Chapter 1
Emerging Perspectives in Stroke Rehabilitation

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Abstract Poststroke characteristics vary significantly between patients and over time, necessitating the introduction of individualized therapy. To provide the appropriate therapy to a patient at the correct time, several theoretical considerations must be taken into account—from a clear delineation of rehabilitation goals to an understanding of how a certain therapy can influence the underlying neuroplasticity. With regard to the differences between upper and lower limb motor recovery, both domains have experienced a change in perspective on rehabilitation.

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In gait training, assist-as-needed rehabilitation paradigms have become more pertinent, allowing each patient to find his/her individual walking rhythm and style within healthy boundaries. With the introduction of robotics in upper limb training (with or without virtual reality games that are attached), the amount of training and feedback that is provided to a patient can be increased without a rise in cost. The emerging consensus is to consider the various motor therapies and pharmacological interventions as part of a single, large toolbox instead of separate entities, guiding us toward a more patient-therapist-tailored approach, which is demonstrating tremendous efficacy.

Keywords Motor recovery · Patient-centered · Stroke rehabilitation · Technology-based interventions

1.1 Introduction

Stroke is not a uniform disease, affecting the motor, cognitive, sensorial, and somatosensory systems. How and to what extent it interferes with these systems depends on many characteristics, such as the nature (hemorrhagic vs. ischemic), location, and size (dominant side, cortical vs. subcortical, cerebral lobe) of the lesion; the condition of the patient before stroke onset; and the time poststroke.

Simply, poststroke characteristics vary between patients and over time. The high variability within and between patients has necessitated individualized rehabilitation. Regarding the current state of stroke rehabilitation, however, most therapies might fail to consider this significant heterogeneity.

Although recovery after stroke is seldom, if ever, complete (Sharma and Cohen 2012), stroke rehabilitation focuses primarily on restoring the exact patterns of movement that existed before the onset of stroke, paying little attention to compensatory strategies. Complicating this matter, the interactions between specific training and spontaneous recovery processes have not been examined extensively. In most rehabilitation centers, a general recovery pattern is projected onto each patient. Clinical studies then aim to evaluate the clinical and functional outcomes of a given therapy.

Given the high variability of stroke patients, however, it was not surprising that a recent large Cochrane review demonstrated that no rehabilitation therapy was superior, with the exception of constraint-induced movement therapy (CI) for the upper limbs (Boddice et al. 2010). Nevertheless, the highly specified inclusion and exclusion criteria of CI distinguish it from other upper limb rehabilitation methods. Thus, CI appears to have been adapted to a specific subgroup of stroke patients and can not be applied to all patients under various circumstances. Unfortunately, this therapy is seldom used in clinical settings, because the energy costs for the patient and therapist might be exorbitant.

Another important aspect that increases the variability between rehabilitation approaches is the interaction between the patient and his/her therapist. An empathic therapeutic relationship might support or interfere with the treatment, the mental state of the patient during rehabilitation, one’s tendency to collaborate, and the general psychological reaction to the stroke (Scott et al. 2012).

Various rehabilitation procedures with disparate underlying neurophysiological assumptions are routinely applied in clinical settings, despite being based on little or no evidence of efficacy (Belda-Lois et al. 2011). In the past decade, several technology-based approaches to stroke rehabilitation have been proposed (Ifejika-Jones and Barrett 2011), but evidence of their efficacy is scarce (Mehrholz et al. 2007; Morone et al. 2012). Nevertheless, the number of novel methods for stroke rehabilitation continues to rise.

This ongoing development in poststroke rehabilitation increases stroke patients’ expectations of recovery but complicates the selection of the appropriate therapy for therapists, due to a lack of treatment guidelines. Thus, a large toolbox must be developed, from pharmacological interventions to technology-based regimens, including guidelines and target specifications for each therapy. When evaluating new methods, one should focus on patient-related disabilities and the expectations and goals of the patient and his/her caregivers for rehabilitation (International Classification of Functioning, Disability and health www.who.int/classifications/icf/en/).

1.2 Current Tendencies in Poststroke Rehabilitation

1.2.1 Theoretical Considerations

After a stroke, no two patients share the same needs, which will likely change during recovery. To illustrate this concept, let us imagine two patients who are undergoing upper and lower limb rehabilitation. One might prefer to focus on the rehabilitation of walking, because the use of only the nonparetic upper limb is sufficient for his/her lifestyle. In contrast, the recovery of hand function might be more important for the other patient, if he is a potter, for example. The needs in motor recovery thus depend highly on the individual’s life perspective and habits, previous lifestyle (e.g., sportsman vs. housewife), and cognitive and mental state.

Many therapists focus primarily on the motor aspect of poststroke rehabilitation, but the influence of cognition and mental state on the potential of motor recovery can not be ignored. Motivation and attention are considered key elements in the success of motor recovery (Cramer et al. 2011). A patient needs to understand why a certain exercise is proposed—specific exercises need to make sense, and goals must be clear to enhance motivation. If one lacks the capacity to understand how an exercise is executed correctly, little effect can be expected. Further, if one is depressed and unable to see the value in recovery of motor function, focusing on such a goal might not be the most appropriate at that time.

Considering the entire interaction of the motor recovery-cognition-mental state system in a patient, it is often claimed that therapeutic interventions should be functional. To ensure adherence and maximum effort by the patient toward rehabilitation, therapeutic exercises should focus on walking or picking up a glass instead of knee flexion and elbow extension. Consistent with this approach, the Institute of Medicine (IOM) defines patient-centered care as “health care that establishes a partnership among practitioners, patients, and their families (when appropriate) to ensure that decisions respect patients’ wants, needs, and preferences and that patients have the education and support they need to make decisions and participate in their own care” (Institute of Medicine (US) 2001).

An important element of this definition is the ‘establishment of a partnership’ between the patient and caregivers to meet the needs of the former. As discussed, we would like to broaden this definition. This partnership comprises more than one individual, and all participants’ needs should be met for it to be successful and for optimal therapeutic profit to be gained.

We are faced with a necessity to develop and investigate treatment modalities that are oriented toward the specific needs of the patient-caregiver system. All developed exercises or technological interventions should be customizable and adaptable. Further, they should be accepted by the entire system. The incorporation of user criteria requires a method that implements user preferences into design specifications. User preferences, however, are related to various factors, from technical acceptance to usability and emotions that a product elicits in a patient. Thus, these complementary aspects require an integrated approach that takes them into consideration. Moreover, in the development of treatment modalities, one should reflect on the possible effect of the therapy and how the effect is established on a neurological level.

