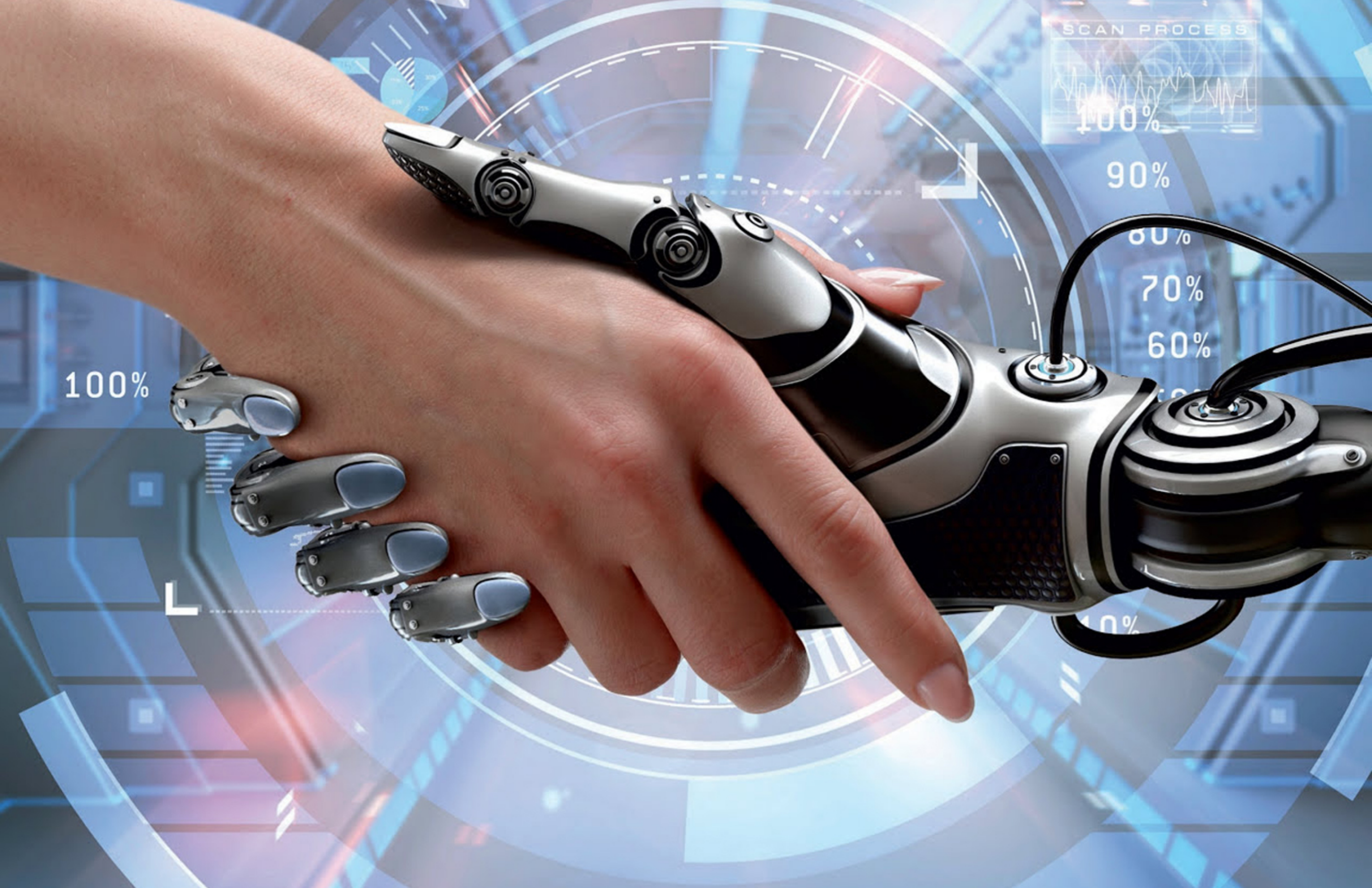
REHABILITATION ROBOTICS

TECHNOLOGY AND APPLICATION



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Technology and Application

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Rehabilitation Robotics: Technology and Applications

The last decades have seen major advances in interventions for neuromotor rehabilitation. Forms of treatment based on repetitive exercise of coordinated motor activities have been proved effective in improving gait and arm functions and ultimately the patients' quality of life. Exercise-based treatments constitute a significant burden for therapists and are heavy consumers of health-care resources. Technologies such as robotics and virtual reality can make them more affordable.

Rehabilitation robotics specifically focuses on systems—devices, exercise scenarios, and control strategies—aimed at facilitating the recovery of impaired sensory, motor, and cognitive skills. The field has a relatively long history, dating back to the early 1990s. Early attempts were part of the general trend toward automating heavy tasks by using "intelligent" machines, with minimal human intervention. The notion of "artificial therapist" was common in early scientific papers and patent applications. However, the most distinctive feature of these devices is not their ability to "automate" treatment but, rather, that of precisely quantifying sensorimotor performance during exercise, in terms of movement kinematics and exchanged forces. This resulted in a gradual shift toward more evidence-based and data-driven forms of treatment. Present-generation rehabilitation robots are designed as complements, rather than substitutes, of the therapist's work. They support the recovery of functions by efficiently exploiting structure and adaptive properties of the human sensorimotor systems and provide rich information on sensorimotor performance and their evolution. Their design, implementation, and modalities of intervention incorporate findings from behavioral studies on sensorimotor adaptation and motor skill learning and their neural substrates.

Rehabilitation robotics is therefore characterized by highly specific design approaches and technical solutions, with roots in both engineering and neurophysiology.

This book addresses both technology and application aspects of Rehabilitation Robotics. Part I focuses on the state of the art and representative advancements in the design, control, analysis, and implementation of rehabilitation robots and the underlying neurophysiological principles. Part II addresses the existing applications and the clinical validation of these systems, with a special emphasis on therapy robots, which support exercise-based treatments aimed at recovering sensorimotor or cognitive functions.

PART I: BACKGROUND AND TECHNOLOGY

NEUROPHYSIOLOGY

Planning and execution of movements results from the coordinated activity of multiple interconnected sensory and motor areas in the cerebral cortex. When an area in this specialized motor network is damaged—for example, through a traumatic brain injury or an ischemic event—the activity of the motor networks can be disrupted, thus leading to functional deficits. How the surviving motor networks reorganize to compensate for the injury depends on the location and extent of the lesion but may be affected by sensorimotor exercise.

Chapter 1 summarizes how neuroplasticity modifies motor networks in response to injury, by focusing on the changes after a cerebrovascular accident in the primary motor cortex. Neuroanatomical and neurophysiological evidence in animal models and human stroke survivors is reviewed to demonstrate how injuries functionally impair motor networks, how motor networks compensate for the lesion to improve motor function, and how selected therapies may facilitate recovery.

Chapter 2 focuses on the hierarchical architecture and synergistic functioning of the motor system. These aspects are crucial for the development of successful robotics applications with rehabilitation purposes. The same framework is used to discuss the mechanisms underlying rehabilitation interventions with a potential to facilitate the recovery process.

TECHNOLOGY AND DESIGN CONCEPTS

Devices for rehabilitation benefit from advances in robot technologies, including sensors and actuators, mechanical architectures, and the corresponding control architectures. These devices are characterized by a continuous interaction with the human body, which poses specific design constraints.

Chapter 3 summarizes the notion of "biomechatronic" design for systems for robot-mediated rehabilitation, encompassing robot structure, musculoskeletal biomechanics, and neural control. Robots for rehabilitation are typically conceived to constantly work in constrained motion with the human body, which represents a challenge for designers. This requires a top-down design approach, in which a model of the human agent guides a concurrent, iterative design cycle of the robot's mechanical, electronic, and multilayered control subsystems. Criteria for the identification of functional and technical specifications and the selection of key components of the robotic system are also derived. Two design case studies demonstrate how these design principles are translated into practice.

Chapter 4 addresses how actuators play a critical role in defining the characteristics of the robot-patient interaction. The different options for actuating and controlling a rehabilitation device are discussed, considering the complex flow of information between the user and the robot during a rehabilitation task. Strategies for both high- and low-level control are presented. Impedance and admittance control modalities are discussed as means of decoding human intention and/or modulating the assistive forces delivered by the robot. Mathematical tools for model-based compensation of nonlinear phenomena (backlash and friction) are also presented.

The way robots are used to facilitate training is crucial for their application to therapy and has important implications for their mechanical and control design. Intensity and frequency of practice are major determinants of the recovery process, but different exercise modalities are possible. Robots may be used for haptic rendering in virtual environments, to provide forces that facilitate task performance or task completion, and/or to make a task more difficult and challenging.

Chapter 5 reviews the control strategies for robotic therapy devices and summarizes the techniques for implementing assistive strategies, including counterbalance techniques and adaptive controllers that modify control parameters based on the patient's ongoing performance.

Personalized treatment is becoming increasingly popular in neurorehabilitation. Two chapters discuss how new design techniques such as exoskeletons or wearable robots are applied to the design of modern therapy robots, for either upper or lower limb rehabilitation.

Chapter 6 specifically addresses the design of exoskeletons for upper-limb rehabilitation. After an introduction of the rationale behind the selection of this robot architecture and a review of the available solutions for actuation, the chapter discusses the state of the art and the most commonly adopted solutions. An overview of clinical evidences of upper-limb rehabilitation with exoskeletons is then provided, discussing evidences in favor of training with exoskeleton devices.

Chapter 7 reviews the current state and clinical effectiveness, safety, and usability of exoskeletons for gait rehabilitation. It provides an overview of the actuation technologies, including compliant and lightweight solutions. Control strategies aimed at guiding the patient according to his/her needs and encouraging his/her active participation are also discussed. Novel perspectives for "symbiotic" human-exoskeleton interaction based on interfaces with neural structures are also introduced.

COMPUTATIONAL NEUROREHABILITATION

One important feature of therapy robots is that they integrate both therapeutic and measuring functionalities. Therapy robots have built-in technology and sensors that measure movement kinematics and kinetics, thus providing an accurate assessment of motor function by which it is possible to diagnose the patient state and to evaluate patient performance and their progress during treatment. The availability of quantitative information has triggered an entirely new paradigm for neurorehabilitation, unifying clinical assessment, and exercise. Computational neurorehabilitation is a new and emerging field, which uses modern data analysis and modeling techniques to understand the mechanisms of neural plasticity and motor learning, and incorporates this knowledge into personalized, data- and model-driven forms of treatment.

Chapter 8 reviews the quantitative measures—encompassing kinematic, kinetic, timing, sensory, and neuromechanical aspects of performance—which are most frequently used to describe motor behavior during robot-assisted rehabilitation of the upper limb. The chapter also analyzes how these indicators are used to monitor motor recovery during exercise, to understand the evolution of performance, and to precisely plan and, if necessary, modify the rehabilitation strategies. The relationship between robot-derived measures and their clinical counterparts is also discussed.

Chapter 9 addresses computational models for neuromotor recovery, with a focus on state-space models that describe the development of functional behaviors through exercise and the relation between neuromotor recovery and motor learning. The chapter first reviews models of the dynamics of sensorimotor adaptation and motor skill learning and then elaborates on similarities and differences with neuromotor recovery. Finally, it discusses how these models can be used to achieve a better understanding of the role of robots to promote recovery and to develop personalized forms of treatment.

Chapter 10 proposes a general framework to model the interaction between robot and patient during robot-assisted training. Human and robot are modeled as two agents, whose respective tasks are described by two cost functions. Optimal interaction strategies are then derived in terms of differential game theory. This approach allows to describe different forms of human-robot interaction. A specific prediction is that optimal interaction requires that the robot maintains a model of the behavior of its human partner. In this case, simulations and empirical studies exhibit more stable, reactive, and adaptive interaction. This form of "symbiotic" interaction is a step toward defining what it takes for robots to behave as "optimal" trainers.

Chapter 11 addresses the strategies implemented in rehabilitation robots to promote patient motivation, which is a major determinant of recovery through exercise. Motivation may be measured with self-report questionnaires or with indirect, more objective measures, such as exercise duration. Motivation may be promoted through interaction with virtual environments, which may consist of activities of daily living, which emphasize relatability, or games, which emphasize enjoyment. The design of these environments must take the hardware, the patients' characteristics, and goal-related feedback into account. Motivation during exercise must be maintained by regulating task difficulty, thus ensuring an appropriate "challenge level."

SOFTWARE ENVIRONMENTS FOR REHABILITATION ROBOTICS

As a natural conclusion of this methodological section, Chapter 12 reviews the software development environments that can be used to implement the different levels of control of a modern rehabilitation robot. The robotic field suffers from a lack of standardization in programming environments. Hence, it is not surprising that even in the specific context of rehabilitation robotics, there is currently no consensus on specific software and hardware platforms. The chapter surveys different solutions used for combining robots (and, more in general, haptic interfaces) and virtual environments. Advantages and disadvantages of each of these environments are discussed, together with typical applications, with a focus on upper-limb rehabilitation.

PART II: APPLICATIONS

The second part of the book addresses the application of rehabilitation robots in different pathologies for training of diverse districts (upper and lower limb) and using different training strategies.

HIGH INTENSITY, ASSIST-AS-NEEDED THERAPY TO IMPROVE MOTOR FUNCTIONS

Chapter 13 provides an overview of 28+ years of efforts at MIT's Newman Laboratory for Biomechanics and Human Rehabilitation for the developments of robotic tools to assist in the neurorecovery process. After a definition of the basic principles that are core for successful rehabilitation robotics technology, the chapter presents a snapshot of few of MIT's rehabilitation robots, discusses the results of metaanalyses for upper extremity robotics, and finally presents two exciting examples for acute and chronic stroke. Overall, the above material points out that robotic therapy for the upper extremity that involves an interactive high-intensity, intention-driven therapy based on motor learning principles and assist-as-needed leads to better outcomes than usual care in both acute/subacute and chronic stroke.

The above principles have been extended to training in a three-dimensional workspace, using robots with an exoskeleton structure. Chapter 14 describes the application of one of the first architectures developed with the purpose of mirroring the anatomical structure of the human arm and of enabling task-oriented training in the 3D space, mimicking activities of daily living.

Hand and finger functions are of critical importance for independence in everyday activities, but their recovery is often limited following neurological injury. This has motivated the development of novel therapeutic and assistive tools. Chapter 15 provides a comprehensive overview of robotic approaches for the rehabilitation of hand function and underlines their potential to complement conventional rehabilitation. First, the design concepts of existing hand exoskeletons and end-effector devices are presented. Then, clinical evidence that underlines the feasibility of robot-assisted rehabilitation of hand function is presented. Finally, promising research directions are discussed to further exploit the potential of robot-assisted rehabilitation of hand function in neurological patients.

Robot-assisted gait training typically involves body-weight support and physical guidance to move the legs into the correct pattern. Gait rehabilitation robots allow greater exercise duration and movement repetitions; improve patient safety and motivation; reduce the therapists' burden; and, eventually, improve the therapeutic outcome. Chapter 16 introduces the rationale for robot-assisted gait training. In particular, existing gait-rehabilitation robots and their control strategies are presented. The available clinical trials are also summarized, showing that training with robotic rehabilitation devices is at least as effective as conventional physiotherapy. Further clinical studies are required in order to define the most appropriate robotic technical features based on the task, patients' type, and degree of impairment.

Wearable systems open new perspectives for rehabilitation in individuals with disabilities, which can lead to difficulty in walking or making arm movements since they could be used to facilitate independent training in the clinic or at home. Wearable systems range from complex rigid exoskeleton structures for the assistance of joints or limbs to hybrid, soft, and interactive systems. The existing solutions are not yet widely used in clinical environments. The aim of Chapter 17 is to review the scientific challenges and the current developments of wearable systems and to discuss their clinical potential.

ROBOTS NOT ONLY FOR STROKE REHABILITATION

Although most applications of robot rehabilitation focus on stroke and traumatic brain injury, these devices may find application in the treatment of other pathologies.

Chapter 18 addresses robot-assisted rehabilitation in multiple sclerosis (MS). Robot-assisted training leads to improved movement quality on reaching tasks, but clinical effects on standard assessment have not been always observed after multiple-session training. An increasing number of studies report effects of a multiple-week training program, but the magnitude of the effect was often similar to conventional training programs. Overall, there is evidence supporting the beneficial effect of robot- and technology-supported training, but its superiority compared with other or conventional treatment programs is still debatable. Research investigating the impact of different technological settings and the motor learning strategies implemented in technology must be encouraged for MS patients.

Persons with cognitive deficits are a completely different target population that can be addressed by therapy robots. Cognitive rehabilitation therapy (CRT) is a set of interventions designed to enhance cognitive performance. Ideally, CRT engages the participant in a learning activity to enhance neurocognitive skills relevant to the overall recovery goals. There is ongoing research to identify the determinants of a positive response to treatment. Chapter 19 addresses the use of rehabilitation robots, socially interactive robots (SIR), and socially assistive robots (SAR), both virtual and embodied, to enhance, restore, or prevent early deterioration of cognitive abilities related to neurodegenerative disease or injury.

INTEGRATING ROBOT THERAPY WITH NEURO- AND PSYCHOPHYSIOLOGICAL TECHNIQUES

All the techniques and devices described until now use robot technology alone. Integration of different approaches and different technologies may improve the outcome, for instance, by training and restoring different functions within the same training session or by using physiological signals to monitor and/or control the recovery process. The following chapters focus on the use of neuro- and psychophysiological signals to enhance or complement robot-assisted therapy.

Chapter 20 presents hybrid FES-robot devices for training of activities of daily living aiming at the parallel restoration of functions by the external activation of paralyzed muscles and external mechanical support of postural functions. The combination of two modalities within the same treatment may multiply their individual effects as the external activation of muscles eliminates the need for large mechanical actuators and reduces the number of degrees of freedom to a controllable domain and, on the other hand, robot guidance removes the need for prolonged, fatiguing stimulation of muscles.

In spite of the acknowledged importance of proprioception for motor control and neuromotor rehabilitation, no effective method for assessment and rehabilitation of proprioceptive deficits has emerged in clinical practice. While there are many clinical scales for assessing proprioception, they all have insufficient psychometric properties and cannot be used in closed-loop treatment paradigms wherein treatment parameters are monitored and adjusted online or with a trial-by-trial frequency. Chapter 21 discusses how robots can simultaneously address two interrelated needs: to provide sensitive and repeatable assessments of proprioceptive integrity and to automate repetitive training procedures designed to enhance proprioception and its contributions to functional movement.

The outcome of a training program can be conditioned not only by the patient's physical conditions but also by his/her psychophysiological state during the whole course of the rehabilitation program. Chapter 22 reviews psychophysiological response modalities that, together with task performance parameters and biomechanical measurements, may be used in a biocooperative approach to rehabilitation. The chapter focuses in particular on electrocardiogram, skin conductance, respiration signal, and peripheral skin temperature. Each signal is described in terms of acquisition modalities, signal processing, and features extraction. The psychophysiological responses in the case of multimodal challenge and physical activity are also examined, with reference to the differentiation of arousal and valence.

Understanding the mechanisms underlying muscle coordination during daily motor activities is a fascinating challenge in neuroscience and may provide important information pertaining to the recovery strategies of the neuromuscular system. Muscle synergies have been hypothesized as a neural strategy to simplify the control of the redundant motor actuators leading human movement and as a method to study motor coordination in healthy and neurological subjects. Chapter 23 presents the theoretical framework for the extraction and the description of muscle synergies. Moreover, it summarizes how neuropathologies impact on muscle synergies and their potential for neurorehabilitation. Finally, it discusses how muscle synergies can be used to assess the effectiveness of robot-aided rehabilitation and the design of innovative control strategies.

ROBOTS AND INFORMATION TECHNOLOGIES ADVANCES TOWARD LONG-TERM INTERVENTION

As the world's population ages, the management of chronic diseases will become more important. This shift will put pressure on health-care systems that often focus on providing effective care while reducing costs. The use of technological advancements to augment health-care services provides a method to meet these demands. Telerehabilitation robotics, addressed in Chapter 24, combines established features of robot-assisted rehabilitation and tele-health care to provide distance rehabilitation services. While there is a growing market of robotic devices used in traditional rehabilitation settings, home-based implementations provide a unique set of challenges (e.g., remote monitoring, deployment constraints, and data management) that has limited the number of successful solutions. Clinical and kinematic outcomes show promising results and support further investigation. Cost analyses have demonstrated that telerehabilitation robotics is a cost-effective alternative compared with clinic-based therapy. While telerehabilitation robotics is a promising addition to conventional care, numerous barriers that limit practical integration will need to be addressed to allow a more widespread acceptance and use of this approach in rehabilitation.

As a final remark, robot rehabilitation involving an interactive high-intensity, intention-driven therapy based on motor learning principles and assist-as-needed leads to better outcomes than usual care in acute/subacute, chronic stroke and other pathologies. For this reason, clinical guidelines recommend the application of these technologies for the recovery of the lost functions.

This book highlights the most important technical aspects and strategies for the design, development, and application of robot technologies for rehabilitation purposes. With their ability to adapt exercise parameters based on physiological signals, objective and sensitive metrics reflecting the state and performance of a patient, the unique possibility to combine motor and somatosensory training, and the perspective of simple and wearable tools for home rehabilitation, robot devices promise further potential for the rehabilitation of neurological patients aiming at an improved motor function, a reduction of their disability, and overall an improved quality of life.

CHAPTER

1 Physiological basis of neuromotor recovery

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INTRODUCTION

Each year in the United States, an estimated 795,000 people experience an acute, localized deprivation of oxygen and nutrient-rich blood that impairs the long-term structure and function of the brain: a phenomenon known as a stroke [1]. While a subset of strokes result from a blood vessel hemorrhage, the overwhelming majority (~87%) of stroke incidences are ischemic, resulting from a partial or complete blockage of a main arterial branch in the brain. Ischemic strokes typically involve the middle cerebral artery, a major arterial branch that supplies blood to the frontal, temporal, and parietal cortices and striatal and capsular subcortical areas. Approximately 51% of strokes occur in the cortex as a result of middle cerebral artery occlusion [2], and overall, there is a large variability in stroke type, injury location, severity, and subsequent cell death or infarction that induces a wide range of sensory, motor, and/or cognitive impairments among stroke survivors. As such, this chapter will focus on the effects of ischemic strokes on motor activity in normal and impaired cortices and further elaborate on potential therapeutic options to restore normal motor function after a stroke.

The emphasis of this chapter is on motor function, both in normal and impaired cortex, and the neurophysiological basis of neuromotor recovery following stroke. This chapter will (1) review the functional connectivity and activity within the motor network that underlies movement generation, (2) describe the phenomenon of infarction and explain how it alters motor network function, and (3) discuss the influence of rehabilitation on motor recovery following stroke.

THE FUNCTIONAL ORGANIZATION OF THE MOTOR NETWORK

Neural processes, such as those that underlie the generation of arm movement, are thought to rely on distributed networks throughout cortical and subcortical brain areas. Though many of the pathways involved in the generation of simple and complex movements require extensive activity from these subcortical areas, the focus here

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Table 1 Motor cortex nomenclature

Modern functional nomenclature	Modern abbreviation	Brodmann area nomenclature	Matteli et al. nomenclature
Primary motor cortex	M1	Area 4	F1
Dorsal premotor cortex	PMd	Area 6	F2,F7
Ventral premotor cortex	PMv	Area 6	F4,F5
Supplementary motor area	SMA	Area 6m	F3
Presupplementary motor area	Pre-SMA	Area 6	F6
Cingulate motor area	CMA	Area 23c, 24c	-
Somatosensory cortex	S1	Area 1,2,3	-
Prefrontal cortex	PFC	Area 8, 9,10	-
Posterior parietal cortex	PPC	Area 5	-

is on the cortex. Studies in humans largely confirm the broad connections between primary motor cortex, M1 (see Table 1 for all anatomical abbreviations), and other cortical motor areas by the extensive white matter connections measured with diffusion tensor imaging and the strong functional interactions observed as part of resting state functional connectivity MRI networks [3]. For a more comprehensive description of connections between motor areas, see Fig. 1.

The M1, premotor, and supplementary motor areas contain a subset of neurons that target spinal motoneurons, and though these corticospinal (CS) neurons are distributed throughout the cortex, about half reside in M1 [4]. Compared with other mammals, primate CS neurons monosynaptically target a greater number of motoneurons that drive distal forelimb musculature, and an overwhelming 80% of these CS neurons originate directly from the caudal half of M1 [4,5]. A subset of CS neurons that target single motoneurons, referred to as corticomotoneuronal cells, functionally encode specific criteria, such that a single corticomotoneuronal cell may fire to activate, rigidly lock, or brake a specific muscle movement, but are unlikely to be involved in all three actions [6]. The functional significance of this organization is that M1 is uniquely specialized to drive fine motor control such as digit manipulation or complex forelimb movements and many other parameters associated with movement. It follows that M1 injury severely impairs these capabilities relative to other motor regions.

