, new robotic systems with innovative design will be conceived for these patients, i.e. patients with peripheral paralysis/paresis, in order to recover muscle force and movement.

As to patients after stroke, robot-assisted training should ideally stimulate motor re-learning of the impaired arm and, consequently, facilitate patients in re-learning motor skills useful in ADLs and social relationships. To date, patients can significantly improve their movement ability with training on such devices, but the improvements typically produce only a small change in functional ability, if any. From this point of view, future research will need to clarify whether through technical design and/or new treatment exercises and protocols, ADL tasks can be enhanced by robotic training.

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