There are two chief approaches to the development of therapies for poststroke rehabilitation: BOTTOM-UP and TOP-DOWN. Whereas the former induces changes at the neural level (up) by acting on the periphery of the body (bottom), the latter focuses on neurological interventions that are based on the state of the brain after stroke to alter peripheral behavioral outcomes (Belda-Lois et al. 2011). Many exercise-based techniques are bottom-up approaches and constitute the benchmark in poststroke rehabilitation, per Bobath (Bobath and Bobath 1957), Brunnstrom (Stern et al. 1970), and Perfetti (Perfetti 2001).

However, a better understanding of the neurological physiopathology can facilitate the introduction of neuroplasticity-modulating therapies, integrating bottom-up and top-down approaches—such as pharmacological, biological, and electrophysiological techniques [e.g., transcranial magnetic stimulation (TMS), direct current stimulation (DCS), functional electric stimulation (FES), and computer-brain interfaces (CBIs)] (Dimyan and Cohen 2010).

In gaining such an understanding with regard to cortical functioning, a challenge lies in correlating brain activation patterns by electroencephalography (EEG), muscle force, electromyography (EMG), and executed movements that are sensed by motion capture (e.g., inertial measurement sensors). Further, new noninvasive brain imaging techniques, such as functional near-infrared spectroscopy (fNIRS), can be used to complement and, in some cases, overcome the technical and practical limitations of EEG as a brain-monitoring technique. Systems that are based on noninvasive methods for brain/neuronal-computer interaction (BNCI) are becoming more common in the development of robotics-based approaches to rehabilitation of motor disabilities (e.g., tremor, stroke, traumatic brain injury, cerebral palsy, multiple sclerosis, and spinal cord injuries) (Iosa et al. 2011; Pichiorri et al. 2012).

The only way to achieve this is by promoting a multidisciplinary approach, whereby researchers, therapists, and patients are challenged to look outside beyond themselves and use each other's specific knowledge to customize the poststroke rehabilitation toolbox.

Robotic-based systems are a good example of technological-based interventions. They are used and tested widely, but there is no consensus on their functional benefits, perhaps because many early-developed devices are considered 'rigid' systems that focus primarily on the strict restoration of healthy motor control to prestroke levels.

For instance, the Lokomat® was designed to treat gait, based on undamaged walking models. Stepping movements are controlled only in the sagittal plane, allowing for limited joint involvement. Considering the specificity of stroke in individuals, this general walking pattern might fail to improve walking capacity. The former physiological pattern can not be restored, because a part of brain function is lost. Instead, new connections should be established, allowing the therapy to vary and adapt to patient-specific walking patterns. As a consequence, several groups have developed walking devices that permit free exploration within boundaries, following the principle of guidance when needed (Wirz et al. 2005).

The upcoming challenge for researchers and clinicians will be to implement one optimal rehabilitation therapy to the right patient at the right time, because certain stroke patients are better responders to a specific therapy than others, solutions must be adapted to each patient. An interdisciplinary step-by-step approach begins with increasing our understanding of physiopathological mechanisms after stroke to favor training-induced plasticity by developing tools that promote functional recovery. Despite the efforts that are being made to develop rehabilitation techniques, there are no accurate guidelines or prescriptions to guide the optimal solution for each patient. One emerging concept likely relies on incorporating objective measurements into the clinical diagnosis before and during treatment to mold the therapy to a patient's individual needs (Backus et al. 2010).

1.2.2 Upper- Versus Lower Limb Motor Control

Although rehabilitation attempts to effect the maximal restoration of patient function as a whole, a distinction is usually made between upper limb and lower limb recovery. Thus, we will discuss the chief neurological processes that underlie upper and lower limb motor control. Although both extremities are involved in voluntary and automatic movements, the function of lower and upper limbs differs.

The upper limb is primarily involved in conscious goal-directed tasks, whereas the lower limb participates in semiautomatic functions, such as gait and postural control. Understanding these differences can mitigate the respective therapeutic challenges.

Movements in humans are controlled by cortical and spinal processes, the functions of which vary by task. Cortical involvement is often linked to conscious control and complex movements, whereas spinal control is generally considered ‘lower control’ for automatic processes and reflexes. For instance, spinal control primarily mediates rhythmic tasks, such as locomotion of the lower limb (Grillner and Rossignol 1978) and scratching for the upper limb (Berkowitz 2008). In contrast, voluntary movements are controlled by cortical processes (Sartori et al. 2012; Carpaneto et al. 2012).

Yet, this apparent dichotomy has been proven to be incorrect, and spinal and supraspinal mechanisms interact in both types of movement. Recent primate research has demonstrated that spinal control is involved in grasping and reaching (Alstermark and Isa 2012). Similarly, cortical processes regulate the monitoring of locomotor patterns, contain important information on the central pattern generation functioning (Cheron et al. 2012), and maintain postural stability, as observed in transcranial magnetic stimulation studies during walking (Rogers et al. 2011).

Taking into account the functional disparities above, it is not surprising that upper- and lower-limb motor control mechanisms differ. Regarding the lower limb and its primary function (gait), the reduced variability in motor pattern and the highly influential theory of central pattern generators (Grillner et al. 2005) support the proposal of locomotion-modeling algorithms (Umberger and Rubenson 2011). This theoretical framework is the foundation of various robotic tools that have been developed for the recovery of walking. Optimal trajectories have been calculated, minimizing energetic costs of the closed chain between hip, knee, ankle, and foot placement, and projected onto the system of the recovering patient.

The clinical picture of the upper limb and its main functions (reaching and grasping) is less clear, because modeling these movements is more complex. There are many effective ways and muscular activation patterns to execute a specific reaching movement successfully, particularly due to the many degrees of freedom in the upper limb. Nevertheless, various modeling approaches have been proposed (Archambault et al. 2009; d’Avella et al. 2011; Sartori et al. 2012), although there is little consensus on the matter. Further, existing models have been applied only to robotic rehabilitation devices with a motor repertoire and limited degrees of freedom (Schmidt et al. 2004).

The developing knowledge base of neurological mechanisms, plasticity, and theoretical models influences our understanding and application of therapies for each limb. Independent of the many therapeutic interventions that have been proposed, both branches of rehabilitation have been affected by the necessary change in perspective—individualizing therapy to the needs of the patient-caregivers system, based on time and severity after stroke. Thus, in the following sections, we will focus on the changing perspective from therapy-centered to client-caregiver system-centered approaches toward lower limb and upper limb rehabilitation.