MOTOR NETWORK ACTIVITY AND MOVEMENT

To better understand the movement parameters encoded by M1, the activity of single CS neurons has been studied for several decades. Early work decoding the activity of individual M1 CS neurons showed that CS activity precedes muscle contraction of small groups of muscles, and the rate of firing of these neurons is related to the force exerted by distal forelimb movements. This suggests that individual CS neurons can

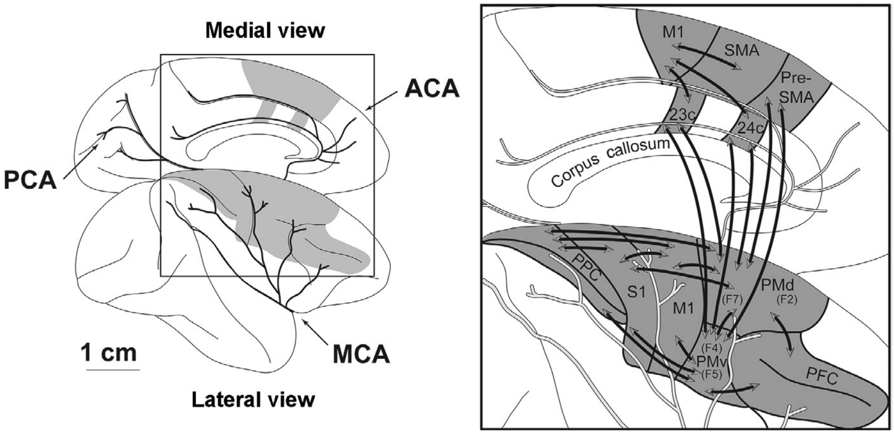

FIG. 1

Neuroanatomical studies in the motor areas of nonhuman primates reveal extensive connectivity between M1, premotor, supplementary, and other association motor areas within each hemisphere. As motor areas are bilaterally symmetrical, the medial view of one hemisphere and lateral view of the other hemisphere are used to show all relevant areas. The smaller, whole brain diagram shows the motor areas with reference to the brain in gray. Medial (MCA), anterior (ACA), and posterior (PCA) arteries are shown in black. The larger diagram shows the connectivity between motor areas. Arrows represent bidirectional connectivity between corresponding motor areas. M1 interconnects with PMd and PMv, SMA, S1, posterior parietal cortex, cingulate cortex, and contralateral M1. PMd and PMv—regions that input extensively to M1—interconnect with SMA, prefrontal cortex, orbitoprefrontal cortex, S1, and CMA. Like premotor areas, SMA and anterior "pre-SMA" similarly interconnect with M1, PMd/PMv, and CMA.

encode kinetic-based parameters, where specific neurons correlate to the contraction of muscle groups involved in functional movement execution, such as arm flexion or extension [7]. While CS activity initiates gross muscle movements, the subset of CS neurons that project directly to spinal motoneurons (corticomotoneuronal cells) are recruited during precision movements that require finer muscle control [8]. Subsequent studies analyzed the population codes of M1 neuronal ensembles to demonstrate that most M1 neurons are tuned broadly to movement direction, with increases or decreases in firing rate during limb movements aimed toward or away from the neuron's preferred direction, respectively. These results suggest that in addition to simple muscle-/kinetic-based parameters, M1 encodes extrinsic movement kinematics that includes related features of direction, velocity, position, orientation, and specific muscle activations related to the completion of movement [9]. Thus, M1 contains neuronal populations that encode both "simple" kinetic activity and more "complex" kinematics [9].

In addition to recording neuronal activity during movement, stimulation of the motor areas noninvasively either via transcranial magnetic stimulation at the cortical surface (electrocortical stimulation mapping) or via intracortical microstimulation (ICMS) at the motor output layers can elicit movements that denote the area's functional representation. ICMS techniques have revealed that M1 contains prominent proximal (e.g., elbow/shoulder) and distal (e.g., digit) forelimb and hind limb representations for the contralateral side of the body [10]. These generated movement representations are not static, and even short-term behavioral experience is sufficient to reorganize the ICMS-defined borders of each representation [11], suggesting that functional organization—and neurophysiological activity generally—may be sensitive to the perturbations by a stroke within the motor network or subsequent recovery and rehabilitation.

While the preceding understanding of motor activity has been largely based on animal models, several human studies have examined motor physiology using noninvasive electrophysiological recordings and functional imaging techniques. Electroencephalography (EEG) recordings reveal a decrease in mu (9–12 Hz) and beta (12–20 Hz) band spectral power, termed event-related desynchronization, starting in the contralateral M1 and propagating bilaterally just before the onset of voluntary movement. This decrease subsequently rebounds in spectral power, termed event-related synchronization, following movement [12]. Furthermore, studies using electrocorticography electrodes on the cortical surface have found a more focal increase in high-frequency spectral power [13]. Similar studies utilizing functional imaging methods such as positron-emission tomography and functional magnetic resonance imaging have demonstrated increases in activity in M1, supplementary motor, and premotor areas, with activations strongest in the cortical hemisphere contralateral to a moving limb but occurring bilaterally in each of these motor areas [14,15]. Unilateral movement recruits motor areas from both hemispheres and suggests that infarction in one unilateral motor area impairs bilateral motor network function that drives movement.

THE PHYSIOLOGY OF ISCHEMIC INFARCTIONS

Arterial occlusion may not induce ischemic infarction immediately. Whether temporary occlusions of blood vessels are relatively minor and go completely unnoticed or more severe and readily apparent, they are considered only a transient ischemia in the absence of tissue infarction. In the minutes that follow ischemia, a gradual and dynamic degradation of cortical tissue develops and is related to both the severity and extent of reduced cerebral blood flow. Reductions in flow rate can negatively impact local neuronal electrical activity, ion channel function, and metabolism within the 5–10 min that follow cerebral artery occlusion [16,17]. It is possible for the arterial occlusion to break apart naturally over several minutes, restoring normal blood flow and rapidly reversing both the onset of stroke-like symptoms and the likelihood of permanent damage. However, there is evidence that when arteries are occluded for longer than 1 h or when blood flow is reduced to below 10 mL/100 g/min, irreversible tissue damage can occur [17]. Prolonged periods of decreased blood flow will eventually lead to tissue infarction of not only the initial ischemic site but also the surrounding area or penumbra. Reinstatement of normal blood flow following occlusion can reperfuse the brain, rescue the tissue within the penumbra, and attenuate both the extent of infarction and severity of impairments [18]. Reperfusion of cortical tissue is not without risk, however, as it may cause an inflammatory response, increase cerebral edema, and exacerbate tissue infarction.

MOTOR DEFICITS FOLLOWING STROKE

Generally, a unilateral infarct in M1 will produce severe muscular weakness in the upper and/or lower limbs and/or the contralateral face muscles and several sensory or motor impairments such as vertigo, ataxia (loss of movement control), hemiparesis (paralysis of one side of the body), aphasia (loss of ability to express or understand speech), or hemispatial neglect (inattention to one side of the body). Studies in both human and nonhuman primates show that infarcts can also produce significant reductions in upper and lower limb strength, grip force, and precision [19,20]. While this effect is most prominent in the contralateral side of the body, the stroke survivor may also experience less severe movement-related deficits in the limbs ipsilateral to the infarct [21]. Location and infarct size can also lead to specific sensorimotor deficits, such that similarly sized infarcts that vary by location within the same motor area can produce different deficits. For example, as demonstrated in a nonhuman primate model, infarcts in rostral M1 can impair proprioceptive feedback, resulting in aiming errors; conversely, caudal M1 infarcts can impair manual motor skill and cutaneous sensation [22].

Across the population of stroke survivors, 15%–30% are left with long-term disability. In one study, approximately 50% of the survivors continued to experience hemiparesis 6 months poststroke [1,23]. While some movement recovery occurs spontaneously, targeted therapies can improve motor function in both clinical populations [24] and experimental stroke models [25]. There is a growing consensus that the amount of neurorehabilitation therapy correlates to the level of functional improvement [26]. Additionally, the timing of therapy is important, as functional recovery is thought to plateau by 3 months poststroke [27], and therapy in the acute (<1 week) and subacute (<3 weeks) phases of recovery is thought to improve recovery. However, there is also evidence that introducing rehabilitation therapy too early in the subacute phase may be detrimental [28]. This information suggests an optimal window of time where therapies most benefit movement recovery. Additional clinical trials are needed to develop an understanding of the underlying changes in the damaged motor area and the interconnected motor network involved in movement control following a stroke. This clarity will contribute to subsequent recovery strategies and appropriate rehabilitation therapies.

MOTOR NETWORK PLASTICITY FOLLOWING INFARCTION

In the aftermath of cortical infarction, intact motor areas utilize innate mechanisms to compensate for damaged motor areas and recover lost motor function. One longstanding premise is that the cortex has vicarious capacity, which allows undamaged cortical tissue to, in some sense, take over the role of focal, damaged tissue [29]. A number of studies have shown that intact regions compensate for injury, but a comprehensive understanding of which processes facilitate vicarious recovery in undamaged cortices is still incomplete. The periinfarct zone, or PZ, is the adjacent, undamaged cortex that surrounds the infarct and undergoes major neuroanatomical changes. Here, the rate of de novo neuroblast formation increases in a regular "wavelike" pattern, and these embryonic neurons migrate to the damaged cortex, at least in rodent cortical ischemia models [30]. In response to infarction, the cortex recruits neuroblasts to compensate for the damaged tissue and, as a result, replenishes the number of neurons in the PZ. The initial 2 weeks postinfarct see an increase in GAP-43, a protein associated with neurite growth, and, subsequently, an increase in synaptophysin, a protein associated with synapse development [31]. The increase in GAP-43 and synaptophysin suggests that the cortical areas surrounding the infarct initially add new neurons, then establish novel connections, and shape these connections into specific pathways as a function of network activity [32]. The sequential timing of neuronal proliferation and synaptic development could provide an avenue to explore potential time-critical drug therapies. For example, systemic administration of dextromethorphan (an NMDA receptor blocker) or lorazepam (a GABA-A receptor-positive allosteric modulator) attenuates training-induced plastic changes and suggests that targeted activation or suppression of NMDA and GABAergic receptors at specific time points of neuronal reorganization could selectively modulate neuroanatomical recovery [33]. Existing neuronal connectivity from intact motor areas is also modified accordingly: In nonhuman primates, afferent axons from more remote PMv and contralateral M1 areas will subsequently redirect from the infarct tissue to the new neurons in the PZ, PMv establishes novel reciprocal connections to S1, and horizontal connections in the PZ redirect to other adjacent, intact M1 subregions [29]. In the intact cortex on the opposite side of the brain (contralateral cortex), GABA-A receptors are downregulated, NMDA receptors are upregulated, dendrites expand or retract, novel synapses are formed, and synaptic morphology changes [34]. Thus, M1 infarction triggers massive neuroanatomical reorganization not only in the injured M1 but also throughout the bilateral motor network.

FUNCTIONAL PLASTICITY FOLLOWING INFARCTION

HUMAN STUDIES

Improvements in motor function following stroke have generally been associated with a "perilesional awakening" of cortex. While fMRI and EEG scans reveal that infarcts initially shift hemispheric activity to the intact, contralesional hemisphere during paretic limb movement, activity between both hemispheres generally normalizes as a function of rehabilitative training [35,36]. The timing of this normalization correlates with the unilateral or bilateral recruitment of sensorimotor areas. However, the role of this intact hemisphere activity is uncertain. In general, the increases in the activity of the unaffected hemisphere during movements following stroke are found to be indicative of motor recovery [37–39], but paradoxically, these increases have also been related to poorer outcomes after stroke [40].

Ultimately, it may be possible to reconcile conflicting evidence about the role of the contralesional hemisphere. Though there are increases in the magnitude of both ipsilesional and contralesional activity during recovery from stroke [37,38], survivors with more complete recovery tend to exhibit a similar asymmetry in the location of this activity between both hemispheres. In contrast, survivors with incomplete recovery that have a greater asymmetry in the location of the activity between hemispheres show better rehabilitative outcomes [41]. This dichotomy may be a pathological consequence of CS loss: greater loss of descending CS connectivity is highly correlated with motor impairment following stroke and likely induces greater development of new cortical and subcortical pathways [42]. Thus, bilateral symmetry is reduced due to atypical and possible asymmetric hemispheric-specific changes in activity. While plasticity in the ipsilesional hemisphere may be optimal for recovery, in the contralesional hemisphere, it appears to be beneficial in survivors with extensive lesions. To this point, there has been evidence to suggest that contralesional inhibition improves motor function when infarct size and impairment are small yet further impairs motor function when infarct size and impairment are extensive [43].

Along with localized measures of cortical activity, there is evidence that the interaction between cortical areas also plays a role in recovery from stroke. Disruptions in interhemispheric connectivity, as observed by resting state functional connectivity MRI, are related to network-specific deficits following stroke [44]. Similarly, inhibition of the ipsilesional hemisphere from the contralesional hemisphere (since callosal connections are largely inhibitory) correlates with motor impairment [45]. Furthermore, lowered interhemispheric inhibition, through impeded contralesional hemispheric activity, can improve motor performance of the paretic hand [46].

While human clinical trials allow for investigation of cortical plasticity in the stroke survivor population of interest, there are also significant limitations. Outcome measures for effects of rehabilitation have been highly variable across experiments, and there is also significant diversity in the location and extent of cortical lesions across individuals within and between trials, making generalizations across studies difficult [47]. For example, one such study found that chronic stroke patients with middle cerebral artery occlusion had deficits in reaching accuracy and velocity in forelimbs, and patients commonly overshot their intended target [48]. Although this study is controlled for the same-type occlusion, there was still massive variation in injured cortical and subcortical motor and nonmotor areas. These studies help inform what features of movement are most impacted by M1 infarction, but for more controlled studies that focus on the consequence of exact injuries, the use of animal models of cortical injury is required.

Though differences exist in the mechanisms of recovery between experimental models of cortical injury and human stroke survivors, studies in animal models provide the ideal settings to both design rigorously controlled studies and examine mechanistic effects not possible in a human population. However, neurophysiological and neuroanatomical differences between human and nonhuman animal motor networks, especially those that may influence rate and extent of recovery, must be considered.

ANIMAL MODELS OF CORTICAL INJURY

Just as short-term behavioral experience can modify motor representations in a normal cortex, it can also modify the motor representations in the infarcted cortex. In the ipsilesional hemisphere, infarcts reduce the somatotopic area of distal forelimb representations and expand proximal forelimb representations in the PZ without rehabilitative training of the paretic limb; but rehabilitative training both preserves and expands these distal forelimb representations [49,50]. PMv motor map representations also reorganize as a function of the M1 infarct size: smaller M1 infarcts reduce the size of PMv distal forelimb representations, while larger infarcts increase distal forelimb representation size [51,52]. There is also evidence to suggest that the supplementary motor area increases in distal forelimb representations following M1 infarction [53]. Therefore, it appears that the intact M1, premotor, and supplementary motor areas compensate for the loss of function following infarction.

Why do motor representations change as a function of rehabilitative training? One possibility is that infarctions induce select changes in GABA-A synaptic or extrasynaptic receptor expression. Downregulation of synaptic (i.e., phasic) GABA-A receptor inhibition can increase phasic channel excitability in both hemispheres [54]. Paradoxically, infarctions also induce an upregulation of extrasynaptic (i.e., tonic) GABA-A receptor inhibition and decrease tonic channel excitability [54–56]. These disruptions in normal channel excitability can modify neuronal potentiation and alter postinfarct motor representations [57].

In the contralesional hemisphere following infarction, studies in rodents show a sudden hyperexcitability that is initiated within a few hours after M1 infarct, suggesting rapid changes in the neurophysiological activity of extant connections [58]. ICMS maps reveal that somatotopic motor representations expand rapidly but usually normalize within 3 days [59]. This hyperexcitability in the contralesional hemisphere appears to facilitate recovery, as functional improvement in paretic limb movement is attenuated following inactivation of the contralesional cortex [60]. Somewhat contradictory is the finding that contralesional inhibitory input to the ipsilesional hemisphere may be maladaptive to recovery [61]. In injured brains where one hemisphere is damaged, there is a loss of a normal interhemispheric inhibitory balance, such that contralesional activity increases and ipsilesional activity decreases. This decrease in ipsilesional activity may impair its own recovery. While these results make clear that more studies are needed to elucidate the role of the contralesional hemisphere in functional recovery of the motor network, they also suggest that future therapies focusing on contralesional hemispheric activity could facilitate recovery of the ipsilesional hemisphere.

CONCLUSIONS AND IMPLICATIONS FOR REHABILITATIVE THERAPIES

This chapter summarizes current research on neuromotor recovery following cortical infarction within the motor network. Both humans and animal models exhibit complex cortical changes in relation to the functional activity and the anatomy of

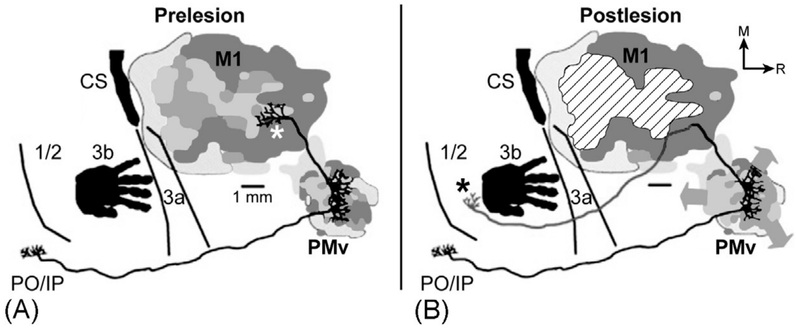

FIG. 2

Cartoon summary of the reorganization that occurs in PMv following M1 lesion. (A) Prior to the lesion, PMv distal forelimb representation is interconnected with M1 and with secondary somatosensory areas in the posterior operculum. (B) Following a large M1 infarct that destroys most of the distal forelimb representation in M1 (represented by diagonal lines), the cortical area devoted to this representation in PMv expands (thick gray arrows in B). These physiological changes are associated with abrupt changes of axon orientation and the border of M1 and novel projections to the primary somatosensory cortex. CS, central sulcus; PO/IP, posterior operculum/inferior parietal cortex.

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intact cortex (see Fig. 2) and support a model for vicarious recovery, where, in part, intact cortical areas take over the function of damaged cortical tissue. In humans, several neuroprosthetic devices have been developed that enhance recovery noninvasively by training a computer to drive movements based on specific cortical signals from the ipsilesional (reviewed in [62,63]) and more recently contralesional [64] hemispheres. Also, given the high variability of stroke location and severity in human survivors, animal models are useful for addressing fundamental gaps in our knowledge and can one day help us understand how to better exploit the plastic changes that are initiated by the brain postinjury. For example, a recent study in rodents with M1 lesion demonstrated the possibility of recovering limb movement by applying stimulation to somatosensory cortex based on the recorded activity in premotor cortex [65]. In conjunction with these animal studies, future work in human stroke survivors will be important for developing therapies that optimize recovery of functional movement by utilizing intact motor areas. Ultimately, it will be a combination of neuroanatomical and neurophysiological research in both animal and human models that helps clinicians better design evidence-based interventions that more effectively restore motor network function after cortical injury.

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CHAPTER

An overall framework for neurorehabilitation robotics: Implications for recovery

2

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INTRODUCTION

As described in previous chapters, the motor system is characterized by a huge number of elements combinable in different modalities to reach the same target. The control of such a high-dimensional system represents a considerable computational problem to be solved quickly and efficiently by the central nervous system (CNS) with the purpose of guaranteeing optimal motor performance in every environmental context. Several models have been proposed in the literature to describe how the motor system acts in its interaction with the external environment [1,2] and to explain intrinsic mechanisms underpinning neurophysiological functions [3]. Those models are commonly based on mathematical functions explaining, in whole or in part, human behavior [4]. A theoretical approach to solve the problem of controlling dimensionality has been based on the concepts of hierarchical architecture of the motor system and its functional synergistic actuation for behavioral output.

HIERARCHICAL ARCHITECTURE OF THE MOTOR SYSTEM

The motor system is organized according to a hierarchical architecture allowing an efficient functionality within its physical constraints (e.g., muscles, bones, and joints). Four major components are recognized as being the motor system scaffolding, each one representing a different level, according to a peripheral-central direction:

- First level: the spinal cord (reflex responses)
- Second level: the brain stem and reticular formation (integration of ascending and descending pathways)
- Third level: the motor cortex (Brodmann's area four representing 30% of corticospinal and corticobulbar fibers devoted to the activation of descending motor commands)

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- Fourth level: premotor cortical areas (Brodmann's area six representing 30% of corticospinal and corticobulbar fibers devoted to programming of movements)

Three common aspects characterize those levels:

1. They contain somatotopic maps.
2. Each level receives information from the periphery.
3. Higher levels control information that reaches them, allowing or suppressing the transmission of the afferent volley by means of a sensory relay.

The cerebellum and the basal ganglia complete the hierarchical architecture of the motor system [5]: the former modulating anticipatorily the activity of the brain stem and of the cortex and the latter intervening in movements' selection and underpinning reward mechanisms related to successful behaviors [6]. This top-down architecture is also regulated by means of parallel circuits (e.g., interneurons, descending fibers from supraspinal regions, and neuronal gating) that, working independently, increase the modularity of the entire system and so its flexibility in accomplishing the demanding requirements coming from an unpredictable external environment.

An exhaustive model of the motor system should take in consideration, in a unique framework, the neuroanatomy, neurophysiology, and computational aspects clinically useful for the interpretation of human motion. With regard to a similar model, it has been suggested that the following anatomical gradients and parallel circuits in the brain are associated with natural motor behavior:

a. In the parietal and premotor cortices, the level of activation smoothly changes according to the difficulty of motor planning and control required by the task.
b. In the frontal lobe, an anterior-to-posterior gradient is responsible for the transformation of an action's intended goal into effective motor commands.
c. Parietofrontal circuits code for a stimulus' location and estimation of body's state (sensory-to-motor transformation) [7].
d. In the premotor areas, medial-to-lateral gradients are involved in planning of internally guided actions (e.g., motor imagery).

FUNCTIONAL SYNERGIES

The architecture so far described is composed of a large number of elements, whose combination can be redundant, thus highly complex to control. To solve this issue, a synergy has been conceptualized as the pooling of different components of the system in stable functional units ready to be activated in larger stable organizations, thus reducing the degrees of freedom that need to be controlled, therefore simplifying the computational demands needed to achieve a successful result. In the field of motor neuroscience, it has been proposed that the CNS might operate exploiting similar strategies to cope with the high dimensionality of the motor system with the goal to produce smooth, well-coordinated, low-energy consumption and targeted voluntary movements. At the muscular level, the pooling of several muscles in one single functional group is called muscle synergy and represents the instantaneous activation of all the muscles, each one activated with its own specific amplitude. It has been postulated that in a similar model, the activation of every single neuron at a higher level induces cascades of events mediating excitatory and inhibitory effects at the same time. The consequent organization should be most probably based on overlapping networks that synergistically produce common effects targeted to set of muscles instead of a one-to-one effectors' control. The synergistic activity of all the mechanisms described so far allows the emergence of human voluntary motor behavior. Nevertheless, the majority of the underlying relationships still remain unknown. Moreover, from an experimental point of view, it is not yet feasible to control for all the interferences occurring while performing a paradigmatic task. Thus, neural solutions that permit the reduction of the musculoskeletal system's degrees of freedom to be controlled are useful not only to clarify control strategies stored in the motor system but also to set up effective approaches for studying human motor behavior especially when affected by neurological disorders. As a general clinical framework, every level potentially involved in closing the loop of voluntary motor behavior should be considered when planning a rehabilitation modality with the aim to favor true instead of compensatory plasticity mechanisms for the recovery of body functions (Fig. 1).

On the left, the basic mechanisms ruling the closed-loop interaction between human motor behavior and external environment are represented. On the right, the reference framework of the closed-loop subject-environment interaction is schematized.

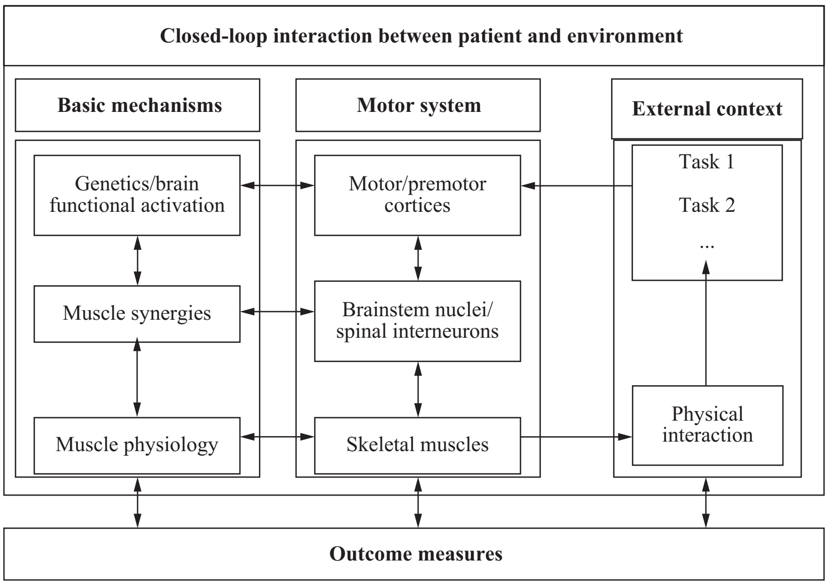

FIG. 1

Scheme for mechanisms mediating the closed-loop interaction between the motor system and the external environment.

NEURAL PLASTICITY AND FUNCTIONAL RECOVERY, AFTER LESION OF THE CENTRAL NERVOUS SYSTEM

After brain insult, both true and compensatory recovery mechanisms spontaneously drive the restoration of normal functionality as best as possible to approximate function before lesion. The probability to regain good motor function of the motor system after injury is influenced by the anatomical areas affected, both in the musculoskeletal system and in the brain. Evidence in humans revealed that when the brain is insulted, cortical lesions (preferably in the primary motor areas) result in milder motor impairment than subcortical lesions, whereas mixed cortical-subcortical lesions have a better chance to recover than pure subcortical brain lesions [8]. It is widely accepted that the recovery process along the rehabilitation course is a combination of both true and compensatory mechanisms mediated by neuroplasticity [9]. The reference goal for rehabilitation, particularly for therapeutic modalities whose rationale is based on neurophysiological principles (e.g., technology-aided therapies), is the facilitation of true recovery against the instauration of compensatory adaptive behaviors, which are generally considered as maladaptive.

THE NEUROBIOLOGY OF MOTOR SKILLS ACQUISITION AND LEARNING FOR REHABILITATION

The possibility of learning new motor skills can be defined, from a kinematic point of view, as the ability to optimize sequences of fast and accurate movements with the aim to accomplish specific tasks [10]. For this purpose, a large variety of different but mostly unknown mechanisms are implicated at several levels (e.g., genetics, neuroanatomy, and neurophysiology). It has been hypothesized that the development of sequences of skilled movements involves the strengthening of the spatiotemporal relationship between specific networks while weakening others. This process may occur through changing the connectivity between specific sets of corticospinal neurons through changes in synaptic efficacy [11]. This spatial and temporal reorganization of synaptic weights is known as a connectivity map, the activation of which has been postulated as the biological substrate for all functional behaviors in animal and humans. Some specific principles characterize the organization of connectivity maps in the motor system: (1) The representation of individual movements is distributed and highly interspersed with adjacent cortical regions (fractured somatotopy); (2) adjacent cortical areas are densely interconnected through the corticospinal tract bundles (interconnectivity); (3) the higher the dexterity of a movement, the larger the proportion of the map represented in the related cortical areas (area equals dexterity); (4) internal and external environmental stimuli are the drivers for dynamic changes of maps' topography (plasticity); and (5) the disruption of motor maps causes inability to produce skilled limb movements but does not abolish movement.

In recent years, a new fundamental property became evident related to plasticity of connectivity maps in the motor system. Since the studies by Nudo et al.

Motor training → neural signalling → gene transcription → protein translation → synaptic plasticity → circuitries changes → map reorganisation → motor skill

FIG. 2

Cascade of neural events from behavioral training to motor skill acquisition.