1.3 Emerging Perspectives in Lower Limb Rehabilitation

1.3.1 Body Weight-Supported (BWS) Gait Rehabilitation

As discussed, lower limb rehabilitation focuses primarily on the recovery of gait. The introduction of electromechanical/robotic-assisted gait rehabilitation techniques in recent years has represented one of the main novelties in stroke rehabilitation. The two best-known robotic commercial devices that conduct ambulation training in hemiparetic patients are the Gait Trainer (GT), which controls endpoint trajectories (GT II, Rehastim, Berlin, Germany), and the Lokomat®, which integrates a robotic exoskeleton and a treadmill (Hocoma Medical Engineering Inc, Zurich, Switzerland) (Jezernik et al. 2003; Peurala et al. 2009). Both devices have been used for stroke and spinal cord injury rehabilitation. Their high cost and uncertain efficacy and the skepticism of certain clinicians have limited their use for inpatient care.

A recently updated Cochrane review (Mehrholz et al. 2007) concluded that electromechanical-assisted gait training (Lokomat® or GT) with physiotherapy raises the odds of recovery of independent walking, based on the functional ambulation category (FAC), compared with conventional therapy without significantly increasing walking velocity or walking capacity. This report included nonambulatory and ambulatory patients at various stages of stroke, from subacute to chronic. A multicenter study by Hidler et al. on Lokomat® demonstrated that conventional gait training interventions are more effective than robotic-assisted gait training in facilitating the recovery of walking ability in subacute stroke patients with moderate to severe gait impairments (Hidler et al. 2009).

The poor performance of robotic approaches might be attributed to the control algorithms that are used. In particular, control systems that are more flexible or adjustable to patients' needs appear to provide better results (Ziegler et al. 2010). This assist-as-needed (AAN) rehabilitation paradigm states that robotic interventions must be tailored to the requirements of each subject and their use minimized only to situations for which the subject truly requires them.

Regarding current assistance strategies for robotic systems, the AAN control concept encourages the active motion of a patient, wherein the robotic device intervenes only when the subject is unable to complete the movement on his/her own. AAN has thus become the benchmark for controlling robotic assistance in stroke rehabilitation. In summary, the first robotic systems used a direct approach, applying a predefined fixed pattern, whereby a patient's singularities were not taken into account; conversely, novel approaches apply the AAN concept.

AAN is assumed to stimulate activation of the efferent motor pathways and afferent sensory pathways simultaneously during training. Current AAN strategies face the significant challenge of providing an adequate definition of the desired assistance to the user during the exercise. To this end, control algorithms that are based on predetermined reference trajectories, mechanical impedance of a patient's effort, or various degrees of body weight support have been proposed (Lunenburger et al. 2004; Hesse and Werner 2009; Gizzi et al. 2012).

Robotic exoskeletons measure the force interactions at several or all joints and support the movement of the patient by reinforcing the 'correct' pattern and impeding the 'incorrect' one (Banala et al. 2009). The crucial step, however, is to define the 'correct' pattern—i.e., to define the trajectory that the robot generates while assisting the patient during the exercise. It has been proposed to return to predefined (recorded from healthy subjects) gait patterns and adapt to them, based on the mechanical impedance that is measured by the robotic device (Abdullah et al. 2007; Pei et al. 2011). An alternative method is to base on the zero-force mode, whereby the device moves compliantly to the movement of the patient (Belda-Lois et al. 2011).

Most popular available robotic devices are position-controlled or impedance-controlled, exerting lower-limb control that varies between "robot-in-charge" and "patient-in-charge." Examples of such approaches are the robot-driven gait orthosis Lokomat® and the LOPES gait rehabilitation robot (Veneman et al. 2007). Another gait trainer, the LokoHelp (Woodway, USA), has been developed to guide the feet of the patient automatically, using harnesses for various applications (Freivogel et al. 2008). The KineAssist™ was developed to increase the challenge in maintaining balance during gait training (Patton et al. 2008). The outcome of rehabilitation with these devices can be enhanced by increasing active participation of the patient in the therapy. Motivation strategies, such as biofeedback measures and virtual reality (presented below), can also improve the outcomes of these therapies.

In addition to control algorithms, other aspects should be considered in refining robotic approaches to gait rehabilitation—the nature of the stroke (hemorrhagic or ischemic), severity of symptoms, poststroke delay, frequency and duration of training, and interactions with other therapies are important elements that should be taken into account. Recent studies have highlighted the significance of this multifactorial approach, demonstrating that only a subpopulation of stroke patients might benefit from electromechanical gait training (Morone et al. 2011, 2012). Moreover, future research should also include cost estimates of the therapy. Dickstein (Dickstein 2008) noted that simple "low technology" and conventional exercises are at least as effective as more complex strategies, such as treadmill- and robotic-based interventions (Dickstein 2008).

1.3.2 Ambulatory Exoskeleton for Gait Rehabilitation

BWS-based robotic systems must be permanently installed in a room and require a treadmill. Overground gait differs substantially from treadmill gait. Further, BWS-based systems do not allow balance training or training that is focused on single joints.

To overcome these limitations, ambulatory exoskeletons are being developed. The WalkTrainer^{TM} is intended for a patient to relearn gait by combining a hybrid orthosis with functional electrical stimulation (Stauffer et al. 2009). It also supports a body weight support system. Alternatively, there is a large group of exoskeletons that support indoor over ground and treadmill walking, such as the IHMC (Institute for Human and Machine Cognition) Mobility Assist Exoskeleton (Kwa et al. 2009), the externally powered lower limb orthosis (Saito et al. 2005), and the Lower Body Exoskeleton (Costa and Caldwell 2006).

Exoskeletons can also target single joints. Thus, instead of actuating the entire lower limb, a single joint or a pair of joints, such as the knee-ankle joint with a knee-ankle–foot orthosis (KAFO) or the ankle joint with an ankle foot orthosis (AFO), is addressed. The powered KAFO is a unilateral KAFO that actuates joints by measuring surface electromyography signals from the patient (Sawicki and Ferris 2009). GAIT is a quasipassive KAFO that was developed as a low-power device (Moreno et al. 2008). The variable impedance AFO (Blaya and Herr 2004), an ambulatory version of AnkleBot (Krebs and Hogan 2006; Wheeler et al. 2004), is an AFO that impedes foot drop.

The BETTER (BNCI-Driven Robotic Physical Therapies in Stroke Rehabilitation of Gait Disorders http://www.car.upm-csic.es/bioingenieria/better/index.htm) project is attempting to develop an exoskeleton that supports entire lower limb movement and single joint approaches. BETTER comprises full and partial approaches in a single exoskeleton that is designed as a modular frame.

1.3.3 Virtual Reality and Games: A User-Centered Approach

Virtual reality is a relatively new approach in neurorehabilitation that can improve scenarios for rehabilitation. It has been defined as the “use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events” (Weiss et al. 2006).

Virtual reality might be advantageous, offering several features, such as goal-oriented tasks and the possibility for repetition, that are important in neurological rehabilitation (Dobkin 2004) and has the potential to provide an enriched environment in which stroke patients benefit from specific problem solving and master new skills. This approach has been used with a neurological rehabilitation bent to improve upper (Henderson et al. 2007) and lower extremity function and gait

(Deutsch et al. 2004), cognition, perception, and functional tasks for daily living (Rose et al. 2005). Although it is uncommon as a rehabilitation method, virtual reality is becoming more accessible and affordable (Burdea and Coiffet 2003). Further, commercial video games are a low-cost alternative (Deutsch 2011; Rand et al. 2008), and interactive video games that are geared specifically toward rehabilitation of stroke patients are being developed (Lange et al. 2010) (for a comprehensive description on virtual reality see also Chap. 13).

Recent studies indicate that robotic-assisted rehabilitation is improved by providing feedback to the patient about his/her performance during training. Virtual reality might be a useful and entertaining means with which to do so and can compensate for diminished proprioceptive capacity. To this end, new metrics that are based on kinematic, kinetic, and physiological measures are being designed and tested (Collantes et al. 2012a, b) that do not rely exclusively on the robot's sensors and can be combined with brain activity (EEG), muscular activity (EMG), and limb motion (inertial measurement units), effecting a more accurate analysis and characterization of the patient's activity, because the biofeedback does not depend on a single source of information. This feedback, based on biological signals, or biofeedback, monitors the patient's degree of activity, involvement, and compliance rendering it a valuable tool in assessing a rehabilitation therapy.

1.4 Emerging Perspectives in Upper Limb Rehabilitation

1.4.1 Examining Upper Limb Recovery

One-third to two-thirds of poststroke patients recover useful upper limb function. Clinical predictors [age, gender, lesion location, stroke volume, time to reassessment, initial Fugl-Meyer (FM) score] explain less than 50 % of the variance in recovery at 3 months poststroke (Prabhakaran et al. 2008). The best predictor of recovery over 6 months remains the initial severity of the impairment (Heller et al. 1987; Sunderland et al. 1989). Up to 86 % of the variance in impairment at 6 months (expressed as the FM) is attributed to the level of impairment at 1 month poststroke, suggesting that subacute rehabilitation has little impact on the impairment in the subsequent 5 months (Duncan et al. 1992).

Arm function at 6 months (expressed as the Barthel Index), however, is best predicted by the functional improvements in the first several weeks poststroke. Notably, only 56 % of variance is explained, which indicates that current rehabilitation strategies target the recovery of function than healing of the impairment. These findings call into question the value of compensatory strategies (Huang and Krakauer 2009) and the therapist in determining whether recovery of function or the impairment should be prioritized.

Nevertheless, the wide variability and poor predictability of recovery over the first 3 months underscore the necessity for developing individualized therapies.

The course of recovery varies tremendously between patients and clinical measurement tools (Kwakkel et al. 2006). Therapists have access to many clinical evaluation scales and tests, ranging from measurements of impairment (Fugl-Meyer, action research arm test, Jebsen-Taylor function test, box and block test, 9-hole peg test) to those of functional performance in activities of daily living (ADL) (functional independence measure, Barthel index). Due to this broad choice of scales, selecting the appropriate therapy at the right time is difficult if the therapist is unaware of the exact state of the deficit. Thus, defining the optimal rehabilitation strategy for a patient within standard therapeutic settings appears to be an impossible task.

The current challenge is to define the clinical predictors of recovery and implement the appropriate rehabilitation strategy to the correct patient at the right time. To do so, one needs to address many questions: What is the main goal of rehabilitation? On what criterion of recovery should the therapist focus? Should we focus on endpoint movements, as they are modeled, or are smooth muscle synergies more important? Is it the time course of recovery that determines the choice of therapy or the severity of the impairment? Since there are many ways to execute the same reaching movement, how do we determine which approach is correct, and what is the value of compensation?

Thus, although we lack well-established theories, a change in therapeutic attitudes has already occurred. In the following section, we will discuss two examples of shifting from the application of a fixed therapy toward a patient-system-centered approach.

1.4.2 Nontechnology-Based Interventions to Restore Interhemispheric Balance

Restoring interhemispheric balance after stroke has an important function in upper limb rehabilitation. Generally, the undamaged hemisphere inhibits the damaged counterpart, further exacerbating the functional limitations of the paretic upper limb. There are several theories on how this negative influence can be overcome: stimulating the damaged hemisphere, inhibiting the undamaged hemisphere, and forcing the 2 hemispheres to interact through bilateral training.

In the early 1990s, Dr. Edward Taub developed the constraint-induced movement therapy, a neurorehabilitation technique that improves use of the paretic upper limb after stroke by inducing plasticity in the damaged hemisphere. Essentially, the nonparetic limb is constrained, forcing the poststroke patient to use his/her paretic limb. The underlying concept behind this technique is the ‘learned nonuse’ theory: discouraged by the difficulties that are faced when using his/her paretic limb, a patient learns to use the nonparetic limb.

Learned nonuse is a type of negative feedback, and CI seeks to reverse this process (Taub and Morris 2001). Overcoming nonuse in the initial phase might be critical—Schweighofer et al. noted the existence of a threshold in recovery, predicting spontaneous use of the paretic upper limb (Schweighofer et al. 2009). When this threshold is not reached during therapy, the function is lost, rendering all therapeutic efforts vain.

In 2006, the first CI placebo-controlled trial demonstrated that after 2 weeks of intensive, treatment spontaneous paretic arm use in a real-world environment increased, as evidence by large effect sizes on the Motor Activity Log (MAL). This change did not occur in the control group, which spent as many contact-hours with the therapist but did not have their nonparetic limb constrained (Taub et al. 2006). This result was later confirmed, singling CI as the only evidence-based therapeutic intervention (Boddice et al. 2010).

The success of CI is often linked to its restrictive inclusion criteria, such as 20° active wrist extension and 10° active extension of each finger that is involved in paretic UL (Taub et al. 1998). These standards render the therapy accessible to a small percentage of stroke patients. Thus, CI is a good example of a clearly targeted therapy for a well-defined subpopulation.