(see Chapter 1), it has been widely accepted that, following anatomical lesions affecting structures of the motor system, both motor maps and skilled movement can be restored by the administration of massed practice motor training and rehabilitation (see Chapter 1). These findings strengthened the idea that motor maps reflect a level of synaptic connectivity within the motor cortex that is required for the performance of skilled movement. At the biological level, this evidence was confirmed by experiments on rats where cholinergic inputs to the motor cortex were removed before task-specific exercise, thus preventing training-dependent map reorganization in their motor cortex with consequent impairment of motor learning [12]. On these bases, skill learning might induce changes in synaptic efficacy exploiting plasticity within the motor cortex with consequent changes in map topography (Fig. 2). At the behavioral level, the main parameter driving this retrograde effect of training on brain plasticity is intensity, defined in the case of motor skill training as the amount of repetition executed for specific tasks. In order to induce an effective brain reorganization, a certain threshold (i.e., number of repetitions) needs to be crossed. This effect is known as experience-dependent neuroplasticity, and in animal models, it was estimated that a range between 1000 and 10,000 repetitions of the same task (trials) is needed to observe a permanent change at synaptic level [13]. Most of the strategies adopted in rehabilitation robotics to vicariate true recovery exploit the experience-dependent neuroplasticity phenomenon, which occurs when a large amount of repetitions is practiced for a sufficient time length (15 days at least).

REHABILITATION MODALITIES

The rapid restoration of deficits after injuries of the CNS and the attainment of a lifestyle as close as possible to the premorbid state are among the main partially unachieved purposes of neurological rehabilitation. Surprisingly, there are many therapeutic approaches to restore lost functions but few of them with clinical evidence of efficacy; thus currently, researchers are working to develop treatments related, as closely as possible, to neurophysiological principles coming from basic science. A large number of approaches (e.g., Kabat and Brunnstrom) based on neurophysiology of the motor system have been proposed for motor rehabilitation in the past decades by many authors [14]. Recently, innovative treatments have considerably increased the repertoire of available therapeutic and rehabilitative strategies. In fact, increasing evidence has sustained the effectiveness of feasible technology-aided approaches aimed at augmenting mechanisms of physiological recovery involved in the production of voluntary movements after a brain lesion. Among them, the best-studied approaches are electromyography (EMG) biofeedback [15], robot-assisted therapy [16], virtual reality (VR)-based interventions [17], constraint-induced movement therapy (CIMT) [18], and functional electric stimulation (FES) [19]. However, despite advances in the understanding of the CNS lesions aftermaths and development of innovative rehabilitation methods, there is no evidence that suggests superior efficacy of one method over others. Several gaps need filling to better understand the relationship between the neuroanatomical structures and the neurophysiological mechanisms involved in human voluntary movements and unravel possible pipelines leading from brain activations to natural behavior.

Following a neurological disease, it is not possible to treat all movement disorders only by physical rehabilitation; in fact, some individuals will benefit also from pharmacological, surgical, or orthotic interventions, and there is no unique consensus on how to deliver motor treatment. Nevertheless, certain general principles are always present in effective rehabilitation treatments independently from the chosen technique. Regardless of the rehabilitative modality chosen, six principles should always encompass every therapeutic program [20]:

1. The establishment of an agreement between patient and the therapy team
2. Analysis of behavioral deficits according to the principles of brain reorganization previously described
3. Reliable measurements of impairment, function, and activity before, during, and after therapy
4. Planning of a rehabilitation program according to the prognosis of a patient
5. Administration of an appropriate amount of therapy in terms of specificity, intensity (dose), and repetitiveness
6. The presence of an appropriate therapeutic environment shaped for motor learning (e.g., modular spaces, possibility to augment feedbacks, adequate to subjects' comprehension, and attention)

Within this framework, it is possible to classify current rehabilitation techniques in three major groups according to the following descriptions (Fig. 3):

- *Priming techniques*: interventions that may prepare the sensorimotor system for increased plasticity promptness through direct stimulation (physical or sensorial) of tissues.
- *Augmenting techniques*: interventions that enhance the effects of sensorimotor interaction during practice.
- *Task-specific practice*: interventions based on massive practice of specific tasks performed in real environment, with the aim of prompting the best generalization of learning in real life [21].

The concept of priming after lesions of the CNS deals with the issue of promoting substitution or restitution strategies for recovery of lost functions due to the lesion

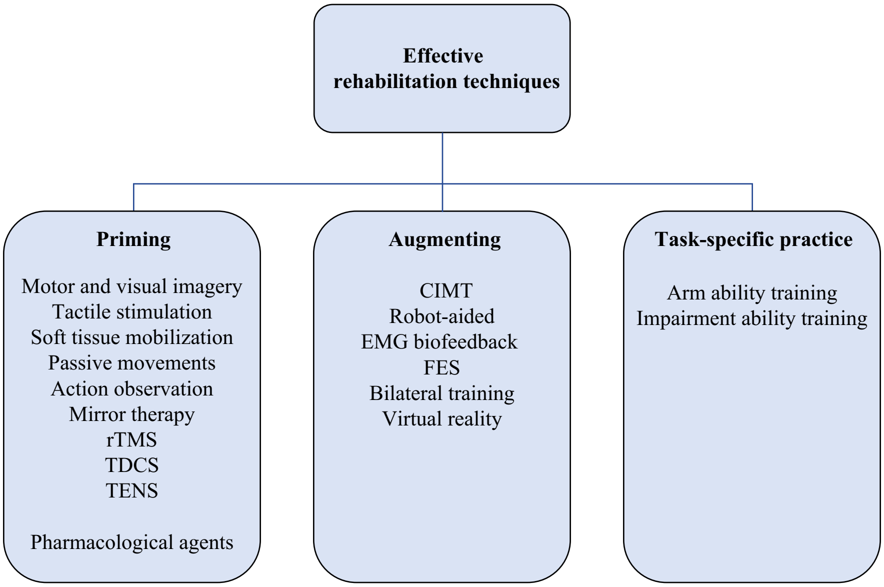

FIG. 3

Classification of motor rehabilitation techniques. *rTMS*, repetitive transcranial magnetic stimulation; *TDCS*, transcranial direct-current stimulation; *CIMT*, constraint-induced movement therapy; *EMG*, electromyography; *FES*, functional electric stimulation; *TENS*, transcutaneous electric nerve stimulation.

location in the brain. With restitution is meant the possibility to reinstate function in the brain structure interested by the lesion with the aim to maximize motor recovery. In this regard, the more is the residual excitability in the lesioned primary motor area (M1), the better the prognosis for motor recovery. When excitability is predominant in the unaffected hemisphere, a substitution strategy is recommended, aimed at inhibiting overactivation of the unaffected side potentially masking the affected one with maladaptive mechanisms. Recent advances in neurophysiological techniques provide methods to temporarily condition neural networks by administration of electric (tDCS) or magnetic (rTMS) fields to the brain through the scalp. This brain stimulation is able to modulate synaptic balance between neurons promoting the so-called metaplasticity (i.e., the plasticity of synaptic plasticity) [22]. With a wider meaning and rehabilitation purposes, all the modalities able to induce a temporary modification of any structure in the musculoskeletal (e.g., passive mobilization of soft tissues and tactile stimulation) and neurological systems (e.g., motor and visual imagery and action observation) are considered as promoting priming of the structures involved in expressing voluntary motor behavior.

The concept of augmented modalities deals with the evidence that enrichment of the external environment, where animals or subjects are requested to interact with, leads to significant modifications of their own functional systems, both at a central (e.g., CNS) and at a peripheral level (e.g., muscles). Experiments in rats demonstrated that animals living in environments providing greater opportunities for physical activity, motivation, and socialization, after experimentally induced stroke, show augmented sprouting and brain plasticity than those living in standard laboratory cages [23]. This evidence has been applied also to stroke rehabilitation, and all the artificial environments (e.g., robot, virtual reality, and biofeedback) augmenting specific features and providing feedback information on results and performance of tasks accomplished are considered as the clinical translation of enriched environments. So far, clinical evidence suggests that this approach is successful particularly for impairment-oriented treatment, but more insights on the mechanisms involved are needed [24].

The concept of task-specific practice comes from the movement and motor-skill-learning literature [25] and has been defined by Teasell and collaborators [26] as training or therapy where patients "practice context-specific motor tasks and receive some form of feedback." This wide definition can be applied to almost all the therapeutic settings available in rehabilitation care; therefore, all the modalities aimed to massive practice of everyday tasks with real-world objects are intended as task-specific practice in clinics. The aim is to achieve optimal function performance that can be replicated in everyday activities, thus improving the quality of life in ecological environments.

CHARACTERISTICS OF SUCCESSFUL STRATEGIES FOR NEUROREHABILITATION: CLINICAL EVIDENCE

The motor system has multiple connections with many nonmotor areas throughout the whole brain; thus, brain injury sequelae usually affect multidomain functions. Currently, it is still difficult to assess exhaustively all the impairments following a lesion of the CNS and even harder to predict their effect on rehabilitation outcomes. Recent reviews updated evidence on motor neurorehabilitation allowing the classification of rehabilitation modalities (i.e., priming, augmenting, and task-oriented) and the identification of the specific target each one is referred to and the respective ICF domain supposed to be tackled (Fig. 4). In the field of neurorehabilitation, time contingency, specificity, intensity, exercise parameters, and therapy doses are acknowledged to be critical aspects to consider for the planning of effective rehabilitation programs regardless of the modality chosen. Several pieces of evidence have been provided on the prominence of exercise features, and as an example, the effect of very early mobilization (i.e., within 24 h from stroke onset) represents the current edge of experimental investigations [27,28] with reference to time contingency. To date, there is still no consensus on which is the best treatment form for regaining motor function after lesion of the CNS [29], but a recent overview of reviews from Pollock et al. [30] provided evidence that the best treatments for the upper limb after stroke are the ones focused on the reinforcement of the visual-motor loop, such as virtual reality (VR), mirror therapy, and mental practice.

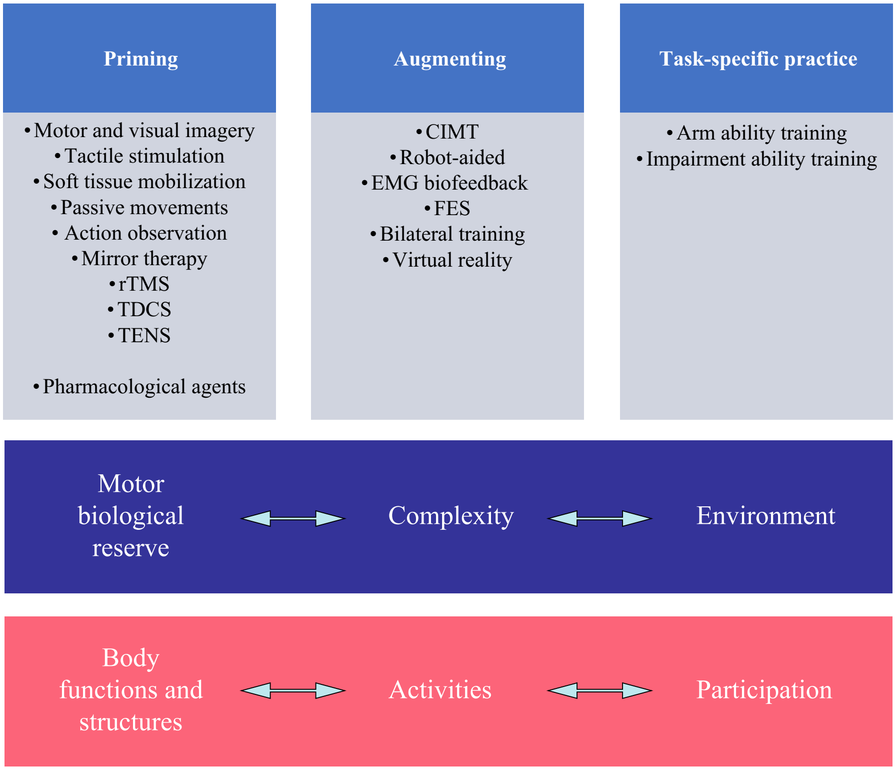

FIG. 4

Biological, computational, and functional purposes of rehabilitation modalities with ICF-related domains.

Clinically speaking, augmenting techniques (e.g., virtual reality and robotics) might be considered like the reference standard for impairment-oriented treatment of the upper limb. For VR-based treatments, efficacy has been demonstrated by Laver et al., whose metaanalyses showed that in stroke patients, this modality is better than conventional rehabilitation therapies to improve upper limb motor function (SMD = 0.29 (0.09 and 0.49)) with some transferability to regained autonomy by patients (SMD = 0.42 (0.18 and 1.29)). Moreover, it was demonstrated that a dose effect exists with a minimum of 15 h of therapy needed for inducing a clinically significant effect (SMD = 0.31 (0.07 and 0.55)) and that specialized VR systems are better than commercial gaming systems (SMD = 0.42 (0.07 and 0.76)). Nevertheless, the mechanisms underpinning this clinical evidence are still unknown and matter for debate.

Each rehabilitation modality group is represented overlying its own alleged purpose and international classification of functioning (ICF) domain so that a bio-computational balance can be achieved for the production of effective voluntary movements.

In general terms, imaging studies carried out with stroke patients have suggested that bilateral hemispheric activation is common after brain lesion, but its persistence when voluntary movements are performed is a predictor of poor motor recovery [31]. Complimentary, preservation of activation in the hemisphere ipsilateral to the lesion at resting state analysis is a good predictor of motor recovery [32]. Still, it remains to be clarified whether the presence of bilateral hemisphere activation should be considered a maladaptive or compensatory phenomenon in motor recovery. Despite uncertainty coming from fMRI studies, this technique remains among the most robust available to study the brain changes occurring during the recovery process after stroke. Some imaging evidence is available for each of the rehabilitation modalities reported above. Indeed, priming approaches seem to increase the activation of both the primary and the extended motor system [33]; augmenting techniques, such as robotics, seem to increase the activation of sensorimotor cortex [34], while virtual reality seems to decrease the activation of premotor cortex contralateral to the lesioned hemisphere [35]; task-oriented practice seems to decrease the activation of the unaffected hemisphere [36].

CONCLUSION

The research field of innovative technologies in rehabilitation (e.g., virtual reality, telerehabilitation, and robotics) has increased hugely in last decades [37]. This trend has been sustained by several recent phenomena like the spreading of low-cost technologies able to monitor physical activities of each subject for 24 h a day, the enlargement of connectivity bandwidth and easy access to cloud services making data sharing feasible and powerful, and the easy manufacturing of experimental prototypes using 3D printers. Other fields of research such as neurophysiology have demonstrated that cortical plasticity and learning can be modulated by other priming techniques like repetitive transcranial magnetic stimulation (rTMS) [38] or transcranial direct-current stimulation (TDCS) [39]. A direction to pursue for future studies should consider the effect of combining priming with augmenting techniques with the aim to augment the effects achievable from the administration of each one independently. Some studies have been recently carried out with this purpose [40]. Several questions remain, however, unanswered about the possible outcome/contribution of using combinations of different treatment modalities: Which is the contribution of each technique? Does the combination empower or interfere with basic mechanisms underpinning recovery and operating at central level? Does the combination increases the risks of side effects? Future research might discuss whether the combination of different known treatment modalities should be considered as a specific modality in itself; thus, experiments exploring whether the same or new basic mechanisms operate when different techniques are merged will be needed.

Finally, future research should take into consideration the inclusion of reliable outcome measures for the detection of patients' quality of life and participation changes due to each rehabilitation modality. In fact, according to the Cumberland consensus model [41], findings coming from all the phases of the research pipeline need to be translated in the delivery of health services only when results have a significant impact on a patients' real life.

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CHAPTER

Biomechatronic design criteria of systems for robot-mediated rehabilitation therapy

3

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INTRODUCTION

Research in biomedical robotic technologies is experiencing a huge development in several health domains, such as wellness, rehabilitation treatment, and prevention of age-related sensorimotor decay [1].

Thanks to technological advancements, such robots are more sophisticated mechatronic systems, equipped with powerful processing units able to exploit real-time information on the human component for enabling patient-tailored assistance during the exercise to be performed. In the most advanced cases, these robotic machines allow real-time tailoring of each exercise and of the whole therapy on the basis of users' residual abilities and online assessment of human performance and of the intended motor-training strategy.

The rationale for robot-aided neurorehabilitation is grounded on the relatively recent scientific evidence in neuroscience that physical exercise and especially action-related movements promote functional recovery even after traumatic lesions of the central nervous system (CNS), having significant positive effects in the process of neurogenesis and speeding up basic mechanisms involved in neural plasticity [2]. In this perspective, robotic machines for motor therapy may play a fundamental role in rehabilitation and promote the recovery of the brain areas devoted to high-level motor control by assisting and guiding the subjects to perform motor tasks while fully exploiting their residual sensorimotor coordination abilities. The user plays a crucial role in robot-aided therapy since the early stage of the design of such systems. Rehabilitation robot design has to meet users' requirements, adapt to human performance and guarantee safety, robustness, reliability, comfort, and freedom of movement while pursuing effectiveness of the treatment.

To start the biomechatronic design process, first, an in-depth analysis of human-activity interaction and interfaces in the target application scenario must be carried out in order to properly identify subtasks and activities of interest, for the introduction of robotic technology in such scenario. Then, optimal reallocation

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of roles must be clearly defined by considering the most appropriate role(s) that each of the agents (the patient, the therapist/physician, and the assistive machine) concurring to the rehabilitation exercise could play. Allocation of roles must be dynamic, that is, depending on different environmental and human-related conditions, roles could be reallocated in order to implement the best solution for stimulating patient recovery.

Once each of the agents has been assigned a specific, dynamic role, interaction design among them must follow by identifying the style and modalities of interaction and what type of interfaces should enable such effective interaction. Fig. 1 depicts the design steps for these machines.

A biomechatronic approach does require a detailed characterization and modeling of the biological system interacting with the robot before the classical, mechatronic design cycle can be started. The aim is the definition of the functional and technical specifications and the consequent concurrent identification of key characteristics of all the robot components in terms of interfaces, mechanical structures, actuators, sensors, control and supervision units. Human component modeling is iteratively used all along the design process to optimize the various subsystems not only in the initial stage but also for simulating and testing viable solutions before translating them to real human subjects.

In Fig. 2, a general functional scheme of a system delivering robot-mediated motor therapy is shown, as the main reference guideline for identifying key subsystems and components to be designed, developed, integrated and tested.

Allocation of roles does play a crucial role for a successful design and eventually for promoting the acceptability of the proposed technology by health-care professionals and end users. Several examples of possible different approaches have been developed both for upper- and lower-extremity robot-aided therapy, such as the Lokomat [3], the KineAssist [4], and the ArmeoPower (Hocoma, AG). In the first case (Lokomat), both the machine and the patient are not accessible to the therapist

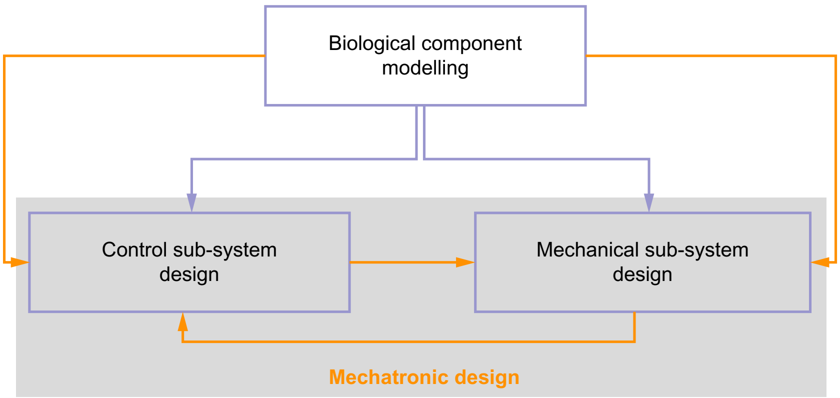

FIG. 1

Biomechatronic design approach.

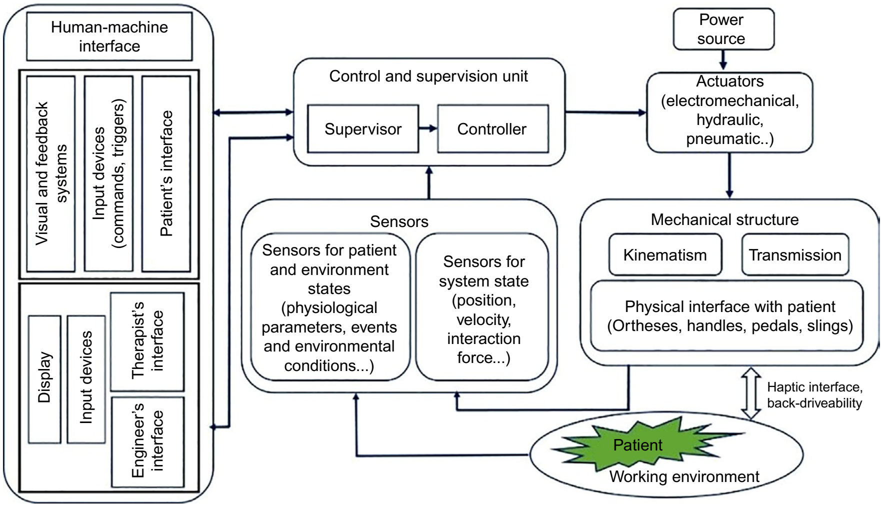

FIG. 2

Typical functional architecture of a robotic machine for neurorehabilitation.

during the exercise that is executed in a highly structured manner. In the second case, both KineAssist and ArmeoPower are machines that help the subject to counterbalance gravity and guide the exercise but without directly controlling synergies among motor districts that remain instead directly accessible to the therapist even during the task execution.

From these examples, it is evident that the successful design and application of a robotic machine for neurorehabilitation depend on an initial in-depth analysis of the scenario in which the machine is being used in order to provide a correct identification of the roles of each component acting in the rehabilitative process, with a particular emphasis on the expected performance of the patient and the therapist versus the machine.

In this top-down approach of robotic rehabilitation machines, modeling and characterization of the human behavior and identification of all the possible human-machine interaction schemes will pave the way for a successful design of exercises.

The objective of this chapter is to provide an overview on the design criteria of biomechatronic systems for robot-mediated rehabilitation therapy focused on both the upper and lower extremities.

Section "Design Criteria of Biomechatronic Devices for Robot-Mediated Rehabilitation" of this chapter presents the basic criteria for the design of mechatronic devices aimed to restore motor function in neuroinjured patients.

In Section "Modeling the Human Component," the human component and its modeling are discussed by analyzing in detail the common approaches pursued for extracting a biomechanical model of the upper and lower limbs. This is just one of the many possible dimensions of modeling to consider.

Section "Overview of Control Strategies" discusses some common control algorithms to be used for implanting safe and effective physical human-robot interaction.

Then, in Section "The CBM-Motus and the LENAR: Two Case Studies," two case studies of biomechatronic design approach are presented: the CBM-Motus, a planar robot for upper-limb poststroke rehabilitation, and the LENAR, a nonanthropomorphic wearable robot for walking assistance.

Final considerations on biomechatronic design of rehabilitation robotic systems and emerging trends are briefly discussed in Section "Conclusions."

DESIGN CRITERIA OF BIOMECHATRONIC DEVICES FOR ROBOT-MEDIATED REHABILITATION

The design of robotic devices for assisted lower- or upper-limb rehabilitation has to strictly cope with a number of biomechanical constraints, dictated by the complex nature of human body dynamics. To this purpose, it is very important to reconsider the technologies and the models that are used in the design and fabrication of biomechatronic devices and bio-inspired robots in order to achieve further progress.

In the field of neurological rehabilitation, the clinical and therapeutic requirements have not been deeply considered so far in the design of rehabilitation robots [5,6]. In fact, rehabilitation robots' design seems to be more oriented toward adding mechanical complexity, that is, increasing the number of sensors, DOFs, and actuators.

Two main categories of systems for robot-mediated therapy can be considered: wearable or operational/end-effector-based machines. The former solution allows direct control and assistance of the motor synergies, whereas the latter category only accounts for the control of the trajectory of human end effector, for example, the foot/ankle or the hand/wrist. Selection of the proper type of machine must be based on the analysis of the estimated residual abilities of the target patient population and of the related therapeutic requirements and specifications.

When the operational-machine category is selected, robot motion in the joint space is not directly constrained by human biomechanics provided that the end-effector trajectory in the operational space is confined within the human-limb workspace. Consequently, kinematic design of such robots can be based on traditional approaches aiming at optimizing dynamic performance, complexity, cost, weight, encumbrance, and other characteristics of the system that might have some priority based on the outcome of the prior top-level analysis of the roles to be assigned to the robot.

The kinematic design of wearable rehabilitation robots, instead, presents in general a twofold possibility: it can follow an *anthropomorphic approach*, that is, the direct correspondence between human and robotic joints and between body segments and robotic links (see Fig. 3 for some examples), or it can pursue the *nonanthropomorphic strategy* that does not necessarily foresee such a direct coupling between human and robot joints.

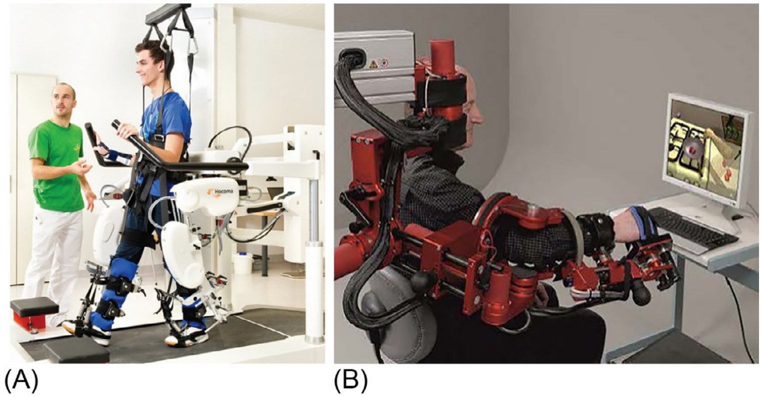

FIG. 3

Examples of therapy robots: (A) Lokomat, a lower-limb exoskeleton for rehabilitation, and (B) ARMin 7-DOF robotic exoskeleton for neurorehabilitation.