Yet, the entire training program is highly intensive for the patient and therapist, and it often fails to suit the needs of the patient and his/her caregivers, resulting in limited use of CI in clinical practice. The need to overcome nonuse and increase spontaneous use, however, remains for all patients. As CI has remained a promising intervention, adaptive versions of CI have been developed, constraining the use of the less-affected limb only during specific tasks that were determined by the patient and therapist to be 'crucial' to activity of daily life (ADL) function.

Another example of a therapy that restores interhemispheric balance is bilateral arm training (BAT). BAT facilitates cortical neural plasticity by treating both arms simultaneously or cooperatively. Bimanual movements activate the primary motor corticospinal tract and are assumed to stimulate ipsilateral uncrossed fibers and facilitate neural plasticity (Cauraugh et al. 2005; de NAP Shelton and Reding 2001). Whereas overcoming nonuse is important during the initial phase of recovery (although the effects of CI have been shown primarily in chronic stroke patients), bimanual therapy is more effective when the plateau phase of motor recovery develops—i.e., when initial spontaneous recovery processes level off (Metrot et al. 2013).

Notably, Stinear et al. suggested an advantage of BAT for patients with low functional potential and poor recovery of upper limb function (Stinear et al. 2007), who are already more likely to engage the contralesional hemisphere during paretic upper limb use. By being forced to use both hands, patients might experience involvement of the contralesional hemisphere in controlling the nonparetic limb simultaneously, facilitating recruitment of the damaged hemisphere.

Thus, CI and BAT restore hemispheric balance, albeit through disparate means and on different time scales. Both therapies have similar benefits on movement smoothness but differential effects on force and functional performance. BAT might be preferred if improvement of force is the provisioned goal. Conversely, CI might be more appropriate for enhancing functional ability and use of the affected arm in daily life in stroke patients (Wu et al. 2011). The ultimate selection of optimal therapy for each patient, however, might depend on goals or preferences with regard to unimanual or bimanual training and follow a logical sequence, wherein various therapies stimulate the correct neuronal process at the right moment.

1.4.3 Technology-Based Interventions that Improve Existing Therapies

Technological tools have been developed gradually to increase the number of possible interventions at the various stages of poststroke. Many technological fields have attempted to improve existing rehabilitation therapies, proposing interventions that are based on robotics (Kwakkel et al. 2008), functional electrical stimulation (Pomeroy et al. 2006), virtual reality (Henderson et al. 2007), and brain-machine interfaces (Buch et al. 2008) and their various combinations (Daly et al. 2009; Fluet et al. 2012; Meadmore et al. 2012).

However, technology experts often design technological interventions without accounting for clinician experience or patient needs, which can unfortunately result in the development of efficient technology that never enters daily practice, because potential users do not understand or agree with its purpose.

One such example is the MIT-Manus robotic system, a robotic device that is designed for upper limb rehabilitation that allows the execution of repetitive movements on planar trajectories. To use this device, the patient sits at a table and attaches his/her arm to the robotic arm. The therapist first guides the arm though a given exercise that is stored by the robotic system so that it repeats the trajectory autonomously during a training session in active (in which the participant moves his/her arm but is corrected when the movement is wrong) or passive mode (the participant’s arm is moved by the system) (Krebs et al. 1998).

Possibly due to the range of movements that are used and the low variability and rigidity of the system, it increased spasticity in certain patients. Updated versions of MIT-Manus allow for various modalities, offering assistance as needed, whereby the therapist is free to define the outer boundaries of a certain trajectory at which the robot influences the natural movement of the hand (Lo et al. 2010). With these adaptations, similar improvements were achieved by patients who used robotic rehabilitation as those who underwent intensive human-assisted therapy (Lo et al. 2010)—the lack of intensive human guidance, however, led to reduced therapeutic costs.

Another innovative tool that has improved therapies is the brain-computer interface (BCI). Pichiorri and colleagues (Pichiorri et al. 2011a) used BCI to improve motor imagery (MI) on the patient and therapeutic levels. MI has been used for many years in stroke rehabilitation, enhancing the therapeutic effects of physical therapy alone (Nilsen et al. 2010). However, the chief drawback of MI interventions was that the therapist lacked an objective measurement of how well the patient was performing an imaginary task or whether the patient was trying to perform it at all.

To overcome this omission, BCI was implemented to monitor the electroencephalography (EEG) of a patient, providing the therapist with feedback of brain activity during task performance (Pichiorri et al. 2011b). With this information, the therapist can guide a patient during the MI exercise and encourage him/her when brain activation drops below a threshold. Using this type of new technology allows the therapist to become part of MI interventions, contributing to the application of such interventions to a larger population of stroke patients and extending their use to clinical environments (Mattia et al. 2012).

These two examples demonstrate how technology improves existing rehabilitation therapies, but technology developers must bear in mind clinicians' attitudes toward elaborate optimal interventions. A new patient-based paradigm must be established, considering that technological tools do not always have to be centered around the patient but the patient-therapist-doctor triad. Thus, a technological intervention is successful if it effects better rehabilitative outcomes results or if similar results are reached faster and more inexpensively, or if it eases the therapist's work in evaluating and selecting patients. Overall it must be possible to tailor to patients characteristics, and within the selected group of patients it should allow standardization

1.5 Conclusion

It is an exciting time for stroke rehabilitation. The longlasting gap between neuroscience data and clinical application is closing rapidly, and many concepts from experimental evidence are guiding everyday activity in stroke rehabilitation centers. This new knowledge is also accelerating the development of new neuromechanical and robotic tools to support and improve the efficacy of rehabilitation. Although the evidence that supports the efficacy of such approaches remains scarce, the knowledge of the causal relationships between rehabilitation approaches and cerebral plasticity with regard to functional outcome is directing us in creating more specific apparatuses and more effective control systems.

The pioneering approaches in robotic rehabilitation, such as the Lokomat® and MIT-Manus, are paradigmatic. After an initial wave of excitement, clinical studies were somehow disappointing and forced to reconsider the mechanical structure and control systems. Further, the possibility of operating in controlled environments and the scientific interest in determining the pathophysiology of poststroke plasticity have effected a surge of data on the specificity of every method, propelling us toward a more patient-therapist-tailored approach that is demonstrating tremendous efficacy. We have highlighted the critical points that are limiting the full implementation of technology-based approaches in clinical neurorehabilitation. Nevertheless, we conclude that such approaches are shaping the present, rather than future, of stroke rehabilitation.

References

Abdullah H, Tarry C, Datta R, Mittal G, Abderrahim M (2007) Dynamic biomechanical model for assessing and monitoring robot-assisted upper-limb therapy. J Rehabil Res Dev 44(1):43–62

Alstermark B, Isa T (2012) Circuits for skilled reaching and grasping. Annu Rev Neurosci 35:559–578. doi:10.1146/annurev-neuro-062111-150527

Archambault PS, Caminiti R, Battaglia-Mayer A (2009) Cortical mechanisms for online control of hand movement trajectory: the role of the posterior parietal cortex. Cereb Cortex 19(12):2848–2864

Backus D, Winchester P, Tefertiller C (2010) Translating research into clinical practice: integrating robotics into neurorehabilitation for stroke survivors. Topics Stroke Rehabil 17(5):362–370

Banala SK, Kim SH, Agrawal SK, Scholz JP (2009) Robot assisted gait training with active leg exoskeleton (ALEX). IEEE Trans Neural Syst Rehabil Eng 17(1):2–8

Belda-Lois JM, Mena-del Horno S, Bermejo-Bosch I, Moreno J, Pons J, Farina D, Iosa M, Molinari M, Tamburella F, Ramos A et al (2011) Rehabilitation of gait after stroke: a review towards a top-down approach. J Neuroeng Rehabil 8(1):66

Berkowitz A (2008) Physiology and morphology of shared and specialized spinal interneurons for locomotion and scratching. J Neurophysiol 99(6):2887–2901

Blaya JA, Herr H (2004) Adaptive control of a variable-impedance ankle-foot orthosis to assist drop-foot gait. IEEE Trans Neural Syst Rehabil Eng 12(1):24–31

Bobath B, Bobath K (1957) Control of motor function in the treatment of cerebral palsy. Physiotherapy 43:295–303

Boddice G, Brauer S, Gustafsson L, Kenardy J, Hoffmann T (2010) Clinical Guidelines for Stroke Management. Melbourne, Australia: National Stroke Foundation. (Published 2012)

Buch E, Weber C, Cohen LG, Braun C, Dimyan MA, Ard T, Mellinger J, Caria A, Soekadar S, Fourkas A et al (2008) Think to move: a neuromagnetic brain-computer interface (BCI) system for chronic stroke. Stroke 39(3):910–917

Burdea G, Coiffet P (2003) Virtual reality technology. Presence 12(6):663–664

Carpaneto J, Raos V, Umiltà MA, Fogassi L, Murata A, Gallese V, Micera S, Zhang W, Johnston JA, Ross MA et al (2012) Continuous decoding of grasping tasks for a prospective implantable cortical neuroprosthesis. J NeuroEng Rehabil 9(1):84

Cauraugh JH, Summers JJ et al (2005) Neural plasticity and bilateral movements: a rehabilitation approach for chronic stroke. Prog Neurobiol 75(5):309–320

Cheron G, Duvinage M, De Saedeleer C, Castermans T, Bengoetxea A, Petieau M, Seetharaman K, Hoellinger T, Dan B, Dutoit T et al (2012) From spinal central pattern generators to cortical network: integrated BCI for walking rehabilitation. Neural plast

Collantes I, Asín G, Moreno JC, Pons JL (2012) Analysis of biomechanical data to determine the degree of users participation during robotic-assisted gait rehabilitation. In: Proceedings of EMBC'12, pp 4855–4858

Collantes I, Asín G, Moreno JC, Pons JL (2012) Analysis of the effect of two different feedbacks on the biomechanical patterns of stroke patients during robotic-assisted gait rehabilitation. In: ICNR'12 (accepted)

Costa N, Caldwell G (2006) Control of a biomimetic "soft-actuated" 10dof lower body exoskeleton. In: Proceedings of BioRob'06, pp 495–501

Cramer SC, Sur M, Dobkin BH, O'Brien C, Sanger TD, Trojanowski JQ, Rumsey JM, Hicks R, Cameron J, Chen D et al (2011) Harnessing neuroplasticity for clinical applications. Brain 134(6):1591–1609. doi:10.1093/brain/awr039

d'Avella A, Portone A, Lacquaniti F (2011) Superposition and modulation of muscle synergies for reaching in response to a change in target location. J Neurophysiol 106(6):2796–2812

Daly J, Cheng R, Rogers J, Litinas K, Hrovat K, Dohring M (2009) Feasibility of a new application of noninvasive brain computer interface (BCI): a case study of training for recovery of volitional motor control after stroke. J Neurol Phys Ther 33(4):203

de NAP Shelton F, Reding MJ (2001) Effect of lesion location on upper limb motor recovery after stroke. Stroke 32(1):107–112

Deutsch JE (2011) Using virtual reality to improve walking poststroke: translation to individuals with diabetes. J Diabetes Sci Technol 5(2):309–314

Deutsch JE, Paserchia C, Vecchione C, Mirelman A, Lewis JA, Boian R, Burdea G (2004) Improved gait and elevation speed of individuals post-stroke after lower extremity training in virtual environments. J Neurol Phys Ther 28(4):185–186

Dickstein R (2008) Rehabilitation of gait speed after stroke: a critical review of intervention approaches. Neurorehabil Neural Repair 22(6):649–660

Dimyan MA, Cohen LG (2010) Contribution of transcranial magnetic stimulation to the understanding of functional recovery mechanisms after stroke. Neurorehabil Neural Repair 24(2):125–135. doi:10.1177/1545968309345270

Dobkin BH (2004) Strategies for stroke rehabilitation. Lancet Neurol 3(9):528–536

Duncan PW, Goldstein LB, Matchar D, Divine GW, Feussner J (1992) Measurement of motor recovery after stroke. Outcome assessment and sample size requirements. Stroke 23(8):1084–1089

Fluet G, Merians A, Qiu Q, Lafond I, Saleh S, Ruano V, Delmonico A, Adamovich S (2012) Robots integrated with virtual reality simulations for customized motor training in a person with upper extremity hemiparesis: a case study. J Neurol Phys Ther 36(2):79–86

Freivogel S, Mehrholz J, Husak-Sotomayor T, Schmalohr D (2008) Gait training with the newly developed 'LokoHelp'-system is feasible for non-ambulatory patients after stroke, spinal cord and brain injury. A feasibility study. Brain Inj 22(7–8):625–632

Gizzi L, Nielsen JF, Felici F, Moreno JC, Pons JL, Farina D (2012) Motor modules in robot-aided walking. J NeuroEng Rehabil 9(1):76