Part (A): © Picture: Hocoma, Switzerland

Anthropomorphic kinematic designs are the most commonly adopted, especially for wearable systems, even though they present some ergonomic drawbacks in terms of micro- and macromisalignments. Due to intersubject anthropometric variability, modeling approximations, and slippage of robot fixations over the body during motion, a perfect alignment can be hardly achieved, thus generating unwanted shear forces on the human skin and reaction forces on the joints. Such limitation can end up with a significant setup time for the system to the patient (up to 15–20 min) that could significantly affect the overall viability of such solutions.

To cope with this issue, nonanthropomorphic architectures have been introduced due to their inherent robustness against alignment errors [7]. Moreover, an increased design freedom resulting from the relaxation of the anthropomorphism constraint offers the opportunity of optimizing the intrinsic dynamics of the robot, for example, through a smart distribution of swinging masses to mimic intrinsic natural efficient pendular nature of body motion during walking and manipulation.

The actuation apparatus represents one of the most important technological bottlenecks in the design of robots for rehabilitation where the challenge is the simultaneous matching of power, accuracy, invasiveness, and safety requirements [8]. In fact, the necessity of equipping robots with high-power/high-impedance actuators able to deliver full torques needed for walking or moving the arm is often in contrast with the need of high kinematic efficiency, low friction, and reflected inertia.

To meet these conflicting requirements, especially for the lower-limb robots, rotary electric motors with high-reduction-ratio gearboxes are often equipped with a series-elastic element (series-elastic actuators, SEAs) that offers several mechanical and control advantages [8]. Passive compliance improves tolerance to mechanical shocks (e.g., resulting from foot-ground impacts) and facilitates control-based disturbance rejection. The elastic component can be also used as a torque transducer that can be used to implement torque controllers preserving stability margins [9].

However, high compliance lowers the controllable bandwidth, because of the saturation effects on motor speed and acceleration. This limitation can be overcome at the cost of an increased design complexity and designing actuators whose mechanical impedance can be regulated (variable-impedance actuators, VIAs) [10]. Walking exoskeletons, for example, very often include only hip and knee actuators as a trade-off between mechanical complexity and functionality; conversely, ankle joint (the one that produces most of the power for propulsion during walking) is only passively supported by elastic elements.

In this context, researchers should consider several important aspects for implementing the following steps in designing robotic devices for neurorehabilitation.

One aspect is related to the goal of the intended therapy. Robot design should therefore emphasize motor activities/exercises to create functional recovery pathways grounded on voluntary movements as part of action-related tasks, for example, for simulated or real activities of daily living (ADLs) scenarios.

Another aspect to take into account is the combination of sensorimotor and biomechanical approaches toward the reduction of abnormal motor responses (applying proprioceptive and vibrotactile stimulations) and the restoration on motor capacities (through passive stretch, active stretch, and isometric exercise with or without resistance).

Moreover, the robot capability to accomplish certain tasks or functions shall be carefully considered and analyzed. In fact, robotic design (including the type and the level of provided assistance) should be patient-tailored in order to address the capabilities, limitations, and the training needs of targeted patients [11].

In order to cope with all these challenges, key additional components to be selected are sensors and interfaces to be integrated in the overall architecture depicted in Fig. 2.

The definition of the type, specifications, and number of sensors must rely on four basic factors:

- Continuous monitoring the status of the human and robot agents and of the working environmental conditions
- Continuous monitoring of human-robot interaction in order to pave the way for effective interaction control
- Safety, fault and error detection and recovery
- Continuous sensory feedback to patients for enhancing relearning, motivation, and involvement in the rehabilitation exercise

As far as the design of the interface subsystem is concerned, one basic challenge is the design of the mechanical interfaces to the human body. Given the need to apply forces, such interfaces should optimize dynamic efficiency of physical interaction while minimizing possible discomfort or unrequired perturbations for the human patient. Selection of materials, morphology, and preliminary simulation of the biomechanics of interaction could be key success factors for designing a successful mechanical interface subsystem, as presented in the case studies reported in Section "The CBM-Motus and the LENAR: Two Case Studies" of this chapter.

Design of the remaining part of the human-machine interface should be driven by an initial basic choice: the use of virtual versus real environment for contextualizing the exercise activities. Virtual reality tools, typically integrated with intrinsic haptic feedback generated via the mechanical interface, could enable the use of a high variety of training scenarios, with high flexibility and opportunities to present to the user situations, which could provide direct stimuli to the relearning and recovery process of sensorimotor coordination capabilities. Training in real-life scenarios could enable direct elicitation of experiences and skills that are still available in the motor and sensory memory of the patient, thus providing possible shortcuts for accelerating the recovery processes.

In any case, the selection and design of the interface subsystem shall be carried out in tight cooperation with medical personnel and involving selected groups of patients at different stages of the design process. This will enable implementing the best possible solution and will pave the way to high compliance of the patients and high level of fulfillment of the clinical end-user actual expectations and needs.

Finally, it is worth to recall and strongly underline that, according to the proposed biomechatronic design approach, all initial design choices of different structural, actuation, sensory, and interface subsystems shall be reconsidered and iteratively optimized in direct combination and, as appropriate, integration with the control subsystems, as presented in Section "Overview of Control Strategies" of this chapter.

MODELING THE HUMAN COMPONENT

Modeling the human component is a fundamental step of the biomechatronic design approach. It plays a paramount role in the initial phase of definition of the specifications and in the design optimization phase, typical of the concurrent design.

For our purposes, hint of biomechanical models of the upper and lower limbs will be provided. Biomechanical models of the musculoskeletal system are powerful tools that allow combining anatomical and physiological data and, also, carry out investigations on neuromuscular control. Several models of the upper extremity, for example, have been used to characterize limb impedance [12], analyze muscle coordination [13], and design neurorehabilitation devices.

The human arm can be modeled as an open kinematic chain composed of a cascade of bones (links) and articulations (joints), actuated by muscles (actuators). The motor commands originated in the CNS generate muscular forces and torques responsible for joints movement. The upper-limb kinematic chain includes seven joints that can be joined into three main groups, the shoulder girdle, the elbow, and the wrist [14]. Due to the complexity of the hand mechanics, in the model of the human arm, the hand is often regarded as an end-effector mounted after the wrist.

In this context, since translations are often considered negligible compared with rotations, all the joints are usually assumed as rotational; in Fig. 4, the biomechanical model of the upper limb is represented.

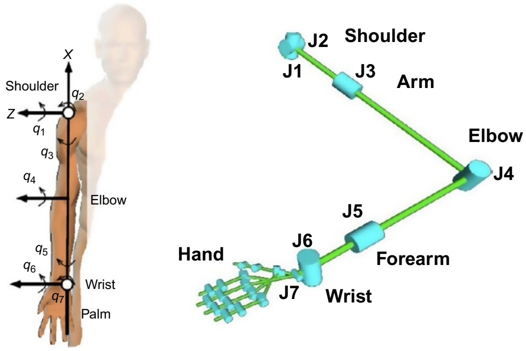

FIG. 4

Biomechanical model of the human upper limb.

The biomechanical modeling of the upper limb assumes the description of the relations that occur between forward and inverse kinematics, including also the muscular space with the muscles' lengths and dynamics. Forward kinematics represents the estimation of the position and orientation of the end-effector (the hand) computed starting from the joint variables (the shoulder, elbow, and wrist). However, inverse kinematics represents the computation of joint variables knowing the information about the end-effector pose.

In adjunct to the evaluation of joint and hand positions corresponding to a desired limb trajectory, the motor system must also estimate the required torques able to produce the desired motor task. To this purpose, the study of the dynamics shows how the motor system translates a desired end-effector motion into advantageous muscular activation patterns.

In particular, the dynamic model of the upper limb refers to the study of the connections that appear between the forces acting on the human arm and its motion. In this context, forward dynamics represents the computation of the arm's motion knowing the internal and external forces acting upon the arm itself.

On the contrary, inverse dynamics allows to estimate the torques and forces acting on the joints starting from the knowledge of the end-effector motion.

On the other hand, the biomechanical model of the lower limb is extensively studied during walking. In fact, the analysis of walking in neurologically impaired subjects is crucial for (i) understanding human motor control mechanisms and injury-related effects and (ii) designing mechatronic machines for neurorehabilitation purposes [15].

Simple walking models are based on the elastic inverted pendulum approach; more complex models can include motion in the sagittal plane, thus considering the lower limb as an open kinematic chain composed of trunk/pelvis, thigh, leg, and foot (end-effector) body segments and the hip, knee, and ankle joints as perfect hinges as interconnections (see Fig. 5). This allows simplifying the model by taking into account only flexion/extension movements, that is, the most relevant one during walking. Complexity can be extended if two additional degrees of freedom are added

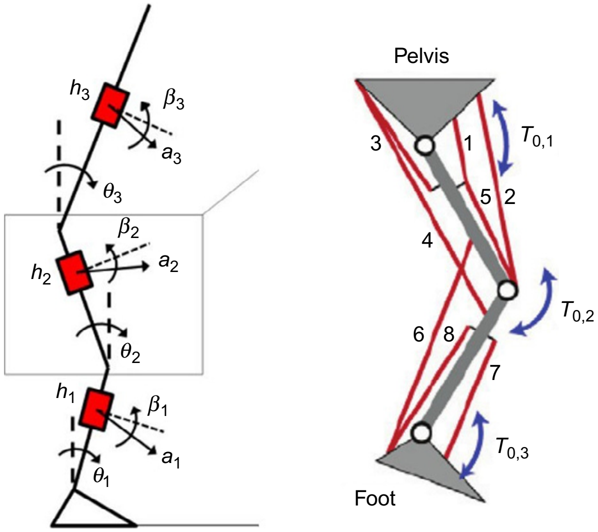

FIG. 5

Biomechanical model of the human leg.

to the hip joint (adduction/abduction and intra-/extrarotation) and to the ankle joint (inversion/eversion and intra-/extrarotation) or if even more realistic rototranslation conditions are considered (e.g., in the case of knee articulation). In most cases, the full complexity of articulation motion is not considered (especially for exoskeletons), and only sagittal-plane motion is taken into account. The model simplification is derived from a trade-off between complexity, wearability, and compatibility on one hand and kinematic compatibility, human-robot joint alignments and ergonomics constraints on the other one.

General features of walking are typically described by means of spatiotemporal parameters (stance/swing duration, walking speed, step length and width, cadence, etc.). Additional and very crucial information for the proper dimensioning of exoskeleton mechanical components and actuators includes joint kinematics (angles, angular velocity, etc.) and kinetics (torques, joint power, etc.), ground reaction forces and muscular activity, the latter depending on the level of complexity of the selected tendon-muscle model adopted. Motor control aspects, on the other hand, have to be mostly considered when interaction control or intention-detection algorithms have to be designed. Finally, anthropometric features [16], average information on body-segment length, mass, center-of-mass position, and moment of inertia, are also crucial to properly rescale models according to the physical size of the subjects under analysis.

In conclusion, leg and arm dynamics can be easily reproduced in physics-based simulation environment, and many research software platforms including extensive full-body musculoskeletal models have been developed and widely used for biomechanical analysis and robot design [17]. However, they often fail to reliably reproduce the active action of the human agent, which can be barely simulated with limited possibilities of mimicking short-term adaptation and long-term learning mechanisms related to the interaction with robotic artifacts. Due to this limitation, simulations of human-robot interaction are very helpful in the initial design phase but need to be confirmed or, more likely, extended through human-in-the-loop validations with real hardware.

OVERVIEW OF CONTROL STRATEGIES

Human-robot mutual adaptation is a key mechanism to be considered in the control of rehabilitation mechatronic systems: robots have to synchronously adapt to the intended motion of the user, who in turn should be allowed to exploit robotic physical support with an active participation and a training activity for the improvement of the residual motor functions. These aspects strongly motivate the need to detect user's motion intention and to adjust robot intervention and interaction forces in a smooth, natural, and compliant way.

In the field of rehabilitation robotics, several control strategies have been developed during the last decades to improve human-robot interaction and point out the best approach to increase clinical recovery. To this purpose, common control algorithms for rehabilitation machines can be grouped into the main following categories:

- *Assistive control*. It provides the patient with the minimal robotic assistance to move their weakened limbs along desired patterns, in a similar manner to "*active-assisted*" exercises performed by physical therapists. Such a control allows promoting user's active involvement.
- *Challenge-based control*. It refers to controllers that provide resistance to the participant's limb movements during exercise, requiring specific patterns of force generation or increasing the size of movement errors (i.e., the so-called "error-amplification" strategies).
- *Haptic simulation*. It is particularly used for the practice of ADL movements in a virtual environment since it offers flexibility, convenience, and safety as advantages compared with performing actions in a physical environment.
- *Non-contact coaching*. Robots are equipped with special mechanisms allowing to play the role of non-contact coaches that decide and direct the therapy program and motivate participants.

Among these categories, the *assistive controller* can be considered as the most widely developed control paradigm [18] in the neurorehabilitation scenario. Moreover, assistive control strategies can be further grouped into four conceptual categories: impedance-based, counterbalance-based, EMG-based, and performance-based adaptive assistance [19]. Chapter 5 of this book provides a comprehensive overview of these control algorithms [20].

Impedance controllers haptically deliver viscoelastic forces/torques considering a reference trajectory, from which a deviation is compliantly allowed. Low values of stiffness and damping coefficients allow the user to deviate from the robot nominal kinematic trajectory, while high gains result in rigidly imparted movements. In lower-limb mechatronics systems, the reference trajectory can be preset based on physiological kinematic data collected with healthy subjects or alternatively can be calculated based on a real-time estimation of the user's intended motion. This can be performed by extracting kinematic anticipatory information from different body districts (e.g., based from arm oscillations [21]) or by directly observing joint kinematics (e.g., by using nonlinear adaptive-frequency oscillators (AFOs) able to intrinsically synchronize themselves with human movements [22,23]).

Interaction control schemes based on the measurement of limb EMG signals have been widely investigated. These controllers can estimate the muscular force, and in turn the joint torques, from EMG measurements by using model-based [24] or model-free [25] approaches, and assist the human with a fraction of the torques needed to perform the task.

It is worth noting that while research on interaction controllers highly pushes toward sophisticated strategies using a number of motion, EMG, force sensors, and very complex control algorithms, commercial robots (e.g., robots from Ekso Bionics and Hocoma) only use very basic solutions. In such solutions, compliance controllers and predefined joint trajectories are implemented, with the sole possibility for the clinical operator to regulate few parameters (joint range of motion, robot stiffness, speed and step length). This results in a very limited possibility for the patient to dynamically deviate from the selected setting or at least to automatically adjust her/his walking patterns and mostly keep the control on the task.

Counterbalance-based controllers are based on the need of balancing the patient's limbs during training in both passive or active modality. Passive strategies assume that the amount of arm weight assistance can be selected by a clinician by adding or removing elastic bands, according to the subject's impairment level. Active strategies allow to generate a counterbalance force through the robot's control system to assist in reaching [26] or walking [27].

For both methods, the amount of weight support can be adaptively chosen and modified adjusting the difficulty of movement task on the basis of patient's impairment level [28]. Performance-based control algorithms are grounded on an error-based strategy that updates a control parameter from trial to trial based on measured participant performance. Such an approach has shown that adapting therapy to specific patient's motor characteristics led to better improvements with respect to conventional therapy [29].

More recently, the fusion of assistive control and haptic simulation has generated the so-called biocooperative control strategy [30]. Objective of this control strategy is to give a central role to the patient who is closed in the control loop thanks to a multimodal interface that collects and processes data coming from different sources.

In particular, information provided by biomechanical, physiological, and psychological measurements as well as intentions and environmental factors contribute to provide a continuous feedback on patients' global conditions [31].

As a result, continuous multimodal measures of the user's state allow to dynamically and real-time shape robotic assistance to the patient's needs. As a consequence, patients' engagement in robotic therapy is expected to increase more than in previously reported studies in the field.

Recently, biocooperative systems have been expanded to non-invasive cortical and non-cortical interfaces with the purpose of detecting user movement intentions and virtual reality environment as well as haptic perception for increasing sensory feedback for the patient.

In this context, robotic devices have been controlled using natural neural commands coming directly from the brain and the body, developing novel brain/neural-computer interaction (BNCI) systems that integrate together electroencephalography (EEG) and electrooculography (EOG) [32]. Such physiological non-invasive signals are intended to be used as a trigger for initiating and stopping movement therapy to provide an online modification/adaptation of robot-aided rehabilitation exercises by real-time monitoring patient's intention.

Multimodal enhanced feedback such as virtual reality (VR) environment often coupled with acoustic and/or haptics represents further aspects that may promote the development of more exhaustive bio-inspired control algorithms. In fact, in a neurorehabilitation scenario, the selection of the optimal task complexity, feedback design and feedback variables is expected to positively challenge the learner, thus contributing to speed up motor learning. It is worth noticing that interfaces for intention recognition based on biosignals (electroneurographic or electromyographic measurements) might be invasive, unreliable, or sensitive to calibration, repeatability and signal acquisition/processing issues.

THE CBM-MOTUS AND THE LENAR: TWO CASE STUDIES

CBM-MOTUS: A PLANAR ROBOT FOR UPPER LIMB NEUROREHABILITATION

CBM-Motus is a planar end-effector machine for upper-limb rehabilitation (Fig. 6) that has been purposely designed for home rehabilitation. The robot main requirements are low and isotropic inertia, simple mechanical structure, lightness (total mass is less than 30 kg) and compactness to enable portability, and low cost to promote home rehabilitation [33].

The machine is designed to have a large workspace (more than $500 \times 500\,\text{mm}^2$) to allow the delivery of several rehabilitation treatments, with interaction forces up to 50 N.

From a mechanical point of view, the robot presents a Cartesian kinematic structure consisting of two modules connected by a double prismatic joint. Each module corresponds to an actuated axis (viz., x and y axes) and includes six pulleys with the same radius (25 mm) and two belts.

A horizontal bar is connected to the first module and allows the movements of the end-effector along the y-direction; a second bar linked to the second module allows

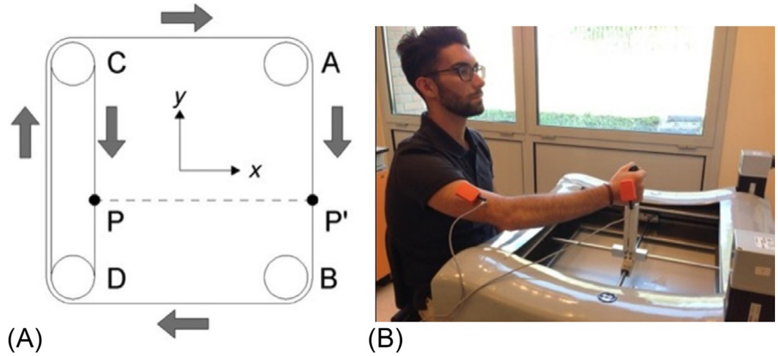

FIG. 6

The CBM-Motus planar robot for upper-limb rehabilitation. (A) Overview of the kinematic structure and (B) a subject performing some state-of-the-art exercises.

the displacements of the end-effector along the x-direction. Motion of the two bars is transferred to the end-effector that is, to the handle of the robot, by a joint obtained by rigidly linking the two prismatic joints.

The double prismatic joint guarantees that only stretching forces are transmitted to the belts. This technical solution ensures that only forces orthogonal to the same bar can be transferred to each bar; in this way, the bar stretches the belts instead of bending them (Fig. 6A).

The robot control strategy belongs to the category of assist-as-needed control that provides the patient with the minimum level of assistance needed to accomplish the task, thanks to the extraction of performance indicators describing the patients' current state.

To this purpose, an impedance control with adjustable parameters has been implemented, as shown in the following:

$$\tau = B(q)y + F_v\dot{q} + F_s\text{sign}(\dot{q}) \quad \text{with} \quad y = M_d^{-1}\left(M_d\ddot{q}_d + K_P\tilde{q} + K_D\dot{\tilde{q}}\right)$$

τ is the torque command; B represents the inertia matrix; $F_v\dot{q}$ and $F_s\text{sign}(\dot{q})$ are the dynamic and static friction torques, respectively, which cannot be neglected in the robot's dynamics.

The following performance indicators have been selected for a quantitative evaluation of the subject's biomechanical behavior and employed to adjust control parameters.

The aiming angle α is the angle between the target direction and the direction of actual travel from the starting point up to peak speed point [34], while *AREA* represents the area between the desired and the actual trajectory performed by the subjects. *nMD* is the normalized mean deviation from desired path, while mean arrest period ratio (*MAPR*) stands for the proportion of time (i.e., the percentage of samples) that movement speed exceeds 10% of the peak speed. Finally, the *speed metric* is the ratio between mean speed and peak speed, and *MD* is movement duration.

Such indicators have been computed by recording hand position and velocity in the planar workspace through incremental encoders and velocity sensors embedded into the robot [35].

The robot control is tailored to the subject's motion abilities by updating stiffness matrix K_P during the therapy and the time t allotted for task execution. In particular, K_P and t have been progressively updated on the basis of the values acquired by two modulation functions C_K and C_t opportunely computed:

$$C_K = \frac{3}{5}\alpha + \frac{1}{4}AREA + \frac{1}{4}nMD \text{ and } C_t = \frac{3}{10}MAPR + \frac{1}{4}speed\ metric + \frac{1}{6}MD$$

They are weighted sums of the aforementioned performance indicators. A trial-and-error approach has been pursuit for choosing the weights, and a threshold strategy is then applied to set the value of control parameters.

The presented control strategy for the CBM-Motus has been developed throughout a modular telerehabilitation system where the patient and the therapist can communicate without a special data interconnection. The implementation of the architecture has been validated on healthy subjects performing simulated poststroke condition (Fig. 6B). The results have shown the reliability of the novel architecture and its capability to be easily tailored to the user's needs, thus guaranteeing a patient-tailored assistance exploiting biomechanical information recorded from the subjects.

LENAR: A NONANTHROPOMORPHIC WEARABLE EXOSKELETON FOR HUMAN WALKING ASSISTANCE AND REHABILITATION

In [7], the Lower-Extremity Non-Anthropomorphic Robot (LENAR), a nonanthropomorphic treadmill-based wearable robot that assists hip and knee motion in the sagittal plane using compliant actuators, has been described (Fig. 7A).

Robot design is based on a novel approach to kinematic synthesis, selection, and morphological optimization: (i) a systematic search of all admissible (i.e., kinematically compatible) planar 2-DOF solutions able to assist hip and knee flexion/extension motion and (ii) the selection of a candidate design solution and the optimization process to improve ergonomics and to minimize static torques demanded to the actuators [36]. Custom SEAs are designed to have low intrinsic impedance and accurate torque control [37].

The resulting design is reported in Fig. 7B. The hip and knee joints (H and K) are represented with blank circles. The robot is composed of one pelvis cuff (hosting joint A) and, for each leg, two rotary SEAs joints A and D; one thigh cuff (hosting joint B); and one shank cuff (hosting joint C). Joints B, C, E, and F are passive. The segment EF can be adjusted to accommodate different user sizes. Additional sliders also allow the regulation of the position of joints A, B, and C.

The architecture of the developed SEAs allows placing motors alongside the human limbs, while only springs and output shafts are located directly on the joints to be actuated. This smart mass distribution, together with the nonanthropomorphic

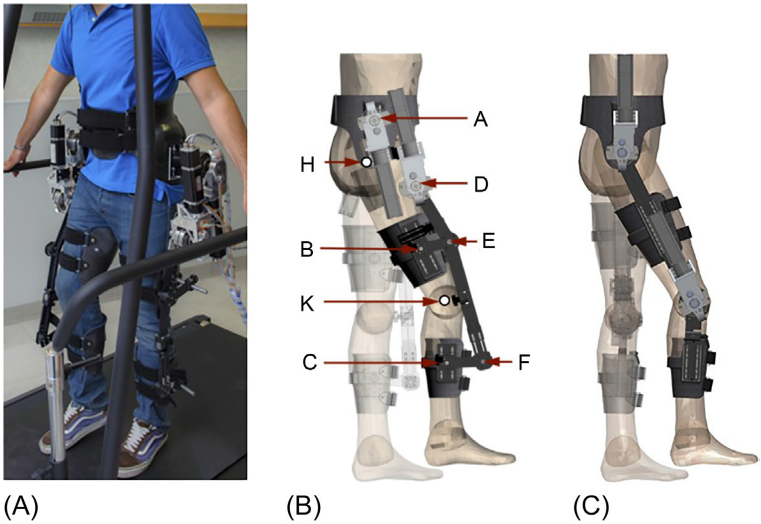

FIG. 7

(A) LENAR prototype worn by a healthy subject. (B) 3D CAD design of the LENAR: blank circles, H and K, represent the human hip and knee joints, respectively. Points A and D are the actuated robotic joints. Points B, C, E, and F are robot passive revolute joints. (C) Schematic representation of an equivalent anthropomorphic robot using the same actuators of the LENAR.

structure, allows locating the heaviest components very proximally (close to the trunk), thus minimizing swinging masses.

Each of the four SEAs of the robot is torque-controlled using as feedback signal the measurement of the spring deflection, that is, the difference between the SEA output rotation and the gear-motor rotation. The low-level control scheme is based on the cascade approach proposed in [38]: it consists of a PI velocity control loop nested in a PI torque control loop. The high-level controller consists of a stiffness control and an intention-detection method based on AFOs described in [23]. Assistive torques are provided following the approach presented in [22]. A pool of AFOs coupled to a nonlinear filter learn periodic joint angles in steady-state conditions during walking. Based on that, the angle corresponding to a certain phase led in the future is derived to be used as equilibrium position for the stiffness controller. With this approach, the user is attracted toward his/her estimated future kinematic status by elastic torques, with the opportunity to continuously adapt his/her walking feature, that is, the frequency and the amplitude/shape of the attractive pattern.

The advantages offered by the LENAR have been demonstrated in [7] both theoretically and experimentally, showing a reflected inertia lower than the one of an equivalent anthropomorphic design (i.e., including the same actuators; see Fig. 7A), a high backdrivability, and an intrinsic tolerance to wearing inaccuracies and misalignments.

CONCLUSIONS

In this chapter, biomechatronic design criteria of generic systems for robot-aided neurorehabilitation have been presented and discussed.

Robotic devices have been proposed as effective machines for delivering neurorehabilitation therapy mainly based on the potential influence that they can have on neuroplasticity, especially when intensive and task-specific clinical protocols are applied.

Modeling the human component is of paramount importance, both for the upper and lower extremities, for proper biomechatronic design of rehabilitation robots able to establish effective, efficient, and safe human-robot interaction. Consequently, in-depth, functional (physiopathologic), biomechanical analysis of the human component should be carried out as the first step of the design process.

Profiling the human factor must include the definition of the optimal role of the physicians before, during, and after each therapeutic session so that the expected performance, functional, and technical specifications for the rehabilitation robots can be consequently identified and iteratively refined following a classical mechatronic design cycle.

As presented in the last section of this chapter, two case studies on the biomechatronic design of rehabilitation robots have been presented with the attempt to provide two practical examples of the application of the proposed approach.

So far, extensive, independent clinical validation (based as long as possible on double-blind, randomized, controlled trials focused on groups of patients) of rehabilitation robots is still needed: evidence supporting such technology needs to be significantly consolidated, so that its application and diffusion could be really boosted.

One key challenge for novel systems to be envisaged in tight cooperation with physicians is how to take into account the different pathological history of each patient.

Such systems will be extended to include human-machine interfaces capable of:

- on one side, detecting from the patient key parameters about his/her physiological status, along with a variety of contextual and environmental factors,
- on the other side, providing the patient augmented sensory feedback.

As a result, the human can be more and more actively included "in the loop," and his/her active role during each single rehabilitation session might be effectively optimized according to the level of performance, attention, motivation, and overall compliance to the proposed, robot-based clinical approach.

Acknowledgments

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CHAPTER

Actuation for robot-aided rehabilitation: Design and control strategies

4

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INTRODUCTION

The importance of the human brain in controlling human movements scarcely needs to be argued. Even a slight damage of nervous system can severely hamper one's ability in performing simple yet crucial activities of daily living. Stroke is the most prominent cause of neurological disorder [1] and is a leading cause of long-term impairment [2]. The incidence of stroke has been shown to increase with age, and as the lifetime expectancy rises, its prevalence and impact on society are deemed to grow. Various strategies have been explored to improve recovery after stroke, and so far, repetitively performing isolated and functional [3] movements in the acute phase of recovery has produced the best outcomes. Robotic devices can relieve the therapists from the demanding task of manually assisting the patient and have shown encouraging results, comparable with the ones achieved with traditional therapy while allowing greater patient compliance and a systematic monitoring of the patient's performance.

In order to be effective, rehabilitation robots need to interact with humans in a gentle but decisive manner. The actuation stage, the overall architecture, and the control strategy, among other factors, play a fundamental role in ensuring the efficacy of the rehabilitation procedure. In this chapter, we provide the reader with an overview of the actuators used for robotic rehabilitation and describe the control strategies used for modulating the interaction with the patient, namely, impedance and admittance control.

Section “Robot Architectures and Actuators” lists the most common choices for the motors, touching on the advantages and drawbacks of pneumatic, hydraulic, and electric motors. The difference between end-effector robots and exoskeletons is defined, with examples from some of the most popular commercially available and researched devices. Sections “Control Strategies” and “Friction and Backlash Compensation” present, respectively, the high- and low-level control strategies used in rehabilitation robotics, emphasizing the difference between traditional servo-controlled robots for industrial tasks and devices that need to interact and exchange

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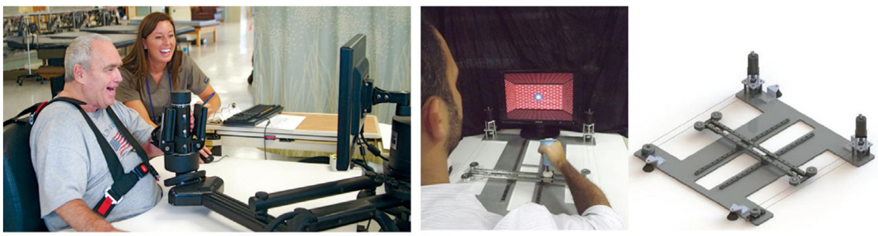
information with and assist movement of human beings. Section "Control Strategies" deals with understanding the user's performance and modulating the level of assistance, in terms of the impedance at the human-robot interface; Section "Friction and Backlash Compensation" presents a brief review of the models used for compensating nonlinearities deriving from the robot's architecture, such as friction and backlash, whose effect could otherwise compromise the performance and stability of the controller. Finally, we focus on the mechanical design choices of the actuation stage of a robot for rehabilitation, dealing with the challenging trade-off between high force delivery and backdrivability and its implications for implementing an effective control strategy.

ROBOT ARCHITECTURES AND ACTUATORS

Rehabilitation robots can be broadly classified in two groups based on the nature of their mechanical attachment to the human body: end-effector robots (examples shown in Fig. 1) and exoskeletons (examples shown in Fig. 2) [6]. In the case of an end-effector robot [5,7,8], the human-robot interface is generally attached at the distal part of the body and does not constrain the kinematics of the human joints but applies a force in the Cartesian space. These devices are much simpler in construction and easier to control when compared with the exoskeleton-type robots.

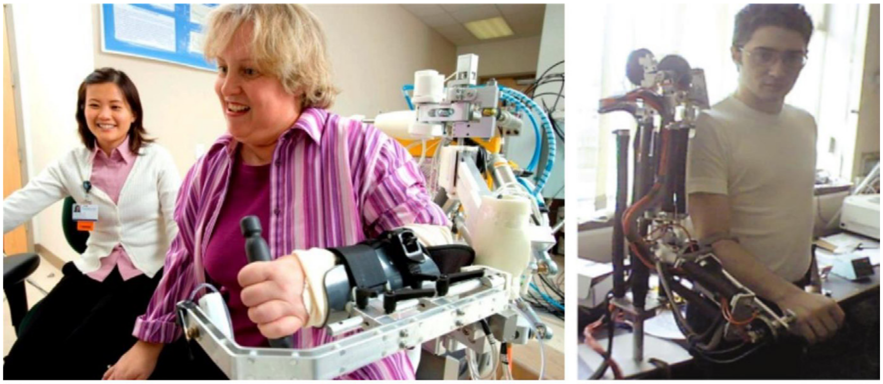
Exoskeletons [9,10], on the other hand, wrap around the human body, acting as an external, parallel skeletal structure and allow for independent control of each individual joint of their wearer. The complexity of the structure increases with the number of degrees of freedom (DoF) to be controlled. One of the key issues with these types of robots is the misalignment between the human joint and robot's counterpart, which leads to undesired interaction forces on the human limb, upsetting the natural smoothness of human kinematics. Recent research has focused on design methodologies to compensate for this issue, but these often result in a more complex and bulky kinematic structure [11].



(A) (B)

FIG. 1

End-effector robots for rehabilitation. (A) MIT-Manus [4] (InMotion ARM, MA, United States) is a serial link end-effector-based robot. (B) H-Man [5] is a cable-driven planar end-effector device.



(A) (B)

FIG. 2

Pneumatically actuated exoskeletons for rehabilitation. (A) Pneu-WREX [13], a four DoF pneumatically controlled device. (B) Salford Arm Rehabilitation Exoskeleton based on PAMs [14].

In both the cases mentioned above, the actuation unit can be placed either distally or proximally, the position of the motors affecting the dynamics of the system. Placing the actuators directly at the joint level strategy avoids the need of a transmission mechanism but increases the inertia of the moving parts, thereby making the control less transparent and more power-consuming. In the case where the actuators are placed proximally [12], a transmission mechanism is required to transmit the torque at the distal location. This helps to reduce the inertia at the joint but introduces the challenge of compensating for the nonlinear dynamics that may arise in the transmission, such as hysteresis and friction.

A wide variety of actuation technologies have been used to develop robotic devices meant for rehabilitation. These can be classified according to the nature of the energy source used to generate mechanical power: hydraulic, pneumatic, and electric motors are among the most common.

In the past, hydraulic actuators have been used for developing rehabilitation robots (examples are shown in Fig. 2), but due to the inherent nature of being bulky, noisy, and prone to fluid leakages, their usage has been declining. Pneumatic actuators in comparison with hydraulic actuators are lighter and quieter but still challenging to embed in a portable system since the compressor unit is quite heavy [15,16]. However, they provide a higher power-to-weight ratio and lower impedance compared with their electric counterpart. Pneumatic artificial muscles (PAMs), based on a bioinspired working principle, have more recently been utilized for developing rehabilitation devices due to their lightweight characteristics and inherent compliant nature [14]. PAMs consist of an inflatable bladder that increases in diameter and shortens in length as compressed air is pumped into them. These pneumatic actuators work only in contraction (unidirectional); therefore, at least two units are required to perform agonist-antagonist motion.

Electric actuators are the most widely used solution mainly because of their high power density and ease of use. High gear reduction can be used to increase the torque output but at the cost of increasing the mechanical impedance of the system, thereby reducing the backdrivability of the system. It is highly desirable to have systems that are backdrivable, for safer interactions between humans and robots and in implementing control strategies, such as impedance control, that are fundamental when assisting human motion.

Simply placing an elastic element in series with an electric motor makes it possible to lower the impedance levels in the system and achieve a more accurate force control. The main advantages of using series elastic actuators (SEAs) are securing safety and improved performance of force (torque) control bandwidth [17]. Indirect force/torque control can also be implemented on stiff actuators with impedance control; however, the main difference between the compliance of SEA and impedance control of stiff actuators is the intrinsic safety [18] of the former, which still applies in the case of control failure.

The main disadvantages of using SEAs are the need of extra components and a deterioration of position control performance. The position control bandwidth is normally lower than that of conventional actuators because the input command of SEA is force/torque [19]. Using SEA in rehabilitation scenarios is a good option because many rehabilitation tasks require precise force/torque control and intrinsic safety. Examples of SEA-based rehabilitation robots are the Lopes [20] and Lokomat [21].

At the current state of the art, most of the implementations make use of traditional electric motors with the addition of a compliant element and/or a controller that modulates the interaction forces with the subject. The rest of the chapter will thus focus on control strategies typically used with electric motors.

CONTROL STRATEGIES

The complex interaction and flow of information occurring between a human being and a robot during a rehabilitation session requires to be addressed via control paradigms different from the traditional servo systems [13,22]. Aside from stability, there are two fundamental requirements that need to be considered, namely, the controller needs to understand the subject's intentions and ensure correct human movements.

In the initial stages of recovery, when voluntary movement is absent or not trustworthy, traditional control methods, defining a desired trajectory/force profile and treating the human interactions as disturbances, may be applied. However, when the subject starts to regain the ability to move, the robot needs to be complementing such actions rather than rejecting or hindering them, assisting the user when needed [22].

Such paradigm, known as assist-as-needed, requires controlling the interaction at the human-robot interface rather than the forces or the position of the device, to both understand the user's intentions and change the behavior of the robot from a very stiff to a compliant interaction.

A conceptual control diagram on the interaction between robots for rehabilitation and assistance and a human being is shown in Fig. 3A [23]. The motion control in a human body can be simplified as a feedback loop, where the brain plays the role of controlling human motions. The brain controls the muscles to follow an arbitrary desired motion X_d. The control output u_h generated by the brain is the motor control signal, sent to the muscles to produce a joint torque F. The input (i.e., human motion intention) to the robot can be extracted from the human-robot interface,

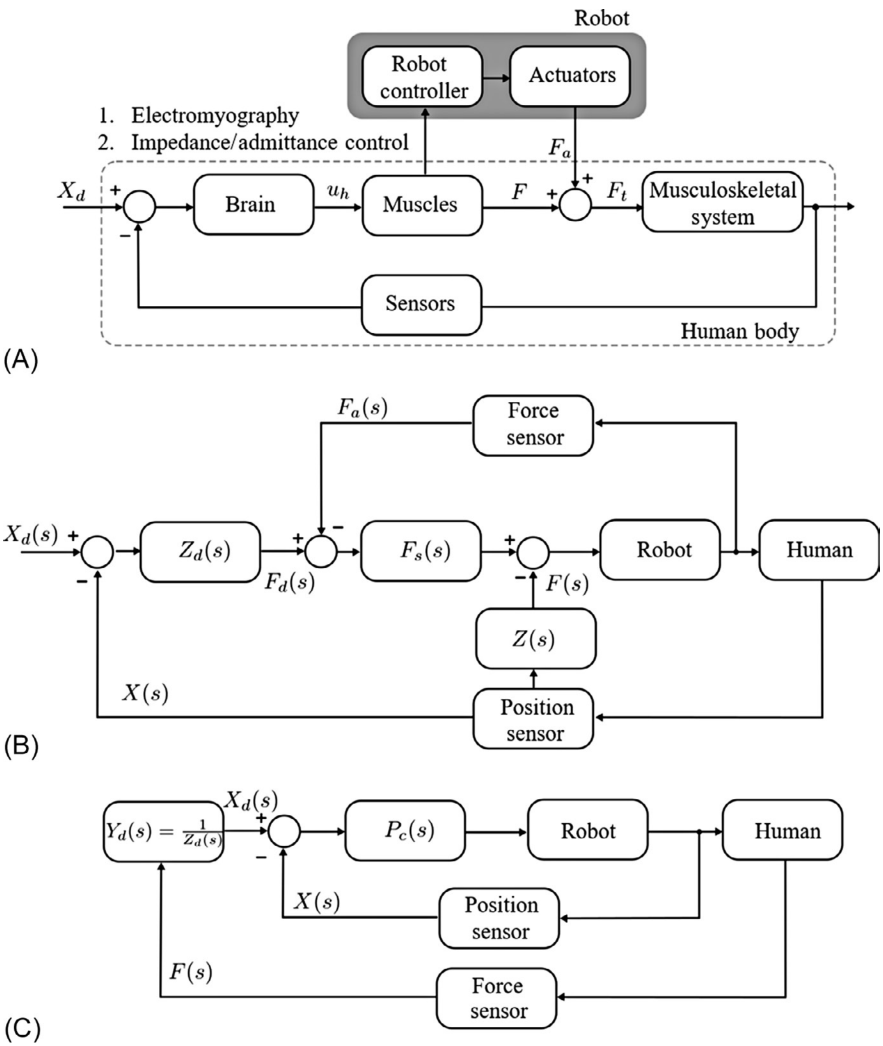


FIG. 3

(A) Human-robot interaction control system. (B) Closed-loop impedance controller. (C) Admittance controller.

through force sensors or muscle-related signals. The robot's controller can then command the actuators to generate an assistive torque (F_a) accordingly, delivered to the musculoskeletal system. In other words, the human body is actuated by the sum of a muscular torque F and an additional assistive torque F_a, complementing its movements. Sensing technologies for detecting the human motion play a vital role, and identifying the exact human intention in a robust and effective way is still an open challenge.

A common sensing method is surface electromyography (sEMG); it is known that the sEMG signals are related to human joint torques and occur prior to the execution of movement [24]. Since this sensing solution may result in a very intuitive usage, sEMG signals have been successfully employed in most of the exoskeleton robots for rehabilitation and assistive purposes. However, sEMG sensors have practical limitations such as subject dependence, sensitivity to the sensing location, low signal-to-noise-ratio, and low repeatability, which do not make them robust enough for daily usage.

A more common and robust method consists in extracting the human intention from the subject's movements, through position sensors, or with force/torque sensors at the human-robot interface. These can then be combined with an impedance/admittance control scheme and a dynamic model of the human limbs [25–27]; the robot can then deliver the appropriate assistance level to compensate for the user's lack of muscular strength. The main advantage of this approach is that it can shape a virtual (or desired) impedance while keeping the patient engaged in the task, allowing to assess his/her movement ability and guaranteeing a safe interaction [28].

In this section, we assume that the robot used for rehabilitation/assistance has a fixed mechanical impedance. The sensing control strategy is addressed using the impedance/admittance paradigm to set the desired stiffness or damping, providing the assistance effort required.

MECHANICAL IMPEDANCE/ADMITTANCE CONTROL

Mechanical impedance is the relationship between the net force applied on a mechanical system and the system's resulting kinematics, that is, position, velocity, and acceleration [29]. If the system is linear and time invariant, the impedance of the system can be expressed in the Laplace domain as the second-order transfer function $Z(s)$ relating the net force $F(s)$ to the position $X(s)$ as in Eq. (1):

$$Z(s) = \frac{F(s)}{X(s)} = Ms^2 + Bs + K \tag{1}$$

where the parameters M, B, and K denote, respectively, the mass, damping coefficient, and stiffness of the system, that is, the coupled system formed by the robot and the human limb. The terms M, B, and K represent the physical mechanical properties of the coupled system, which are passive and constant. Under the robot's control and actuator force $F_a(s)$, the actual dynamic behavior of the system can be modified and replaced by a set of virtual (or desired) parameters M_d, B_d, and K_d. This form of control is referred to as the impedance/admittance control.

Shaping the desired mechanical impedance not only effectively provides an assistance but also allows the user to safely interact with the robot. In addition to the acting force $F(s)$, the system is subject to the actuator effort $F_a(s)$ generated by the motor. The impedance/admittance control can adjust the actuator's force $F_a(s)$ such that the user feels a different impedance, defined in Eq. (2):

$$Z_d(s) = M_d s^2 + B_d s + K_d \tag{2}$$

where the terms M_d, B_d, and K_d represent, respectively, the desired mass, desired damping coefficient, and desired stiffness. The implementation of a compliant controller can be accomplished in two ways, usually referred to as indirect force control strategies: impedance-based force generator and admittance-based trajectory generator.

Although various alternatives have been proposed for these two schemes, we will herein focus only on their most general implementations, that is, the closed-loop impedance and admittance schemes, which rely on the feedback from both a position and on a force sensor, and the open-loop variation of the impedance control, which has found broad application in rehabilitation robotics.

Impedance control

The goal of impedance control is to define the desired impedance between a desired input position $X_d(s)$ and the actuator force $F_a(s)$. The impedance control comprises an inner force control loop $F_s(s)$ and an outer position feedback loop with a position sensor [30]. The control diagram is illustrated in Fig. 3B.

The measured position $X(s)$ is used as an input to an impedance control containing the desired impedance parameters in the form $Z_d(s)$. The impedance control generates a desired force $F_d(s)$ as in Eq. (3). The desired actuator force $F_d(s)$ and the actual kinematic trajectory $X(s)$ are used to control the robot through the inner force control loop. As a result, the robot executes the command and applies an assistive force $F_a(s)$ on the user to perform the desired motion:

$$F_d(s) = \left(M_d s^2 + B_d s + K_d\right)\left[X_d(s) - X(s)\right] \tag{3}$$

where $X_d(s)$ is the desired position of the system.

The issue of the impedance control is related to the high-performance requirement for the inner force control loop. Depending on the coupled system dynamics, a low gain for the force control can cause inferior performance, whereas a high gain tuning can lead to instability.

The open-loop version of impedance control avoids stability issues in the inner force loop by removing the feedback from the force sensor. This implementation practically translates in an outer position loop the implements the desired impedance and delivers forces through the motor in current mode. Note that such framework requires the actuator to be backdrivable, relies on accurate modeling of the robot's dynamics, and is not suitable to render high impedances.

Admittance control

The admittance control scheme comprises an admittance-based trajectory generator and a force sensor in a feedback loop. The admittance control scheme shown in Fig. 3C is a common solution to guarantee *backdrivability by control* when nonbackdrivable actuators are used.

The huge advantage of the admittance control is its robustness thanks to the inner position control $P_c(s)$, the objective of the inner control loop is to accurately track the desired trajectory $X_d(s)$ as fast as possible, while the outer force loop is responsible for modifying the force-position relation (4) [30]:

$$X_d(s) = \frac{F(s)}{Z_d(s)} = \frac{F(s)}{M_d s^2 + B_d s + K_d} \tag{4}$$

where the outer force loop computes the desired motion $X_d(s)$ when the acting force $F(s)$ is sensed based on the desired impedance parameters. Thus, the admittance control paradigm is the preferred approach, showing considerable advantages, for applications requiring large stiffness (such as haptic devices) or exoskeleton robots with nonbackdrivable actuators [31]. The main drawback of the admittance control arises when a low impedance is desired. This is because a low desired impedance implies high desired admittance, which may result in instability. A further limitation is inaccurate impedance-rendering due to the imprecise inner position control loop; this can be caused by numerous factors, among which nonlinear phenomena such as friction and backlash play a key role.

FRICTION AND BACKLASH COMPENSATION

All mechanical systems, independently of the nature of their actuation stage and transmission components, and no matter how well designed, will exhibit some degree of unwanted friction and backlash. These phenomena, deriving, respectively, from the interaction between contiguous surfaces and a play between adjacent movable parts, can significantly affect the performance of the device, reducing its tracking accuracy and bandwidth and influencing the stability of a closed-loop controller [32]. Addressing these issues is particularly relevant when one requires accurate position controlling or force rendering and in applications, such as rehabilitation robotics, where safety in the human-robot interaction is of paramount importance.

When the effect of backlash and friction is significant, it leads to nonlinear behaviors such as stick-slip and hysteresis, making common linear control strategies such as proportional-integrative-derivative (PID) unsuitable to meet the application's requirements. More elaborate controllers thus need to be designed, including a model or a strategy that accounts and compensates for the effects of nonlinearities [33].

If a sufficiently accurate mathematical description of the system is available, the essence of compensation comes down to using a feedforward command that is equal and opposite to the instantaneous force/position deficit caused by friction and backlash, respectively. This has resulted in a rich and varied literature on modeling nonlinear systems with complex dynamics [34,35]. Alternatively, one could use a strategy that is not based on any model for counteracting unwanted effects, by opportunely choosing the control gain parameters or using nonmodel-based observers [36].

In this section, we'll review the most common model-based strategies adopted to control mechanical systems with friction and backlash, focusing on the mathematical formalisms developed to describe these phenomena and on their practical usage.

FRICTION

Although friction may be a desirable property, it is often an impediment for servo control. Tribology, that is, the science of rubbing contacts, has produced a vast variety of descriptive mathematical tools that can be exploited when controlling systems with friction. This section is by no means complete and will only touch on some of the most common and practical approaches for engineering. An elegant and exhaustive review of such tools can be found in Armstrong-Helouvry et al. [35].

The first known studies on the science of rubbing contact surprisingly date back to the pre-Newtonian era, when Leonardo da Vinci first recognized friction as being a force proportional to the load, opposed to motion and independent of contact area [29]. After the elucidation of Newton's first law, da Vinci's model was formalized by, among others, Amonton and Coulomb [37,38]. The Coulomb model for friction is widely used for its simplicity and can easily be formalized as an ideal relay:

$$F = F_c sgn(v) \tag{5}$$

$$F_c = \mu F_N \tag{6}$$

with μ being a constant friction coefficient, F_N the normal load and $sgn(v)$ the sign function of the velocity.

In 1833, Morin introduced the idea of static friction [39] that was later combined with the viscous models introduced by Reynolds [40], resulting in one of the most commonly used friction models in engineering, shown in Fig. 4A. The model incorporates the concept of static friction (or stiction), that is, friction at zero velocity, breakaway force, that is, the force required to overcome the stiction, and the velocity-dependent nature of friction for nonzero velocities. A common formalization of this model takes the form

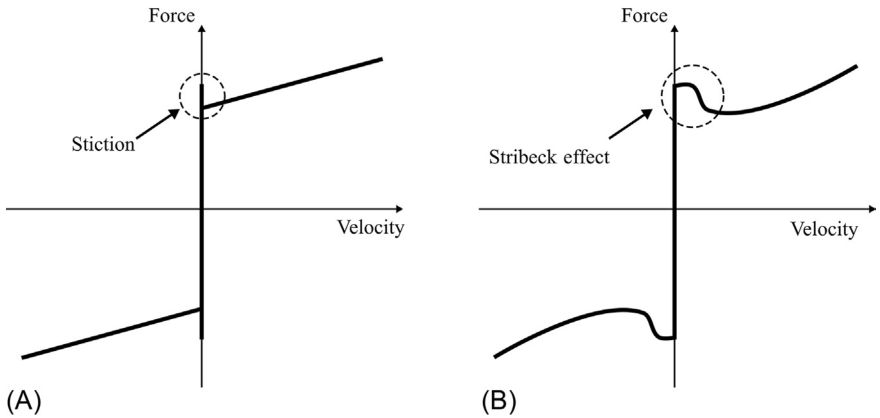


FIG. 4

Static friction and Stribeck effect. (A) Stiction model with viscous friction. (B) Stiction model with Stribeck effect and viscous friction.

$$F = \begin{cases} F_e & \text{if } v = 0 \text{ and } |F_e| < F_s \\ F_s\, sgn(F_e) & \text{if } v = 0 \text{ and } |F_e| \geq F_s \\ \beta v & \text{if } v \neq 0 \end{cases} \tag{7}$$

with F_e being an external force, F_s the breakaway force, and beta a viscous coefficient.

Stribeck [41] later observed that the drop in force at the initiation of motion is not a discontinuous function but depends on the velocity:

$$F = \begin{cases} F_e & \text{if } v = 0 \text{ and } |F_e| < F_s \\ F_s\, sgn(F_e) & \text{if } v = 0 \text{ and } |F_e| \geq F_s \\ F(v) & \text{if } v \neq 0 \end{cases} \tag{8}$$

with $F(v)$ being an arbitrary function for which many parametrizations have been proposed and which may take the form shown in Fig. 4B. A common formalization is

$$F(v) = F_c + (F_s - F_c)e^{-\left|{v}/{v_\sigma}\right|^{\delta_\sigma}} + \beta v \tag{9}$$

where $F(v)$ is known as the Stribeck velocity and $\delta\sigma$ is a parameter that can be tuned to best fit the shape of the Stribeck effect.

Although widely used for their simplicity, the discontinuities at zero of the previous models make them impractical for friction compensation at motion stop and inversion, where some of the most unwanted effect (e.g., stick-slip) can arise. Dynamic models that include a smooth transition between the two friction regimes instead of a switching function have thus attracted interest from the control community.

Many attractive features for model-based friction compensation have been shown by the LuGre model [42] that is probably the most widely used choice in the research community for both its fidelity in simulating realistic friction behaviors and its ease of implementation. The LuGre model has been used for friction compensation with complex nonlinear systems such as robotic manipulators [42] and wearable assistive devices [27], its simplicity making is suitable for adaptive frameworks.

The underlying reasoning of the LuGre model is not unlike that of the Bristle model: friction derives from the deflection of bristles at the contact points of the moving surfaces. Friction force is a function of the bristles' average deflection, described by a state variable z:

$$\dot{z} = v - \frac{|v|}{g(v)}\sigma_0 z \tag{10}$$

$$F = \sigma_0 z + \sigma_1 \dot{z} + f(v) \tag{11}$$

where σ_0 and σ_1 are constant parameters and $g(v)$ and $f(v)$ model the Stribeck effect and the viscous friction, respectively. The most common choices for these two functions are those that result in a steady-state force similar to Eq. (9):

$$g(v) = \alpha_0 + \alpha_1 e^{-\left({v}/{v_0}\right)^2} \tag{12}$$

$$f(v) = \alpha_2 v \tag{13}$$

with α_i and v_0 being coefficients determining the characteristics of the friction curve such as the stiction force and the Stribeck effect's profile.