Grillner S, Rossignol S (1978) On the initiation of the swing phase of locomotion in chronic spinal cats. Brain Res 146(2):269–277

Grillner S, Markram H, De Schutter E, Silberberg G, LeBeau FEN et al (2005) Microcircuits in action–from CPGs to neocortex. Trends Neurosci 28(10):525–533

Heller A, Wade DT, Wood VA, Sunderland A, Hewer RL, Ward E (1987) Arm function after stroke: measurement and recovery over the first three months. J Neurol Neurosurg Psychiatry 50(6):714–719

Henderson A, Korner-Bitensky N, Levin M (2007) Virtual reality in stroke rehabilitation: a systematic review of its effectiveness for upper limb motor recovery. Topics Stroke Rehabil 14(2):52–61

Hesse S, Werner C (2009) Connecting research to the needs of patients and clinicians. Brain Res Bull 78(1):26–34

Hidler J, Nichols D, Pelliccio M, Brady K, Campbell DD, Kahn JH, Hornby TG (2009) Multicenter randomized clinical trial evaluating the effectiveness of the Lokomat in subacute stroke. Neurorehabil Neural Repair 23(1):5–13

Huang VS, Krakauer JW (2009) Robotic neurorehabilitation: a computational motor learning perspective. J NeuroEng Rehabil 6(1):5

Ifejika-Jones NL, Barrett AM (2011) Rehabilitation emerging technologies, innovative therapies, and future objectives. Neurotherapeutics 8(3):452–462

Institute of Medicine (US), Committee on Quality of Health Care in America. (2001) Crossing the quality chasm: a new health system for the 21st century. National Academies Press

Iosa M, Cincotti F, Pisotta I, Tamburella F, Mattia D, Molinari M (2011) What users need. Requirements in BNCI-driven robot for gait rehabilitation after stroke: a pilot study. Int J Bioelectromagnetism 13:13–15

Jezernik S, Colombo G, Keller T, Frueh H, Morari M (2003) Robotic orthosis lokomat: a rehabilitation and research tool. Neuromodulation: technology at the neural. Interface 6(2):108–115

Krebs HI, Hogan N (2006) Therapeutic robotics: a technology push. Proc IEEE 94(9):1727–1738

Krebs HI, Hogan N, Aisen ML, Volpe BT (1998) Robot-aided neurorehabilitation. IEEE Trans Rehabil Eng 6(1):75–87

Kwa HK, Noorden JH, Missel M, Craig T, Pratt JE, Neuhaus PD (2009) Development of the IHMC mobility assist exoskeleton. In: Proceedings of ICRA '09, pp 2556–2562

Kwakkel G, Kollen B, Twisk J (2006) Impact of time on improvement of outcome after stroke. Stroke 37(9):2348–2353

Kwakkel G, Kollen BJ, Krebs HI (2008) Effects of robot-assisted therapy on upper limb recovery after stroke: a systematic review. Neurorehabil Neural Repair 22(2):111–121

Lange B, Flynn S, Proffitt R, Chang C, Rizzo AA (2010) Development of an interactive game-based rehabilitationtool for dynamic balance training. Topics in StrokeRehabil 17(5):345–352

Lo AC, Guarino PD, Richards LG, Haselkorn JK, Wittenberg GF, Federman DG, Ringer RJ, Wagner TH, Krebs HI, Volpe BT et al (2010) Robot-assisted therapy for long-term upper-limb impairment after stroke. N Engl J Med 362(19):1772–1783

Lunenburger L, Colombo G, Riener R, Dietz V (2004) Biofeedback in gait training with the robotic orthosis Lokomat. In: Engineering in Medicine and Biology Society, 2004. IEMBS'04. 26th Annual International Conference of the IEEE, vol 2, pp 4888–4891

Mattia D, Pichiorri F, Molinari M, Rupp R (2012) Brain computer interface for hand motor function restoration and rehabilitation. Towards Practical Brain-Computer Interfaces, pp 131–153

Meadmore KL, Hughes AM, Freeman CT, Cai Z, Tong D, Burridge JH, Rogers E (2012) Functional electrical stimulation mediated by iterative learning control and 3D robotics reduces motor impairment in chronic stroke. J NeuroEng Rehabil 9:32

Mehrholz J, Werner C, Kugler J, Pohl M (2007) Electromechanical-assisted training for walking after stroke. Cochrane Database Syst Rev 4(4)

Metrot J, Mottet D, Hauret I, Bonnin HY, VanDokkum L, Torre K, Laffont I (2013) Changes in bimanual coordination during the first 6 weeks after moderate hemiparetic stroke. Neurorehabil Neural Repair 27:251–259

Moreno JC, Brunetti F, Rocon E, Pons JL (2008) Immediate effects of a controllable knee ankle foot orthosis for functional compensation of gait in patients with proximal leg weakness. Med Biol Eng Comput 46(1):43–53

Morone G, Bragoni M, Iosa M, De Angelis D, Venturiero V, Coiro P, Pratesi L, Paolucci S (2011) Who may benefit from robotic-assisted gait training? A randomized clinical trial in patients with subacute stroke. Neurorehabil Neural Repair 25(7):636–644

Morone G, Iosa M, Bragoni M, De Angelis D, Venturiero V, Coiro P, Riso R, Pratesi L, Paolucci S (2012) Who may have durable benefit from robotic gait training? A 2-year follow-up randomized controlled trial in patients with subacute stroke. Stroke 43(4):1140–1142

Nilsen DM, Gillen G, Gordon AM (2010) Use of mental practice to improve upper-limb recovery after stroke: a systematic review. Am J Occup Ther 64(5):695–708

Patton J, Brown DA, Peshkin M, Santos-Munné JJ, Makhlin A, Lewis E, Colgate EJ, Schwandt D (2008) KineAssist: design and development of a robotic overground gait and balance therapy device. Top Stroke Rehabil 15(2):131–139

Pei, Y., Kim, Y., Obinata, G., Hase, K., and Stefanov, D. (2011). Trajectory planning of a robot for lower limb rehabilitation. In Engineering in Medicine and Biology Society, EMBC, 2011 Annual International Conference of the IEEE, pages 1259–1263. IEEE

Perfetti C (2001) L'exercice thérapeutique cognitif pour la rééducation du patient hémiplégique Elsevier Masson

Peurala S, Airaksinen O, Huuskonen P, Jakala P, Juhakoski M, Sandell K, Tarkka I, Sivenius J (2009) Effects of intensive therapy using gait trainer or floor walking exercises early after stroke. J Rehabil Med 41(3):166–173