Details about other parametrizations for $g(v)$ and $f(v)$ and about identification procedures for the LuGre model can be found in [43]. Once a good model of friction in the robot is available, friction can be predicted and compensated using a feedforward term in the control block.

BACKLASH

Backlash is present in any mechanical system where the driving member is not directly connected to the load. The most common case occurs with gears, where the loss of contact between teeth at motion inversion causes a backlash gap to open. When this occurs, the load is uncoupled from the motor, and the actuator's torque drives only the components before the backlash. This can result in a significant deterioration of motion control and, in the worst case, in loss of stability.

Some of the most important developments in control of systems with backlash was pioneered by Tao and Kokotovic [44], who proposed to use an inversion of the backlash nonlinearity in the control to cancel out the physical phenomenon. Since backlash causes position hysteresis, useful tools for identification and control have been proposed from the extensively researched field of hysteresis modeling.

Several mathematical formalisms exist for modeling backlash-induced hysteresis, but the Bouc-Wen model has been proven to capture a wide range of hysteresis phenomena while retaining a low level of complexity and computational effort and has been successfully used for accurate position control of wearable robotic devices [45].

The Bouc-Wen model represents the hysteresis cycle using a mapping between an input variable $x(t)$ and an output $y(x, t)$ using an auxiliary state variable z:

$$y(x,t) = \alpha kx(t) + (1-\alpha)Dkz(t) \tag{14}$$

$$\dot{z} = D^{-1}\left(A\dot{x} - \beta|\dot{x}||z|^{n-1}z - \gamma\dot{x}|z|^{n}\right) \tag{15}$$

with $n \geq 1$, $D > 0$, $k > 0$, and $\alpha \in 0, 1$. A, β, and γ are dimensionless parameters that can be tuned to control the size and shape of the hysteresis loop and n governs the smoothness of the transition between the elastic and plastic response. Note that the output is given by the sum of a purely elastic term ($kx(t)$) and a hysteretic contribution ($Dkz(t)$), with α controlling the weight of each on the output.

Identification strategies for the model's parameters include least mean square, genetic algorithms, particle swarm optimization, and neural networks. The feedforward term, deriving from the model, can be used in an open-loop scheme alone, combined with a feedback term or combined with feedback information for continuous adaptation.

IMPLICATIONS FOR THE CONTROL OF REHABILITATION ROBOTS

One of the most profound engineering challenges in designing robots for rehabilitation is achieving the dual goal of delivering high forces while retaining the backdrivability of the device. Backdrivability has been shown to be a fundamental feature for keeping the patient engaged in the task, for assessing his/her movement ability and for guaranteeing the system's safety. Yet the requirements of minimizing the intrinsic dynamics on one hand and providing high force output on the other are at odds since the latter requires bulkier actuators or reduced transmissions, which compromise the efficiency of the system and reduce its dynamic transparency.

For stationary robots, where portability is not paramount or devices that need not render extremely high forces, using larger actuators in a direct drive (or small reduction) configuration is probably the most convenient choice. The absence of complex transmission mechanisms will not diminish the efficiency of the motor, allowing it to be back-driven. For such systems, one could implement an open-loop impedance controller, well-known for its stability, simply using the position sensors on the motors' axes. Modeling the robot's dynamics and compensating for backlash and hysteresis is, here, critical.

A device designed for portability or for rendering high impedances, on the other hand, will most likely require a highly reduced and thus nonbackdrivable transmission. An open-loop impedance control in this configuration becomes unfeasible, and a force sensor between the device and the subject is needed to monitor the interaction forces and achieve backdrivability by control. Both the closed-loop impedance and admittance controllers are viable options, but the former is more prone to stability issues, while the latter is robust thanks to the inner position control loop. The drawback of admittance controllers, that is, low accuracy, can be dealt with through accurate identification and compensation of nonlinear phenomena that could upset the inner position feedback loop, for example, friction and backlash in the transmission.

Finally, a significant advantage in terms of intrinsic safety, low-cost force measurement by spring displacement and, most of all, increased force control robustness can be achieved using SEAs. The drawback is the compulsory need for force sensing between the robot and the subject.

CONCLUSION

In this chapter, we gave an overview of the most commonly used actuation strategies for rehabilitation robots, where the characteristics of the interaction between the robot and its user play a key role. Being electric actuators the most commonly employed solution, we briefly described the two frameworks used to achieve compliant control with DC motors.

Both frameworks require compensation of nonlinear phenomena, such as friction and backlash, to ensure stability and accurate force rendering; we gave the reader an overview of what we believe to be the most practical and effective tools to compensate for such phenomena. Finally, the last section explores the difficult trade-off between high force rendering and backdrivability in rehabilitation robots.

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CHAPTER

Assistive controllers and modalities for robot-aided neurorehabilitation

5

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INTRODUCTION

Therapy robots have been specifically designed to deliver and/or support rehabilitation exercises for neurological patients, in particular stroke survivors. The existing robot therapy devices differ widely in terms of their mechanical design, number of degrees of freedom, and control architectures [1]. One feature common to all is that they incorporate sensors of different types, including movement sensors. Hence, both therapeutic and measurement functions are integrated into the same device. As therapeutic devices, robots can be programmed to implement a variety of highly reproducible, repetitive exercise protocols and/or interaction modalities. As measuring devices, they are capable of detecting and quantifying many aspects of both the movement and the physical interaction with the user (movements, forces, and possibly also physiological signals).

Therapy robots are conceived and designed to promote neural plasticity processes through motor learning/relearning; such learning is considered a key element for successful neurorehabilitation. This is based on recent findings showing that it is not the movement per se (such as obtained through passive mobilization) that is effective in promoting plasticity but rather movement associated to *volitional effort*, that is, involving purposeful actions and tasks [2,3]. There are two different ways to enhance the voluntary control during neuromotor rehabilitation of an impaired limb: (1) by providing (electric) assistance through functional electric stimulation or (2) by using robots to facilitate goal-oriented exercise. The two methods of assistance (electric and haptic) are complementary, and the literature provides some examples showing increased beneficial effects when the two modes are used in combination [4,5]; see also Chapter 20 for details. In the following sections, we discuss the different types of haptic assistance that a therapy robot can provide to the patient during training.

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THERAPEUTIC EXERCISES

Different approaches have been proposed for the use of robots to promote neuromotor recovery. Early approaches were mostly heuristic and limited by the available hardware that had been designed for industrial applications. More recent applications are based on an improved understanding of the physiology of the nervous system reorganization after a lesion. Following the taxonomy proposed by Marchal-Crespo et al. [6], existing approaches to robot-assisted exercise can be summarized into three broad scenarios: haptic simulation, challenge-based, and assistive.

HAPTIC SIMULATION

Robots are used for haptic rendering in virtual environments—in the virtual environment, the subject can exercise with a variety of interaction tasks, generally inspired by activities of daily living (ADLs). Robots in combination with visual displays allow the joint visual and haptic interaction with virtual objects. The advantages of a virtual environment over practice in a real-life context include greater safety and flexibility, better adaptation to the individual subject ability, and the possibility to quantify performance.

CHALLENGE-BASED

The robot provides disturbances and/or perturbations to make a task more difficult or challenging with respect to performance without the robot. Several approaches have been proposed. During exercise, the robot can generate perturbations that oppose the subject's movement or compel the subject to provide a greater force. The robot may also be programmed to generate dynamic environments that have a destabilizing effect, for example, negative viscous forces [7]. Another possibility is to visually amplify motor errors. The rationale underlying challenge-based scenarios is that making the task more difficult during training will later result to an improved performance in unassisted or unperturbed exercises.

A number of studies have pointed out that training within negative viscous fields, that is, destabilizing forces that are proportional to movement velocity and equal direction, has a facilitatory effect on sensorimotor adaptation [8]. It has been suggested that the greater variability induced by negative viscosity leads to a greater amount of exploration and therefore a faster and more accurate adaptation to unfamiliar dynamics [9,10]. Training within negative viscosity was also found to facilitate neuromotor recovery from stroke [11].

ASSISTIVE

The robot provides forces that facilitate task performance or task completion. The goal is to help the subject move the impaired limb in specific goal-oriented tasks such as grasping, reaching, and walking.

These categories are not mutually exclusive, in the sense that they can be combined in a given application. In addition, there is no immediate association between one or other approach and specific robots. Rather, all robots can be programmed to work according to each of the above scenarios. For a comprehensive review of robot therapy scenarios, the reader is referred to [6].

ASSISTIVE SCENARIOS

Assistive scenarios are widely used in rehabilitation because they are flexible enough to fit a wide range of impairments. In assistive scenarios, robot devices have been frequently used to enforce passive movements. Repetitive passive training may improve recovery, at least in specific clinical conditions, as it counteracts the deterioration of the mechanical properties of tendon and muscle tissues that are an indirect consequence of the reduced mobility associated with limb paresis. However, better results are obtained when exercise takes into account the adaptive nature of the nervous system and forces the patient to execute voluntary movements.

The notion of "assistance," whether electric or haptic, is closely related to the patient's intention to move. Intention to move can be assessed either directly or indirectly. Direct approaches rely on recording the brain or muscle activity (EEG or EMG), and motor intention can be inferred even from extremely reduced mobility patterns [12,13]. In some devices, the recorded signal is used as an indicator of effort generation to trigger assistance [14]. Other devices generate assistive forces proportional to the amplitude of the processed EMG so providing a sort of "proportional myoelectric control" for the arm [15].

Indirect approaches rely on the notion that robot action must be controlled/modulated in such a way to avoid the phenomenon of "slacking" (see below for details), that is, a reduction of the subject's voluntary control as a consequence of the minimization of effort in assisted movement or passive mobilizations [16,17]. Irrespective of the detection method adopted, when the subject's intention to move is recognized, it triggers the robot controller to provide and/or modulate the proper form of assistance through specific modalities.

ASSISTIVE CONTROLLERS

Like haptic rendering, assistance (or resistance) is obtained through the use of controllers in which the robot guides the movement along a desired path. For an end-effector robot for upper-limb rehabilitation, for example, assistance is described by the following linear proportional-derivative controller:

$$F(t) = K_P \cdot \left[x_d(t) - x_H(t)\right] + K_D \cdot \left[\dot{x}_d(t) - \dot{x}_H(t)\right] \tag{1}$$

where $x_d(t)$ is the desired trajectory, $x_H(t)$ is the trajectory of the hand, and K_P and K_D are the proportional and derivative constants of the controller. More often, the controller does not specify the desired trajectory, but simply constrains movements to be directed toward a target, x_T:

$$F(t) = K_P \cdot \left[x_T - x_H(t)\right] - K_D \cdot \dot{x}_H(t) \tag{2}$$

where K_P and K_D are, respectively, the position and velocity gains (i.e., the controller's apparent stiffness and viscosity).

One problem with the above controller is that it does not limit the force magnitude. For safety reasons, a constant-magnitude assistive force is often preferred:

$$F(t) = F_A \cdot \frac{x_T - x_H(t)}{\left|x_T - x_H(t)\right|} \tag{3}$$

In this way, the force is always directed toward the target but has a constant magnitude, F_A.

One special case of assistive controller is the situation in which the robot simply counteracts the effects of body dynamics, either partly or totally. The T-WREX device, commercialized as ARMEO (Hocoma, Switzerland), is a passive orthosis that uses springs to counteract the effect of gravity in three-dimensional arm movements [18]. In a similar way, all gait robots are equipped with weight support devices that compensate for body weight during robot-assisted gait movements. These weight compensation devices represent a form of assistance. Using the ACT^{3D} device, Ellis et al. [19] imposed forces on the arm to either increase or decrease the amount of limb support required to the subject and measured the workspace explored during planar free reaching movement as a function of active limb support. They concluded that progressive shoulder abduction loading can be utilized to ameliorate the reaching range of motion against gravity. Based on the above taxonomy of robot assistance scenarios, the provided force/torque can be used either to assist (constant assistance) or to disturb (challenge-based assistance) the patient during motor task execution.

ASSISTANCE MODALITIES

Assistive modalities also differ in terms of when and how the assistive force is provided.

The different types of assistance can be summarized as follows:

Continuous assistance

An assistive force is continuously provided starting from the target onset [20]. The assistive force comes into play gradually, in a ramp-like mode of duration T:

$$A(t) = F(t) \cdot R(t;T) \tag{4}$$

where $R(t; T)$ is a ramp-and-hold function (t is the rise time) that enables a gradual onset of force within the time interval T.The magnitude of the assistive force (expressed as stiffness or maximum force) must be carefully set at the minimum magnitude enabling the patient to initiate the movement. In this assistance modality, there are no explicit constraints on the maximum duration of the movement. This assistive modality is the simplest form of assistance and is suitable for subjects who are initially unable to autonomously initiate movements. It is applied in the most severe patients when no "intention to move" detection strategies are included in the robot device. The disadvantage is that in order to keep the task challenging, the magnitude of the assistive force needs to be continuously regulated by the therapist and adapted in step with the patient's improvement on a session-by-session basis.

Time-triggered assistance

At the beginning of the trial, the patient is free to move the arm within the workspace. After a predefined time, t_0 (e.g., 2 s) from target onset, the assistive force gradually comes into play in a ramp-like mode, up to a predefined value (soft application of assistance). The force is then maintained at that magnitude for a time T so as to guide the patient's arm to the target:

$$A(t) = F(t) \cdot R(t - t_0; T) \tag{5}$$

In this way, the patient is challenged to autonomously initiate the movement. Assistance only comes into play after a delay to help the patient complete the movement, thus motivating the patient to be actively engaged in the exercise [21] but, at the same time, enabling a minimum dose of exercise within the duration of the training session. As before, time-triggered assistance is typically used with the more impaired patients.

Activity-triggered assistance

The objective of this type of assistance is to stimulate and enhance the patient's voluntary motor activity. In active-triggered techniques, the robot provides assistance only if the subject is unable to complete the task by herself/himself.

The patient is required to move the arm from the starting point to the target, the only restriction being the working plane supporting the arm for an exercise carried out in two dimensions. If the patient cannot complete the task autonomously, the robot evaluates the current position of the arm/end effector depending on the type of robot and, after a predefined period of time in which there is no movement, guides the patient's arm to the target position [21,22]. The scheme can be represented by the following function:

$$A(t) = F(t) \cdot k(v_H, t) \cdot R(t - t_0; T) \tag{6}$$

where $F(t)$ is the assistive force, $R(t-t_0;\, T)$ is a ramp-and-hold function, and $k(v_H, t)$ is the output of a finite-state machine that outputs one when hand-speed v_H remains below a threshold value for a predefined interval (e.g., 3 s) and zero otherwise.

Pulsed assistance

The aim of this type of assistance is to provide an assistive force that is pulsed in time, with a predefined repetition frequency (e.g., 2 Hz) that is compatible with recent theories on intermittent control [23]. The assistive force consists of a constant component plus a periodic sequence of force pulses. It can be assimilated to a force field that is turned on smoothly (by gating the field generator with a ramp-and-hold function) and is turned off suddenly as soon as the target is reached. In this case, the force field can be represented by the following function:

$$A(t) = \left[k + (1-k) \cdot \sum_{n=1}^{N} \varphi_{\Delta t}\left(t - nT_p\right) \right] \cdot F(t) \cdot R(t) \tag{7}$$

where $F(t)$ is the assistive force (see Eq. 3) and $R(t)$ is a ramp-and-hold function and $\varphi_{\Delta t}(t)$ is a smooth peak function (pulse) with unit amplitude ($\varphi_{\Delta t}(0)=1$) and duration Δt. The pulse train has N pulses and period T_p, both adjustable in accordance with the distance from the target; k is a weighting factor ranging from 0 to 1, which selects between a pure pulsed field ($k=0$), a mixed continuous and pulsed field ($0<k<1$) and a continuous field ($k=1$). Preliminary findings suggested that pulsed assistance allows subjects to reach a similar performance level to that obtained with continuous assistance after a single training session [24].

Negative assistance

In this type of assistance, the patient is required to execute the reaching task while working against a negative force of constant or variable magnitude. This can take the form of the robot resisting the desired movement or creating an unfamiliar dynamic environment that the subject has to adapt to. This type of assistance may be implemented by using a continuous or pulsed paradigm, but the force magnitude F_A or the position gain K_P are negative. This modality is intended for less compromised patients or for those who have already made a significant motor recovery and need mainly to improve the quality of their motor control.

Fig. 1 shows a graphic representation of the different types of assistance as a function of time. The fact that robots can provide different types of assistance should increase the number of patients who can benefit from robotic treatment.

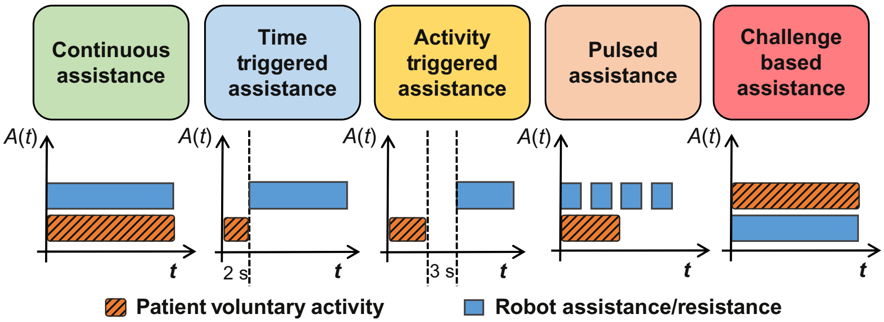

FIG. 1

Types of assistance as a function of time. The figure reports, for each type of assistance, the time of activation of the assistive force and its relationship to the patient's voluntary activity. Note that in the challenge-based assistance case, in contrast to the other cases, the patient needs to exert a force (voluntary activity) that is generally higher in magnitude than that exerted by the robot.

REGULATION OF ASSISTANCE

In the foregoing section, we have shown that the different forms of assistance provided by the robot can be broadly categorized into discrete and continuous regulation of assistance depending on their modality of activation. Of course, this is only a broad categorization, because often the same device can implement different forms of assistance depending on the type of exercise required during training.

A recent study on locomotion [25] suggested that the motor system acts like a "greedy" optimizer, quickly incorporating the assistive forces generated by the robot into the motor plan in order to reduce the degree of voluntary control (and therefore muscle activation) while keeping the position error small. This phenomenon is known as "slacking" and is likely to occur during active-assisted exercises (and, even more, during passive training) when assistive forces are set independently from the subject intervention. A continuous assistive force, if not properly regulated, can induce a reduction of voluntary control that could have adverse effects on recovery. To prevent slacking, assistance should only be provided "as needed", that is, the subject should perform the task with only the minimal amount of robot assistance necessary for task completion. As patients improve their performance, the amount of assistance needs to be adjusted accordingly.

Several robot control strategies have been designed to satisfy this requirement, for both upper limb and gait training [6]. They usually imply the presence in the robot of a controller that provides an appropriate regulation of the assistive force, either continuously or on a trial-by-trial basis.

Hogan et al. [26] found that a treatment protocol that continuously adapts to the subject's motor ability achieves a better recovery than a training protocol in which assistive forces are not adapted. In Casadio et al. [20], the therapist manually selected the assistance level in order to keep it to the minimum level required to evoke the functional response needed to accomplish the task. In Vergaro et al. [27], a linear controller continuously and automatically regulated the assistive force provided by the robot, based on the online performance measures. Similar mechanisms have been proposed for both the upper limb (i.e., the performance-based progressive robot-assisted therapy used by the MIT-Manus robot [28]) and the lower limb (i.e., the patient-cooperative training modality used by the Lokomat system [29]).

Squeri et al. [30] designed an adaptive Bayesian regulator that adjusts the magnitude of the assistive force (or other task parameters) to keep the average performance around a target magnitude (performance clamp). In this way, as performance improves, the controller automatically reduces the amount of assistance.

Another determinant of neuromotor recovery is the regulation of task difficulty or equivalently the "desired" or target performance. This can be implemented by regulating assistance, providing different forms of assistance or changing the properties of the assigned motor task [21]. To this end, regulation requires a proper estimation of patient performance through measurement of movement kinematics and kinetics. The idea behind this concept is to control the motor recovery processes through the performance-based regulation of the training parameters. We can represent the whole system through a control loop in which the motor control system of the patient influences the performance of the motor task using voluntary activity (voluntary control). The resulting performance influences both the motor control system through the sensory system and the robot, which in turn can modify the amount of assistance provided and the properties of the motor task. Fig. 2 shows a schematic representation of the control loop.

Computational models of motor learning further suggest that large initial errors may prevent learning [31]. The challenge point theory states that “optimal” learning is achieved when the difficulty of the task is matched to the subject's level of expertise (i.e., learning is optimal when the individual's challenge point is reached) [32]. This would imply that giving a difficult task to a less skilled person would result in less learning after a similar amount of practice, as compared with training when the task difficulty is adjusted to the skill level. This theory is supported by a recent study that demonstrated that a force field that guided subjects through a desired movement was more beneficial for less skilled participants [33]. Similar effects have been observed in the neurorehabilitation field.

Overall, these considerations suggest that a controller that (i) maximally promotes the subject's involvement, (ii) provides enough assistance so that the subject completes the desired movements, and (iii) is adapted to the subject's skill level and to his/her improvements will maximize motor skill learning and neuromotor recovery.

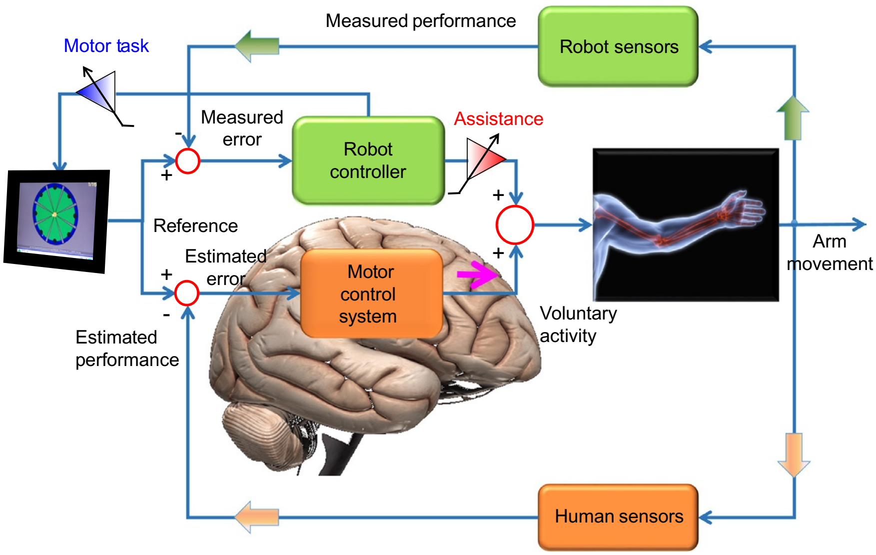

FIG. 2

Control loop for task difficulty regulation. The motor control system of the patient influences the execution of the motor task by voluntary activity (voluntary control). The resulting performance influences both the motor control system through the sensory system and the robot that can modify the amount of assistance and the type of motor task.

However, translating this into actual mechanisms of regulation is far from easy. The problem of "optimally" regulating assistance is currently an open research area, and only heuristic, ad hoc solutions are currently available. The task of deriving an optimal (i.e., "assist-as-needed") controller would be relatively straightforward if the dynamics of the learning or recovery process were completely known. Although there have been attempts to model this process, these models are currently not accurate enough to allow the design of robust controllers [34].

The general goal of regulation of assistance is to decrease assistance as performance improves. This is often achieved through simple linear control models [28,29]. Controller parameters are usually set heuristically. However, stability of the closed-loop recovery process is critically dependent on these parameters, which may be a problem as very little prior information is available on the dynamics of the learning/relearning process. Moreover, the latter may be highly subject-dependent.

Model-based controllers rely on the exact knowledge of the parameters of the trainee learning model. These parameters can be obtained by observing how the dynamics of recovery is affected by varying amount of assistance. Moreover, the recovery process is nonlinear and inherently noisy (it includes a random component accounting for exploration of action space), which makes this approach quite problematic. Another possibility is to use adaptive controllers, which do not require a detailed knowledge of the learning process and automatically adapt to it.

OTHER TYPES OF ASSISTANCE

BILATERAL TRAINING

Bilateral trainers represent a special category of therapy robots. The focus of the first bilateral device was on shoulder and elbow movements [35]. Control was based on the mirror-image movement enabler (MIME) concept: a modified industrial robot applied forces to the impaired arm using position control, with the goal of replicating the movements of the other arm in a mirror-symmetrical way. Another device based on a similar bilateral approach is the Bi-Manu-Track, used for training of pronosupination of the forearm and flexion extension of the wrist [36]. The control of the impaired side can be either passive or active, and the movement may be in a mirrorlike or parallel fashion. Regarding the lower limb, the LOPES gait training robot uses a bilateral approach whereby the unimpaired leg determines the state of the other leg through a method called complementary limb motion estimation [37]. To date, in the majority of bimanual control schemes, the two sides are not required to cooperate, but rather interact in a master-slave fashion, with few exceptions [38].

SENSORY TRAINING

Finally, some experimental training protocols include sensory stimulation and training. For training of proprioception, for example, subjects are instructed to move their arm from the start to the end targets of the reaching path without assistance of vision.

Specifically, the subject's vision of the arm and robot handle is blocked through a specific opaque plane or by a special mask. In this case, the assistance may assume the form of a sensory feedback exploiting a different sensory channel. For example, the robot can provide vibratory feedback to the ipsilateral or contralateral arm to assist the patient in selecting the proper direction of movement (see Chapter 20 for more details).

CONCLUSIONS

We have shown that robot therapy is effective in promoting neuromotor recovery, but what about its mechanisms of action? Several studies have demonstrated that exercise facilitates the recovery of motor functions following stroke. Intensity and frequency of practice are major determinants of recovery. However, mere repetitive task training results in only modest increases in lower limb function and no improvement in the upper limb.

Robot-assistive therapy may be beneficial because (a) its assistive forces can help subjects to complete the motor task even in the early phases of the recovery process, which in turn may increase motivation; (b) it elicits the “right” afferent signals (proprioceptive and tactile), thus promoting the emergence of the appropriate associations in sensory and motor cortical areas; (c) it may induce a sensation of greater stability of the external environment, a necessary condition for long-term, more stable adaptation to occur; (d) it interleaves effort by the patient (essential to provoke motor plasticity) with stretching of muscles and connective tissue that is helpful to prevent stiffening of soft tissues; (e) it may help induce brain plasticity through moving the limb in a manner that self-generated effort cannot achieve; (f) it may help to perform more movements in a shorter amount of time, potentially allowing more intense practice; and (g) it allows subjects to practice a task more intensively by simply making it safer. All these factors may contribute to the recovery in robot-assisted exercise, but none of them has been tested empirically.

A better understanding of the way robot therapy works and, more generally, how physical assistance can facilitate motor skill learning and relearning may lead to novel, more innovative approaches and consequently to a wider range of applications and even more effective recovery.

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CHAPTER

Exoskeletons for upper limb rehabilitation

6

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INTRODUCTION

Motor recovery after stroke with consequent regain of function is promoted by physical therapy and exercise, thanks to the changes in cortical reorganization according to residual neuroplasticity. Four main factors are considered as the major determinants of motor recovery: early intervention, task-oriented training, amount and scheduling of practice, and degree of participation [1,2].

Stroke rehabilitation is being vastly improved through advanced robotic and neuroscience technology. As the entire rehabilitation process is time-consuming and labor-intensive, robots function as an alternative and a supplement to the one-to-one therapy.

There are two options available for upper-limb rehabilitation: on one side simpler devices, that is, one or two DOF, that can be used to train specific function or single-articulation movements, for example, elbow or hand planar movements, and on the other side multi-DOF robots that can train spatial and more complex movement. In this second category, exoskeletons represent the most advanced robot as they drive not only the end effector of the human arm, that is, hand, but also the full kinematic chain, that is, providing single-joint robotic assistance during movement execution, and so, they can be specialized and tailored to patient's needs.

However, the field of robotic exoskeleton technology remains in its infancy, since rehabilitation-robot markets at $221.4 million in 2015 are anticipated to reach $1.1 billion by 2022, with an exponential growth (source WinterGreen research), of which the current share of upper extremity is 13% and expected to grow up to 18.3% in 2021. Exoskeletons alone represent a share of 15% now and expected to reach 17.9% in 2021.

We can define upper-limb robotic exoskeletons as wearable robots characterized by suitable shape, kinematic, and weight factors that can be worn on the patient's arm [3,4]. In order to accomplish this function, the exoskeleton kinematics is characterized by multiple points of connection between the human limbs and robot-exoskeleton links so that often the exoskeleton kinematics is defined as isomorphic to that of human arm and it appears like an outer structure covering the human arm ("exo-", prefix,

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as used for naming insect exoskeletal structure). In this way, exoskeletons can provide a tailored assistance to patient's needs, providing selective joint control at the level of human articulations and acting in symbiosis with human movement. In order to accomplish this function, it becomes evident how appropriate kinematic constraints should be satisfied. Moreover, since exoskeletons are intended to be used for the rehabilitation of patients, with particular reference to neurological patients, it is clear that they should also exhibit a smooth, low friction, dynamic behavior, with overall requirements for the actuation similar to those adopted in the design of haptic devices [5].

In this chapter, we will deal with the main design issues of upper-limb exoskeleton for rehabilitation both in terms of mechanical design from kinematic, actuation, and control point of view in Section "Design of Exoskeletons" and we will analyze their clinical application in stroke rehabilitation in Section "Clinical Evidences of Upper Limb Rehabilitation With Exoskeletons."

DESIGN OF EXOSKELETONS

Upper-limb exoskeletons are typically used for rehabilitation of arm and hand function [6]. Another field of application of robot exoskeleton is human-power augmentation where a number of powered exoskeletons have been already developed [7] such as the Hercule by RB3D, the NASA X1 Exoskeleton [8], the XOS 2 exoskeleton by Sarcos, or the Body Extender from PERCRO, SSSA, Italy [9].

As shown in Fig. 1, there is a large variety of technologies used for exoskeletons. Rehabilitation and human power-augmentation exoskeletons make use of different actuation solutions, such as geared solutions, tendon drives, hybrid solutions (screw and cable actuators), or variable-impedance actuators.

We will briefly analyze in the following sections some of the main issues concerning the kinematics and actuation issues in rehabilitation exoskeleton design.

KINEMATIC ISSUES IN EXOSKELETON DESIGN

In order to accomplish training of motor function, upper-limb exoskeletons should be accurately designed from an ergonomic and biomechanics point of view. In particular, since exoskeletons are thought to act in symbiosis with the human operator, the kinematics is not less relevant than actuation. The following issues need to be properly analyzed: (1) nonideal equivalence of human joints to simple kinematic joints, (2) need of adjusting exoskeleton dimensions to human arm size, and (3) joint implementation should take into account the bulk of human arm.

Of course, it is well-known that the real anatomy of human joints do not correspond to ideal rotational or spherical joints: if we restrict, for instance, to upper limb, the shoulder complex involves the glenohumeral, the sternoclavicular, the acromioclavicular, and the scapulothoracic joints, so the human shoulder complex can be considered only as a generalized spherical joint with a floating center.

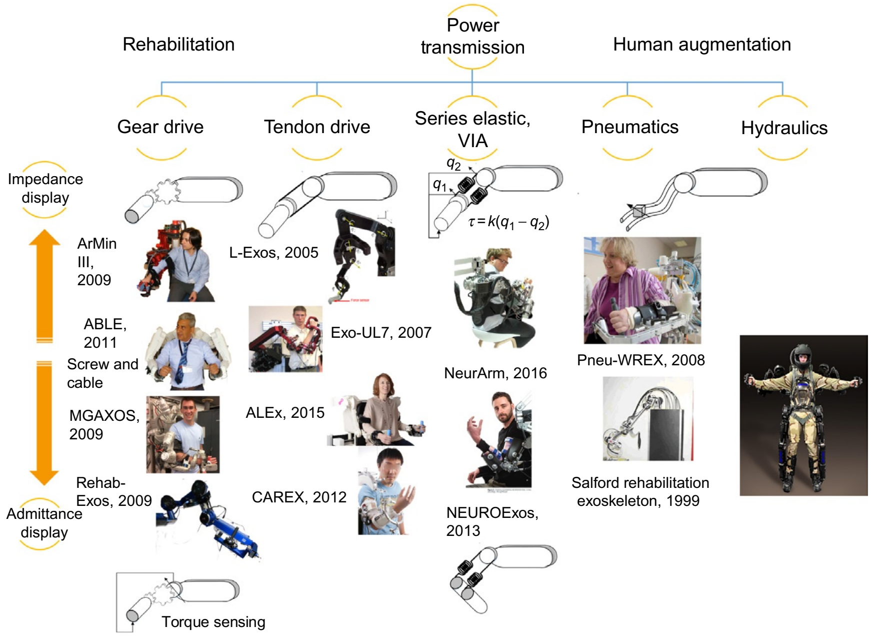

FIG. 1

Exoskeletons divided by category of actuation.

Pictures courtesy of Prof. Robert Riener for ARMin III; Prof. Craig Carignan for MGA Exoskeleton; Eng. Philippe Garrec for ABLE; Prof. Jacob Rosen for Exo-UL7; Prof. Sunil Agrawal for CAREX; Prof. Antonio Frisoli for ALEx, Rehab-Exos, and L-Exos; Prof. David Reinkensmeyer for Pneu-WREX exoskeleton; Prof. Nikos Tsagarakis for Salford Rehabiltation Exoskeleton; and NEUROExos to Massimo Brega. Right-most image used with permission from Sarcos Corp.

Axis misalignment can lead to undesired interaction loads (UI loads) that can render training uncomfortable. Moreover, the perfect alignment of joints requires that either to adapt robot-link size to human anthropometric dimensions or to use self-alignment mechanisms based on passive joints. A first systematic approach to the synthesis of self-alignment mechanisms was proposed by Jarrasse et al. [10] by studying the general problem of connecting two similar kinematic chains through multiple passive joints.

A further generalization [11] of this approach in terms of the type synthesis of self-adapting upper-limb exoskeletons considers the application of the mobility formula to multiloop linkages $\#F = \#f_{\text{active}} + \#f_{\text{human}} + \#f_{\text{passive}} - dl$ where l denotes the number of loops, equal to 2, for instance, for shoulder-elbow exoskeletons (one for shoulder and one for elbow complex), $d = 6$ for spatial case, $\#f_{\text{active}}$ indicated the active degrees of freedom of known joints (4 DOF), $\#f_{\text{human}}$ the human joints (4 DOF), and $\#F = 4$ degrees of freedom considering shoulder (3 DOF) and elbow (1 DOF). By solving for $\#f_{\text{passive}}$, it is easy to derive that eight passive degrees of freedom should be added to the kinematic chain as passive joints in a shoulder-elbow exoskeleton,

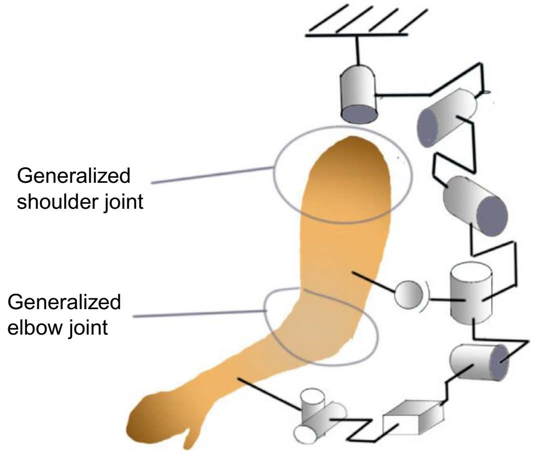

FIG. 2

Example case of an isostatic connection between human arm and shoulder-elbow exoskeleton.

with a distribution on shoulder-elbow # DOF subchains that can vary in the range of 3/5, 4/4, and 5/3. One example is reported in Fig. 2 where a $3R_a$-C-S chain is used for the shoulder and then a R_a-P-U chain is used for the elbow, where R, C, S, P, and U symbols stand, respectively, for rotational, cylindrical, spherical, prismatic, and universal joint kinematic pairs, while the subscript a indicates that the joint is actuated.

ACTUATION ISSUES

There are several technological issues to be taken into account in the construction of upper-limb robotic exoskeletons, of which a relevant one is the choice of the actuation principle.

Fig. 3 shows a summary map of the different technological options that are available to the design. First, the choice of the actuation principle represents a fundamental choice. Electric motors have several advantages; they are commonly used in the form of brushless DC motors to reduce the electromagnetic emission as required for medical devices.

Hydraulics has a better power density, but it poses problems in terms of safety due to the high pressure required by the oil circuit, and it is not always compliant to guarantee patient's safety.

Pneumatic actuation has been used in several designs; see, for instance, in the form of artificial pneumatic muscle [12] or for the actuation of shoulder and elbow in Pneu-WREX [13]. In this particular application, the inherent compliance due to air transmission might increase also the safety for a human-worn exoskeleton.

In fact, it has been already pointed out that for physical human-robot interaction, the risk of human injury in case of collision with a robot increases with the stiffness and mass of the moving parts of the robots [14]; so that in reducing the effective

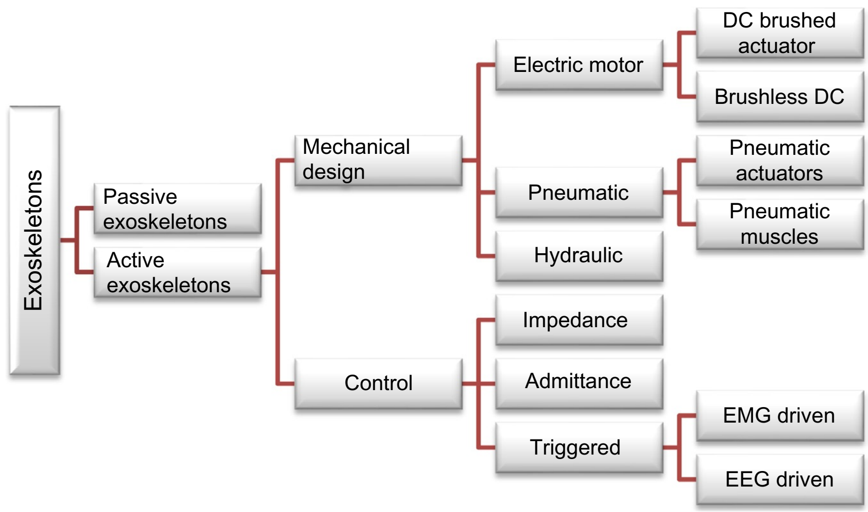

FIG. 3

Actuation and control solutions for design of exoskeletons.

impedance of the robot while maintaining high-frequency torque capability, it is possible to satisfy the competing design requirements of performance and safety.

Recently, we have assisted in the advances in the direction of new actuators for human-robot cooperation, and this is particularly relevant in the fields of exoskeletons, with the introduction of different solutions. We will focus mainly on the electric actuation, as this represents the most commonly adopted solution.

The simplest class of exoskeletons is the fully passive, where a system of springs or counterweights are used to compensate the weight of the patient's arm, reducing the role of abnormal synergies [15].

On one side, the requirements of transparency and high fidelity of forces, such as the concept of Z width [5], require that actuator solution is chosen to prevent anisotropic behavior and low perceived reflected inertias. If we consider that for a given gear ratio τ, we will achieve at the end effector an equivalent increase in terms of motor inertia I_m proportional to the square $\tau^2 I_m$.

Since in the case of electric actuation we need to adopt usually transmission systems to achieve the rate torque values, there are different approaches that have been developed to comply with this requirement (Fig. 4).

Gear drive designs

Direct-drive actuators are electric motors coupled with a transmission/reduction system; they can be classified according to the backdrivability and sensing system.

More commonly, joint torque solutions can be implemented by means of gear-drive designs, where Harmonic Drive speed reducers can provide important gear ratios for force amplification. The ArMin III exoskeleton [16] makes use of additional

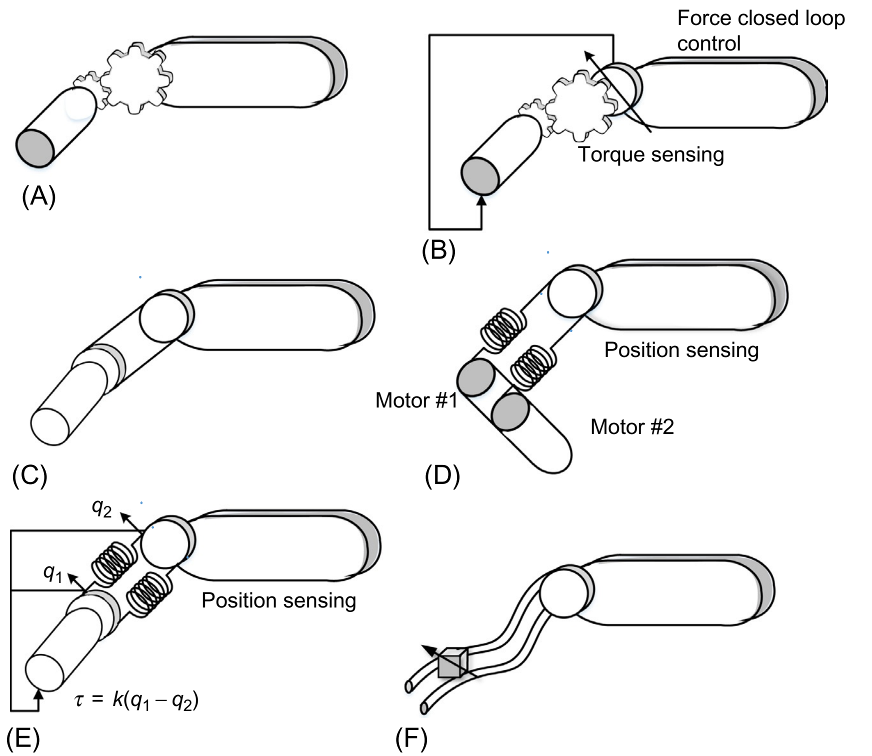

FIG. 4

Principles of actuation for exoskeletons. (A) Geared transmission. (B) Force sensorized joint. (C) Tendon transmission. (D) Variable impedance. (E) Series elastic. (F) Hydraulic-pneumatic.

passive degrees of freedom for compensating scapula elevation movement. In this case, actuators are located at joints and are composed of electric DC motors connected with Harmonic Drive (HD) gearbox with different reduction ratios according to joint location, while an open loop control can be used with feedforward compensation schemes for inertia and friction disturbances.

A hybrid approach successfully employed is a combination of ball-screw actuators and tendon actuation, such as in the case of ABLE exoskeleton [17]. In this case, the ball screw, thanks to the low friction, leads to an overall high backdrivability, while tendons are used for torque transmission at joints and motion conversion from linear to rotational.

Alternatively, to increase the backdrivability of the systems, hand force/torques and elbow load cells can be introduced at the connection points with the human, so that a closed-loop force control can be used, as in the case of MGA [18] exoskeleton.

Also, specifically designed joints can be used to obtain high-fidelity joint torque, by means of joint torque sensors integrated at the level of joints, so that impedance

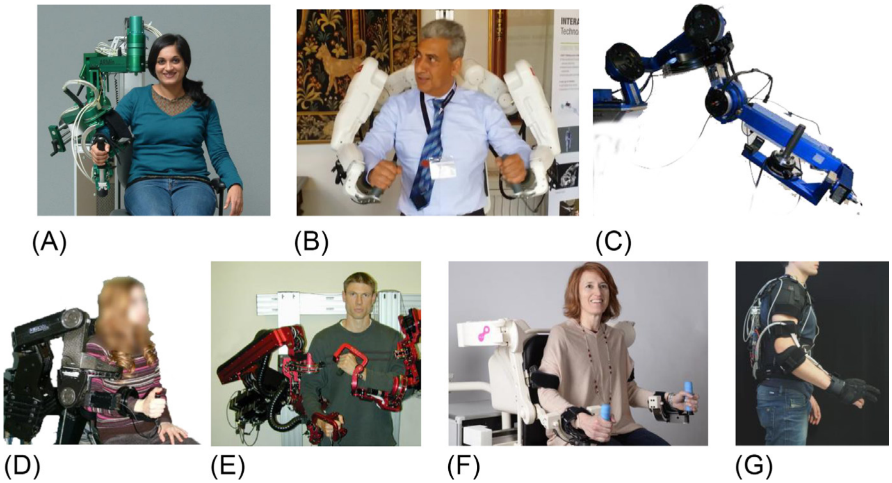

FIG. 5

Top, gear-drive designs, (A) ARMin III [16], (B) ABLE exoskeleton [17], (C) Rehab-Exos [19] at bottom tendon drive designs, (D) L-Exos [20], (E) EXO-UL77 [21], (F) ALEx [22], and (G) soft-arm compliant exoskeleton [23].

(A) Courtesy of Prof. Robert Riener, ETH. (B) Courtesy of Eng. Philippe Garrec, CEA. (E) Courtesy of Prof. Jacob Rosen, UCLA. (G) Courtesy of Prof. Lorenzo Masia, NTU.

behavior is achieved by closed-loop control. One of the issues with the design of integrated torque sensors is however the residual sensitivity to other force components and the bandwidth of the closed-loop controller that depends on actuator dynamics. The Rehab-Exos [19] makes use of a joint torque sensor to provide accurate torque control and increase backdrivability, while high torque can be delivered thanks to almost 1:100 Harmonic Drive gear reduction (Fig. 5).

Tendon transmission designs

Using tendon transmission allows to physically separate the motors from the joints where the actual torque is transferred: this has as strong effect on the reduction of moving masses, since motors can all be located at the level of a fixed frame, still achieving some force reduction according to the ratio between motor- and actuated joint-driven pulleys.

The tendon-driven designs have been proposed first with the L-Exos [20], characterized by four degrees of actuation for shoulder and elbow joints. The system is characterized by having all motors located at the back on a fixed frame, while steel metal tendons are used to transmit the torque to each joint. This design requires that the cable transmission system is characterized by a constant length, and this is achieved by a set of idle pulleys that drive the cable all over the joints. This leads to a consistent reduction of weight and inertia of the moving parts and smooth dynamic behavior.

Later, the Exo-UL7 was introduced [21], a seven-degrees-of-freedom tendon-driven exoskeleton based on the same principle of actuation, extended also to include wrist actuation. In both designs, the shoulder pronation/supination is implemented by means of an open circular guide to allow the compatibility with human arm.

Recently, Frisoli et al. proposed Alex [22], a bimanual tendon-drive exoskeleton that is based on a tendon transmission, exploits a novel kinematic solution to implement the shoulder joint, and is based on innovative patents remote of center mechanism.

Tendon transmission represents an ideal mean to achieve high backdrivability of the system and so typically adopts an open-loop impedance control scheme, meaning that there is no closed-loop control on joint torque.

Recently, the soft-exoskeleton concept has been introduced as well. Masia et al. [23], for instance, introduced sheathed tendons to control a shoulder exoskeleton, where the system is worn by the user as a garment and tendons can provide assistive torques directly at the level of the joint. To take into account the variability of friction due to change of configuration of the geometry of sheaths, calibrated dynamic friction models, e.g., LuGre model are used to compensate in feedforward.

In alternative, another example of a massless cable-driven design is the CAREX exoskeleton, where in this case it is exploited the principle that a minimum of $n+1$ cables are required to control n degrees of freedom [24].

Series elastic and variable impedance

One of the research lines to advance wearable robots is to develop and incorporate an adjustable compliance (i.e., stiffness) actuation that assists the human body to the desired dynamic motions.

The general traditional actuators, due to the absence of elastic or damping elements, can be lighter and more compact than variable-impedance actuators, and they better adapt to predefined trajectory control, but their time response and dynamic bandwidth are limited by control and electric properties of actuators, such as maximum reachable velocity by an electric motor.

In the context of research, some exoskeleton designs have been proposed based on VIA (variable-impedance actuators) actuators: they can be further divided in two categories, depending on whether the electric motor is coupled to a spring with fixed (series elastic actuator, SEA) or variable stiffness (variable-stiffness actuators, VSA) [25]. All the variable-impedance actuators have the advantage of absorbing impacts, and in addition, adding a series elastic element reduces the peak power demand on the motor, with consequent reduction of the motor size.

However, a strong limitation to adopt VIA actuators in exoskeleton design is due to their complexity, size, and/or weight.

The LOPES [26] at the University of Twente has been the first exoskeleton, for lower limb assistance, using series elastic actuation, and is capable to provide over mill gait assistance with the capability of adapting to user's motion, for example, walking and running. Recently, VIA has been successfully adopted for elbow exoskeleton in the NEURARM by Vitiello et al. [27]. Table 1 provides a summary of the main pros and cons of different electric actuator solutions.

Summary of actuation solutions

We present in Table 2 a short summary of the examined exoskeletons with indication of their actuation and adopted control solution.

Table 1 Pros and cons of SEA, VSA, and direct-drive solutions

	SEA	VSA	Direct drive
Pros	Capacity to store and restore the energy in the mechanical compliance	Variable stiffness	More compact design, high efficiency in torque transmission
Cons	Low bandwidth in position control, closed-loop bandwidth depending on two sensor readings	They generally use two motors that increases the size, weight, and complexity of the actuator in comparison with an SEA	Dynamic bandwidth limited by amount of speed reduction and speed limits of electric actuators

Table 2 Classifications of upper-limb exoskeletons according to actuation and kinematic

Exoskeleton	Actuation solution	Control	Anatomical districts	Number of DOFs
L-Exos [28]	Tendon drive	Impedance control	Shoulder and elbow	4
Exo-UL7 [21]	Cable-driven, tendon, and pulley	Impedance control	Shoulder, elbow, and wrist	7
Masia et al. [23]	Soft exoskeleton with sheathed tendons	Friction compensation	Elbow and shoulder	1
MGAXOS [18]	Gear drive	Force closed-loop control	Shoulder-elbow	4
ABLE [17]	Ball screws and cable	Impedance control	Shoulder-elbow-wrist	7
Rehab-Exos [19]	Gear drive	Closed-loop interaction joint control	Shoulder-elbow	4
Armin III [16]	Gear drive	Impedance control	Shoulder-elbow-wrist	7
T-WREX [15]	Passive exoskeleton	Spring passive behavior	Shoulder-elbow-wrist	5
Pneu-WREX [29]	Pneumatic	Nonlinear force control	Shoulder-elbow	4
BONES [13]	Pneumatic	Nonlinear force control	Shoulder-elbow	4
Salford exoskeletons [30]	Artificial pneumatic muscle	Force closed-loop control	Shoulder-elbow	7
Sarcos [31]	Hydraulic	Admittance control	Shoulder-elbow	7
NEUROExos [27]	Variable-impedance actuation	Torque control	Elbow	1

CLINICAL EVIDENCES OF UPPER LIMB REHABILITATION WITH EXOSKELETONS

There are evidences that exoskeleton can lead to significant improvement in the rehabilitation due to their capability of performing selective joint control and three-dimensional spatial training [32].

The first studies in chronic stroke with active exoskeletons were conducted with L-Exos [28,33] and ARMin II [34] exoskeletons showing significant increase in upper-extremity Fugl-Meyer score.

The rehabilitation training with L-Exos exoskeleton [6] in the recovery of spatial reaching movements, with a focus on point-to-point reaching movements performed in different directions, produced positive effects in movement execution, in terms of decreased execution time, improved movement smoothness, and increased active joint ranges of motion. In particular, the observed functional changes were found to be associated to an improvement in the cocontraction index of proximal joints, in particular for shoulder extension and flexion.

One of the earliest randomized controlled trials with exoskeletons [15] was conducted with T-WREX (31 chronic stroke patients divided in two groups), a passive instrumented arm orthosis, finding a statistically significant difference in Fugl-Meyer assessment of the upper-extremity (FMA-UE) scale between T-WREX and the conventional therapy.

A subsequent controlled study made use of a pneumatic actuated exoskeleton version, the Pneu-WREX [29], used to assist patients also in movement completion, and confirmed how in patients with chronic and moderate-severe deficits (26 chronic stroke patients divided in two groups) exoskeleton training in three-dimensional virtual tasks was more effective than conventional tabletop training.

More recently, a larger controlled study conducted with the ARMin [35] exoskeleton (77 patients with moderate to severe paresis divided in two groups) confirmed that robotic training performed with task-specific training in three dimensions reduces motor impairment more effectively than conventional therapy, since patients assigned to robotic therapy had significantly greater improvements in motor function as measured by FMA-UE.

Also, the UL-EXO7 [36] with seven DOF was applied in a clinical trial for the rehabilitation of chronic stroke patients (>6 months since acute event). The study reports the results of the comparison of unilateral robotic training (five patients), bilateral robotic training (five patients), or usual care (five patients) and showed that bilateral-movement training scheme obtained better outcome in wrist-joint movement and other quantitative parameters compared with the unilateral training group.