Pichiorri F, Fallani FDV, Cincotti F, Babiloni F, Molinari M, Kleih SC, Neuper C, Kubler A, Mattia D (2011a) Sensorimotor rhythm-based brain–computer interface training: the impact on motor cortical responsiveness. J Neural Eng 8(2):025020

Pichiorri F, Cincotti F, de Vico Fallani F, Pisotta I, Morone G, Molinari M, Mattia D (2011b) Towards a brain computer Interface-based rehabilitation: from bench to bedside. In Proceedings of the 5th international brain–computer interface conference, Verlag der Technischen Universitat Graz, Graz, Austria, pp 268–271

Pichiorri F, Morone G, Cincotti F et al (2012) Clinical trial design to validate a BCI-supported task-specific training in neurorehabilitation after stroke. Eur J Neurol 19:566

Pomeroy VM, King L, Pollock A, Baily-Hallam A, Langhorne P (2006) Electrostimulation for promoting recovery of movement or functional ability after stroke. Cochrane Database Syst Rev 2

Prabhakaran S, Zarahn E, Riley C, Speizer A, Chong JY, Lazar RM, Marshall RS, Krakauer JW (2008) Inter-individual variability in the capacity for motor recovery after ischemic stroke. Neurorehabil Neural Repair 22(1):64–71

Rand D, Kizony R, Weiss P (2008) The Sony PlayStation II EyeToy: low-cost virtual reality for use in rehabilitation. J Neurol Physl Ther 32(4):155–163

Rogers L, Madhavan S, Roth H, Stinear J (2011) Transforming neurorehabilitation of walking following stroke: the promise of non-invasive brain stimulation–a review. Restor Neurol Neurosci 29(6):507–516

Rose FD, Brooks BM, Rizzo AA (2005) Virtual reality in brain damage rehabilitation: review. Cyber Psychol Behav 8(3):241–262. doi:10.1089/cpb.2005.8.241

Saito Y, Kikuchi K, Negoto H, Oshima T, Haneyoshi T (2005) Development of externally powered lower limb orthosis with bilateral-servo actuator. In: Proceedings of ICORR’05, pp 394–399

Sartori L, Camperio Ciani A, Bulgheroni M, Castiello U (2012) Reaching and grasping behavior in Macaca fascicularis: a kinematic study. Exp Brain Res 1–6

Sawicki GS, Ferris DP (2009) A pneumatically powered knee-ankle-foot orthosis (KAFO) with myoelectric activation and inhibition. J NeuroengRehabil 6:23

Schmidt H, Hesse S, Werner C, Bardeleben A (2004) Upper and lower extremity robotic devices to promote motor recovery after stroke-recent developments. In: Engineering in medicine and biology society, 2004. IEMBS’04. 26th annual international conference of the IEEE, vol 2, pp 4825–4828 (IEEE)

Schweighofer N, Han CE, Wolf SL, Arbib MA, Winstein CJ (2009) A functional threshold for long-term use of hand and arm function can be determined: predictions from a computational model and supporting data from the Extremity Constraint-Induced Therapy Evaluation (EXCITE) trial. Phys Ther 89(12):1327–1336

Scott CL, Phillips LH, Johnston M, Whyte MM, MacLeod MJ (2012) Emotion processing and social participation following stroke: study protocol. BMC Neurol 12(1):56

Sharma N, Cohen LG (2012) Recovery of motor function after stroke. Dev Psychobiol

Stauffer Y, Allemand Y, Bouri M, Fournier J, Clavel R, M′etrailler P, Brodard R, Reynard F (2009) The WalkTrainer-a new generation of walking reeducation device combining orthoses and muscle stimulation. IEEE Trans Neural Syst Rehabil Eng 17(1):38–45

Stern PH, McDowell F, Miller JM, Robinson M (1970) Effects of facilitation exercise techniques in stroke rehabilitation. Arch Phys Med Rehabil 51:526–531

Stinear CM, Barber PA, Smale PR, Coxon JP, Fleming MK, Byblow WD (2007) Functional potential in chronic stroke patients depends on corticospinal tract integrity. Brain 130(1):170–180

Sunderland A, Tinson D, Bradley L, Hewer RL (1989) Arm function after stroke. An evaluation of grip strength as a measure of recovery and a prognostic indicator. J Neurol Neurosurg Psychiatry 52(11):1267–1272

Taub E, Morris DM (2001) Constraint-induced movement therapy to enhance recovery after stroke. Curr Atheroscler Rep 3(4):279–286

Taub E, Crago JE, Uswatte G (1998) Constraint-induced movement therapy: a new approach to treatment in physical rehabilitation. Rehabil Psychol 43(2):152

Taub E, Uswatte G, King DK, Morris D, Crago JE, Chatterjee A (2006) A placebo-controlled trial of constraint-induced movement therapy for upper extremity after stroke. Stroke 37(4):1045–1049

Umberger BR, Rubenson J (2011) Understanding muscle energetics in locomotion: new modeling and experimental approaches. Exerc Sport Sci Rev 39(2):59

Veneman JF, Kruidhof R, Hekman EEG, Ekkelenkamp R, Van Asseldonk EHF, van der Kooij H (2007) Design and evaluation of the LOPES exoskeleton robot for interactive gait rehabilitation. IEEE Trans Neural Syst Rehabil Eng 15(3):379–386

Weiss P, Kizony R, Feintuch U, Katz N (2006) Virtual reality in neurorehabilitation. In: Selzer M, Cohen L, Clarke S, Duncan P, Gage F (eds) Textbook of neural repair and rehabilitation. Cambridge University Press, Cambridge, pp 182–197

Wheeler JW, Krebs HI, Hogan N (2004) An ankle robot for a modular gait rehabilitation system. In: Proceedings of IROS'04, vol 2, pp 1680–1684

Wirz M, Zemon D, Rupp R, Scheel A, Colombo G, Dietz V, Hornby T et al (2005) Effectiveness of automated locomotor training in patients with chronic incomplete spinal cord injury: a multicenter trial. Arch Phys Med Rehabil 86(4):672–680

Wu C, Chuang L, Lin K, Chen H, Tsay P (2011) Randomized trial of distributed constraint-induced therapy versus bilateral arm training for the rehabilitation of upper-limb motor control and function after stroke. Neurorehabil Neural Repair 25(2):130–139

Ziegler MD, Zhong H, Roy RR, Edgerton VR (2010) Why variability facilitates spinal learning. J Neurosci 30(32):10720–10726

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