But what is the effect of wearing an exoskeleton on human movement performance?

Pointing movements toward target were evaluated [31] under the exposure to space artificial force field generated with Sarcos hydraulic exoskeleton. They were found to be altered in healthy subjects until sufficient adaption is reached to return to null-field trajectories. But interestingly, it was found that subjects do not return to the same null-field trajectories in the joint space, making speculation that our motor control does planning of reaching movements in extrinsic (task space) coordinates. This task was further analyzed in another study [32] by making use of the ABLE exoskeleton, where natural interjoint coordination in pointing movement was measured by means of principal component analysis (PCA), confirming the absence of joint-space adaptation but evidencing also the lack of end-point movement adaptation and the capability of using exoskeletons to teach new upper-limb synergies in pointing and tracking tasks. These are considered relevant features for the application of exoskeletons for rehabilitation of poststroke patients.

Another study, conducted with the Alex, showed that motor synergies, assessed by EMG recordings, are not altered by the usage of the exoskeleton [22].

It is moreover reported in literature that the usage of exoskeletons allows to monitor the levels of spasticity by isokinetic movements at various angular velocities within the capable range of motion for both joints [37] or perform specific training against spasticity. The results suggested that intense early rehabilitation could contribute to prevent elbow spasticity from occurring at a later stage (3–4 months after stroke) of recovery [38].

CONCLUSIONS

This chapter has presented an overview of the main issues for the design of upper-extremity exoskeleton for rehabilitation, analyzing the main aspects of choice of kinematics, actuation, and relevant results of clinical evaluation.

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CHAPTER

Exoskeletons for lower-limb rehabilitation

7

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INTRODUCTION

Powered lower-limb exoskeletons have been proposed as wearable systems to enable daily-life bipedal locomotion in patients with muscular weakness or paralysis and to facilitate the reacquisition of motor skills required for walking. Wearable robots, introduced as person-oriented systems that directly interact with the users, can support the clinicians to optimize retraining of physiological movement patterns with activity-based interventions.

Most common neurological diseases that can affect the lower-limb motor function are cerebral palsy in children, sclerosis, Parkinson's disease, stroke, and spinal cord injury (SCI). Appropriate therapy can promote greater autonomy in the chronic phase recovering motor skills through active muscle activation. These facts put robotics as one key candidate solution to the socioeconomic pressures of an aging world, improving the recovery process.

The goal of this chapter is to revise the state of the art and status of most advanced designs in the rapidly evolving field of wearable robots for gait rehabilitation. We will provide an overview of designs and control solutions in existing robots and the existing evidences (that are commercially available) of usability and clinical efficacy. We will emphasize a new variety of solutions for bioinspired actuation and control that promise to consolidate wearable robots as a new way to deliver rehabilitation therapy.

LOWER LIMB EXOSKELETONS FOR REHABILITATION: STATE OF THE ART

There has been an increasing interest in the development of lower-limb exoskeletons to relieve the drawbacks of the traditional rehabilitation interventions, namely, the lack of repeatability, short training sessions, and assessment only based on observation [1,2]. The aim of rehabilitative exoskeletons is to safely facilitate the restoration

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of the human-legged mobility by providing a task-oriented and repetitive gait training and monitoring the patient progress [3].

Currently, there are a number of wearable exoskeletons at various stages of development such as ReWalk (ReWalk Robotics, Inc., Marlborough, MA, the United States) [4,5], HAL [5,6] (Hybrid, Assistive Limb, Cyberdyne Inc., Japan), Ekso (Ekso Bionics, Richmond, CA, the United States) [7], Indego (Parker Hannifin Corp., Cleveland, OH, the United States) [8], and HANK (GOGOA, Urretxu, Spain) [9]. Recent studies disclosed that Indego, ReWalk, and HAL enable different modes to support the gait training during sitting, walking, and stand transitions [8,10,11].

To investigate the clinical effectiveness, safety, and usability of the task-specific robotic training supplied by wearable exoskeletons, clinical trials with neurological patients have been carried out. Inspection of the protocol designs across studies revealed considerable variations in the frequency, intensity, and number of sessions performed [3,12,13]. Typically, the robotic gait training comprised 1–3 sessions of 1–2 h per week [3,12].

While some studies relied on standardized tests and timed measures to assess functional (e.g., 10-m walk test, 6-min walk test, and timed up and go test (TUG)) and physiological (muscle stretch, spasticity, and energy expenditure) measures, others relied on questionnaires or subjective observation-based assessments [3,13].

The effects on gait function of exoskeleton-based therapy are an open matter of research. HAL introduced positive and significant contributions in the gait speed, cadence, TUG test, and balance in patients suffering from stroke and SCI [6], and it was well tolerated by hemiparetic patients [11]. Ekso training improved mobility and energy expenditure of patients with SCI [7]. The use of exoskeletons has also introduced secondary benefits across multiple physiological systems, such as improved bowel/bladder function and spasticity, and decreased chronic pain [3,12]. Such findings have been highlighted in the rehabilitation with ReWalk [4,10].

Usability outcomes also showed that the neurological patients learn to use Indego quickly and manage a variety of indoor and outdoor surfaces [8]. No reports of considerable adverse events were observed during exoskeleton-assisted ambulation by HAL [6,11,14], ReWalk [4,10], Indego [8], HANK [9], and Ekso [3,13]. The existing designs of HAL and ReWalk enabled intensive training of gait in patients with severely impaired gait function, which encourages their potential for independent ambulation. Ekso and HANK open the possibility to mitigate the common impairments of SCI and stroke, respectively [7,9].

Current challenges for the clinical interventions based on rehabilitative exoskeletons comprise the long-term investigation of chronic exoskeleton use and the application of comprehensive metrics for assessing safety and usability.

NEW HORIZONS FOR WEARABLE EXOSKELETON TECHNOLOGY: SYMBIOTIC INTERACTION

The possibility of interfacing the human body with artificial devices to optimally rehabilitate gait function is a fascinating technological challenge. Neurological patients would benefit from wearable robotic systems that could automate the assist-as-needed physical rehabilitation paradigm. This principle assumes that training should be accomplished with the minimal amount of external guidance possible. In this way, in the decade of 2010, assist-as-needed robotic training algorithms to rehabilitate walking on the treadmill were proposed and tested, including error weighting functions that allowed minimization of robot guidance and at the same time continuously challenge the subject.

The approaches proposed for human-machine interaction are not yet taking into account the symbiotic interaction between the user and the wearable exoskeleton (ReWalk, Ekso, and Indego). From the emerging directions, we highlight the evolution of human-robot interfaces for rehabilitation exoskeletons for overground training. Patient-cooperative devices are proposed via new interfaces with brains and muscles that allow for detailed assessment and monitoring of biomechanics and neuromotor deficits [15]. Adaptability and learning approaches are also under investigation to balance safety with a more versatile function to handle multiple situations[1]. In the following section, we describe bioinspired actuation and control approaches for symbiotic interaction in lower-limb exoskeletons.

BIOINSPIRED ACTUATION IN WEARABLE EXOSKELETONS FOR WALKING

Conventional actuator technologies

In wearable robotics, actuator technologies are commonly designed and applied to move the exoskeleton by converting a source of energy into a mechanical motion. Electric, hydraulic, and pneumatic actuators are predominantly used in current wearable exoskeletons [2,16,17].

Electric actuators are easily controllable and power efficient but still required for most gait-related application gear reductions to achieve the desired torques [2,16,18]. Exoskeletons electrically actuated are Ekso, Indego, ReWalk, HAL, and HANK [2,16].

Hydraulic and pneumatic actuator technologies include variable volume pressure chambers to convert a pressurized liquid or a pressurized gas, respectively, in a mechanical torque to create motion. Due to their inherent benefits, hydraulic and pneumatic actuators are silent, precise, smooth, and impervious to dusty and wet environments; support high specific power and force; and enable backdrivability and twice lightweight than electric actuators [2,16]. Nevertheless, electric actuators are 92 % more power efficient than hydraulic actuators for robot-assisted walking applications [2].

The wearable exoskeleton community has pointed out that actuators should exhibit high specific power and force, natural motion behavior, ease of control, efficiency, and safety mode [16]. Key physical requirements include low mass, low cost, modularity, and portability [16].

[1]The BioMot Project “Smart Wearable Robots with Bioinspired Sensory-Motor Skills,” FP7-ICT-2013.2.1-611695

In general, conventional actuation technologies still result in heavy and rigid systems [16,17,19]. To overcome these issues, alternative actuation mechanisms are under investigation.

Compliant actuators

Traditional nonbackdrivable electromechanical actuators can be limited to provide more accurate stable force control or exploit energy storage-release principles for energy efficiency.

Including elastic (or compliant) structures in the electromechanical actuators was originally proposed and widely adopted with the introduction of *Series Elastic Actuators* [20]. Such compliant actuators have been proposed to develop exoskeletons with variable impedance functions to compensate for a capability gap. In such systems, the control system is used to drive the exoskeleton movement and set to control the displayed force and the compression in the elastic element through the motor's angular rotation. Thus, the compliant actuator in the exoskeleton can exhibit low impedance, low friction, and acceptable dynamic range. The major benefit of this scheme, thanks to the elastic component, is that it allows implementing a torque control loop through a position control. This results also in a better resistance to impact, which can, in turn, benefit comfort and safety.

Among the multiple design choices including transmission type and gear box, other important factors affect the bandwidth of the actuator, such as actuator size and stiffness of the compliant element. The choice of stiffness is a compromise between minimal endpoint impedance and high force control bandwidth.

Lightweight, low power controllable actuators

The development of actuators that behave like human muscles is of major importance for the advancement of rehabilitation robotics. Applications in exoskeletons include timed application of springlike behavior with quasi-passive mechanism at joints. Such semiactive mechanisms that allow varying the joint stiffness could be deployed in rehabilitation exoskeletons to adaptively change the demand of muscle forces and joint moments during walking.

A great deal of research has been conducted in the field of orthotics to design passive mechanisms to resist knee flexion in weight bearing while allowing free knee extension and enabling free knee rotation in flexion and extension when the leg is unloaded [21]. Furthermore, more advanced designs have tried to also incorporate control of knee flexion at early stance and provide knee extension assistance with recovery of elastic energy [22]. Shamaei et al. developed a quasi-passive mechanism integrated in a powered exoskeleton that provides assistive moments to the knee joint in the weight acceptance phase of the gait [23]. Interestingly, Elliot et al. investigated the addition of a spring at the knee of an exoskeletal brace, engaged by a clutch to supplement weak knee extensors during walking in subjects with increased joint stiffness [24]. Recently, passive clutch-like structures have been demonstrated to be feasible to improve walking economy with mechanical clutch technology that enables spring elements in the ankle joint [25]. Recently, the potential to use the electrostatic adhesion to achieve lightweight, low-power, and controllable holding forces has been demonstrated in an ankle exoskeleton [26].

BIOINSPIRED CONTROL

Biomechanical principles

There is still a limited understanding of how people adapt to walking with robotic devices. Basic observations can be performed in patients with partial paralysis, by comparing with respect to healthy groups, to determine the seven minimum actuation requirements (Fig. 1).

With regard to user's adaptation to robotic assistance, preliminary research reveals a reduction in net muscle moments about the joint, altering joint kinematics. However, such bandwidth and power capacity have not been clearly attributed to subject's adaptation or actuator mechanical limitations. Further physiological adaptation has been seen in the whole leg stiffness during hopping, in which the biological leg stiffness is modulated in order to achieve a combined linear stiffness, with a reduction in energy consumption. The design of the exoskeleton control can greatly alter how humans adapt to robotic assistance during walking. Recent preliminary evidence with an ambulant exoskeleton (H2, Technaid) is showing that in patients with incomplete SCI, walking assisted with a compliant controller could improve the metabolic cost compared with a stiff trajectory control [27]. Further research is expected to validate such hypothesis and to reveal how control modes should be tuned to tackle specific deficits.

Admittance and impedance controllers

The mechanical interaction between a wearable exoskeletons and the human is arguably one of the most fundamental exoskeletons' behaviors. This interaction may be solved through impedance control and admittance control, both disclosed by Hogan [28].

The mechanical interaction can be characterized by mechanical impedance, which seeks to establish a dynamic relationship between an output force and an input trajectory, using dynamic properties, such as stiffness, damping, and inertia [28,29]. The first implementation of the impedance control in robotic devices for rehabilitation of lower limbs was proposed in the Lokomat (Hocoma, AG) through an inner PI control loop [30]. A PD-computed torque controller form of the impedance control was also implemented in [31]. Fig. 2 presents an impedance control scheme for lower-limb rehabilitation using a wearable exoskeleton.

Conversely, the mechanical admittance may be considered as a dynamic extension of compliance since it determines the output trajectory (angular position) from a mechanical interaction by monitoring the force (mechanical torque) involved in this interaction [28]. Aguirre-Ollinger et al. [32] implemented an admittance control to modulate the trajectory command for a 1-DOF exoskeleton [32]. This control was also implemented in [33,34].

In ambulatory robotic applications, the human-robot interaction is most often solved through the impedance control to maintain the interaction force below safe

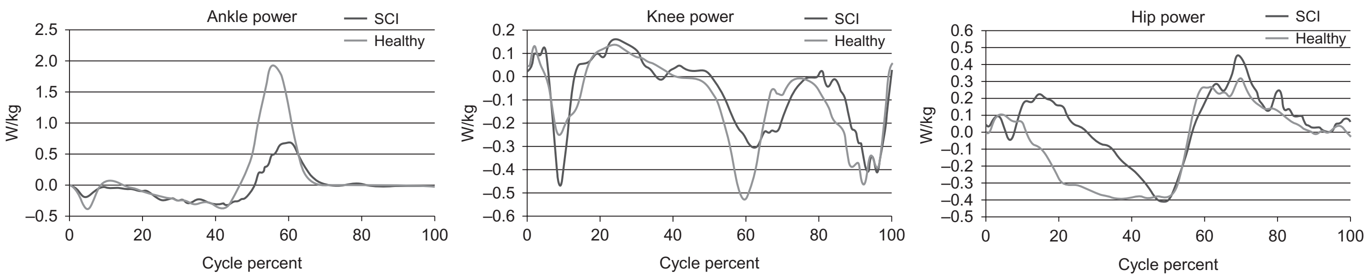

FIG. 1

Comparison of lower-limb joint power during walking (sagittal plane) between incomplete SCI and healthy groups. The sample vas composed of nine incomplete spinal cord injured patients that were able to perform unassisted walking for at least 10 m. The experiment compared the lower-limb joint dynamic data in the sagittal plane (joint power) with a sample of 10 healthy people. Both groups were height matched. The healthy group walked in a slow walking in order to better match the characteristics of the i-SCI group.

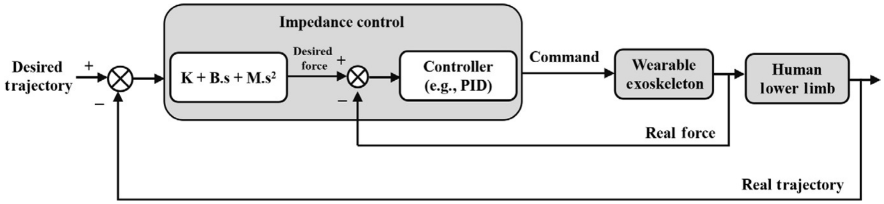

FIG. 2

Impedance control scheme for wearable exoskeleton.

levels for the patient and, simultaneously, to control the limb position according to the desired trajectories determined by the therapy [29]. This impedance can be thought of as a dynamic generalization of a physical or virtual spring. Nevertheless, the performance of an impedance control is determined by the precision of the position sensor and the actuator torque precision and bandwidth. When the actuation system of the exoskeleton augments the total inertia apparent, the robot hardly behaves as a spring, and it is usually more feasible to make it behave as a mass [28,35]. The apparent inertia of a wearable exoskeleton can be minimized through gravitational compensation.

The performance of admittance controllers beneficiates the application of stiff and powerful actuators with low backslash since this control scheme is stable toward the displayed high stiffness. Therefore, the main issues concerning the final choice of a control architecture depend on the characteristics of mechanical systems and goals pursued.

Setting references for robotic control

Wearable exoskeletons require a prior personalized definition of the default targeted movement. Reference kinematic patterns could be shaped for individual subjects and range of desired gait speeds in training, based on normative gait databases. In an attempt to simplify the process of personalization of speed-dependent reference trajectories, it has been proposed to apply regression-based models for reconstructing body-height and speed-dependent angular trajectories [36]. It has been shown possible to record patterns from healthy subjects walking with a lower-limb exoskeleton and then reconstructed for different walking speeds and key events to create a reference pattern for the robot. Asín et al. found, in healthy individuals, that such model-based generated kinematic patterns can contribute to improved human-robot interaction in terms of average interaction joint torques during overground gait training [37].

Neuromusculoskeletal (NMS) modelling for feedback and control

The successful development of wearable robotic devices for rehabilitation of human locomotion requires that both human and robot are treated as a truly cooperative system. The ability of measuring muscle forces and joint variables is therefore needed to quantify and predict joint function. Neuromusculoskeletal modeling has become a popular tool for predicting these variables from movement data. An approach is to record EMG to translate the measured individual's neuromuscular patterns into muscle and joint force estimates via EMG-driven musculoskeletal modeling. This

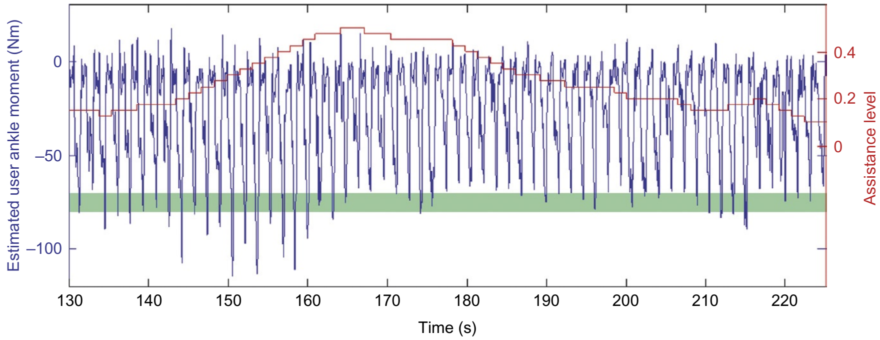

FIG. 3

For robot-aided human walking, estimated ankle moment (*blue* line: positive, dorsiflexion; negative, plantarflexion). In *green*, the target plantarflexion moment range is shown. The adaptable robot guidance (increased when the user exerts an excessive ankle plantarflexion moment and decreased when the user relaxes) is shown in *red*.

is one of the solutions adopted in the BioMot project (Smart Wearable Robots with Bioinspired Sensory-Motor Skills) to estimate user's contribution to motion generation during robot-aided walking through the use of EMG-informed models. In this context, a subject-specific musculoskeletal model continuously estimates the state of each muscle and estimates the forces of the muscles and how they overall contribute to motion generation when walking with the wearable exoskeleton. Preliminary results with runtime NMS model show agreement in estimated joint moments and furthermore demonstrate the feasibility of adapting robot guidance as a function of actual user contribution to the movement (Fig. 3).

CONCLUSION

This chapter has provided an overview of the state-of-the-art wearable rehabilitation exoskeleton technology and research. Significant progress has been done, and relevant step changes are foreseen in the horizon to create clinically efficient gait rehabilitation exoskeletons. However, innovations are still pending until these robotic tools embed computational tools for the recognition of patient's motor skills, detection of user intention and compliance, and unobtrusive means to provide positive feedback. Further, wearable robotic exoskeletons ought to handle the potential mismatch between cause and consequence that would lead to usability or even safety issues. A trade-off between stimulation of patient involvement and cognitive burden should be investigated to allow for efficient and comfortable interventions.

Clinical evaluation of the effects of wearable robots must be focused to demonstrate the functional, clinical, and economic benefits of these technologies, considering patient's and clinician's end user's perception through clinically validated functional scales and protocols.

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CHAPTER

Performance measures in robot assisted assessment of sensorimotor functions

8

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INTRODUCTION

In robot-assisted therapy, standardized clinical scales evaluating specific aspects of the patient's motor behavior are generally used to measure the motor function and the effect of therapeutic interventions. At present, the array of outcome measures used to assess the effectiveness of the robotic intervention is quite scattered, as reviews in the literature have pointed out [1,2]. For this reason, two recent papers based on consensus methods, such as the Delphi survey technique, sought to define a shared assessment protocol for use in clinical practice and research to evaluate the real improvement related to robot-assisted rehabilitation of the upper and lower limbs [3,4]. Both papers proposed an appropriate combination of outcome measures covering all domains of the International Classification of Functioning Disability and Health (ICF) framework and based on patient characteristics.

Although existing clinical measures are widely accepted, standardized, and validated, they are subjective and nonlinear and have a low resolution due to the use of ordinal scales. In addition, the lengthy time required to perform them is a disincentive to their regular use to track and understand motor recovery. On the contrary, therapy robots have built-in technology and sensors that automatically measure movement kinematics and kinetics, providing the opportunity for an accurate assessment of motor function that can be used to diagnose the patient's status, measure therapy progress, and evaluate patient performance in real time. The robot-measured parameters are generally used in healthy subjects to assess the outcome of motor learning experiments, but in patients, they can be used to monitor improvements in motor performance during robot-assisted rehabilitation. These objective measures can be computed automatically during therapy, and, in contrast to ordinal scales, they provide continuous data that can be treated with parametric statistics.

This chapter will analyze the parameters—which encompass kinematic, kinetic, timing, and neuromechanical metrics—most frequently used to describe motor

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behavior during robot-assisted rehabilitation of the upper limb, in particular to monitor motor recovery components, identify the performance acquisition model, and precisely plan and, if necessary, modify the rehabilitation strategy.

CLASSIFICATION OF ROBOT-MEASURED PARAMETERS

Two different approaches can be used to extract information about body functions from sensors. The first uses raw sensor data to directly extract the relevant information; the second uses a feature extraction approach to obtain characteristic properties of the subject's motor behavior. The information conveyed by a specific robot-measured parameter depends on three main factors: (a) the robot device (e.g., a two-degree-of-freedom (DoF) device will support only planar tasks), (b) the motor behavior for which it is developed, and (c) the method used for its computation. Thus, when we define robotic measures, it is fundamental to describe the motor behavior associated to it and the type of device used to implement it. There are three categories of motor behavior that are relevant to the field of neurorehabilitation [5], namely:

- Point-to-point reaching—this is a discrete movement task performed with the upper limb. It is identified by specific start and end positions in the 2D/3D workspace, whereas the trajectory traveled by the subject is generally fully free or bounded to a desired path region by means of haptic virtual walls. This task may be part of a more complex sequence of reaching movements and may involve single- or multijoint coordinated movements.
- Tracking—this is a task involving tracking of a specific trajectory of the workspace. It is generally continuous in space but not in time. So the subject, even if requested to execute a continuous movement, can start and stop several times during task execution when no robot assistance is provided to complete the task.
- Manipulation—this task typically includes manipulation of specific objects with the hand and fingers. Generally, it is used to test precision, dexterity, or power.

For the computation of parameters describing the subject's movement ability and motor performance, no assistance should be provided by the robot device during the task execution. Alternatively, the parameters can be computed only during that part of the task executed without robot assistance. A list of parameters commonly measured to assess motor recovery during the course of robot therapy of the upper limb is reported below. The parameters are grouped according to the different domains explored.

MEASURES DESCRIBING MOTOR FUNCTION

Active workspace: This represents the spatial extent of the voluntary movements made during task execution (i.e., the voluntary reachable workspace). This parameter depends on the type of robot used; for example, with a 2-DoF device, only a planar workspace can be explored. Conversely, with a 3 (or more)-DoF device, a cubic or more complexly shaped workspace can be measured. The active workspace is measured in different orthogonal planes or by exploring a planar workspace with the arm extended at different heights [6,7]. This parameter is a typical example of the feature extraction approach, in that it is obtained by measuring the active explored area or volume computed starting from the raw position sensor data. It is a measure relevant to acute and subacute patients who initially have a very limited active range of motion (ROM) and also to chronic patients with persistent impairments.

Movement velocity: It measures the velocity of the arm during task execution. The mean and the peak value of the end-effector speed are two popular measures of movement velocity. It is sometimes considered as an indirect measure of movement smoothness (see below).

Movement accuracy: This is assessed by measuring the mean absolute value of the distance (MD) of each point of the actual path traveled by the subject from the theoretical path. It is referred to sometimes as movement deviation (Fig. 1). When this parameter approximates zero, movement accuracy will be very high. It is actually a measure of the error of accuracy; hence, a decrease in this index during training indicates an improvement of accuracy in the motor task execution [8,9].

Movement smoothness: It measures how the arm movement is gradually changing. This measure is very commonly used in the rehabilitation robotic literature and can be estimated by many different methods/parameters [10]. It can be computed from the integral of the squared magnitude of jerk that is the third derivative of position. Actually, stroke survivors tend to exhibit large oscillations in the velocity profile, which can be interpreted as functional "submovements." The number of these submovements can be used as a measure of smoothness. The simplest way to measure these oscillations is to count the number of peaks (nPK) in the tangential speed profile of a reaching movement, expressed as a negative value so that increases in the peak metrics equal increases in smoothness; another method computes the ratio between the peak tangential speed and the mean speed of the end effector [9,11]. Smoothness can also be measured by quantifying the complexity (spectral arc length) of the Fourier magnitude spectrum of a movement speed profile. It assesses the small oscillations in the trajectory speed profile that correspond to higher frequencies than the underlying movement [10]. This spectral metric is a valid, robust, and sensitive measure of movement smoothness.

Normalized path length (nPL): This is obtained by computing the path length of the trajectory traveled by the subject to reach the target and is normalized to the theoretical path [12]. It is a measure of the error of movement efficiency; therefore, decreasing values during training reflect an improvement of efficiency in the motor task execution. It is also an indirect measure of the patient's effort during task execution.

Movement efficacy: This metric measures how effective the movement is with respect to the task requested. It can be computed considering either the patient's behavior or the robot's behavior. In the first case, it quantifies the subject's ability to execute the motor task without robot assistance. The computed parameter reflects the proportion of theoretical path (i.e., the straight line connecting the starting point to the target) traveled by the end effector in response to the patient's exerted force and it is referred to sometimes as "active movement index". It increases only with the patient's voluntary activity. Alternatively, one can measure the "target error," that is, the endpoint error of a subject's movement relative to the target location. Both these kinematic measures

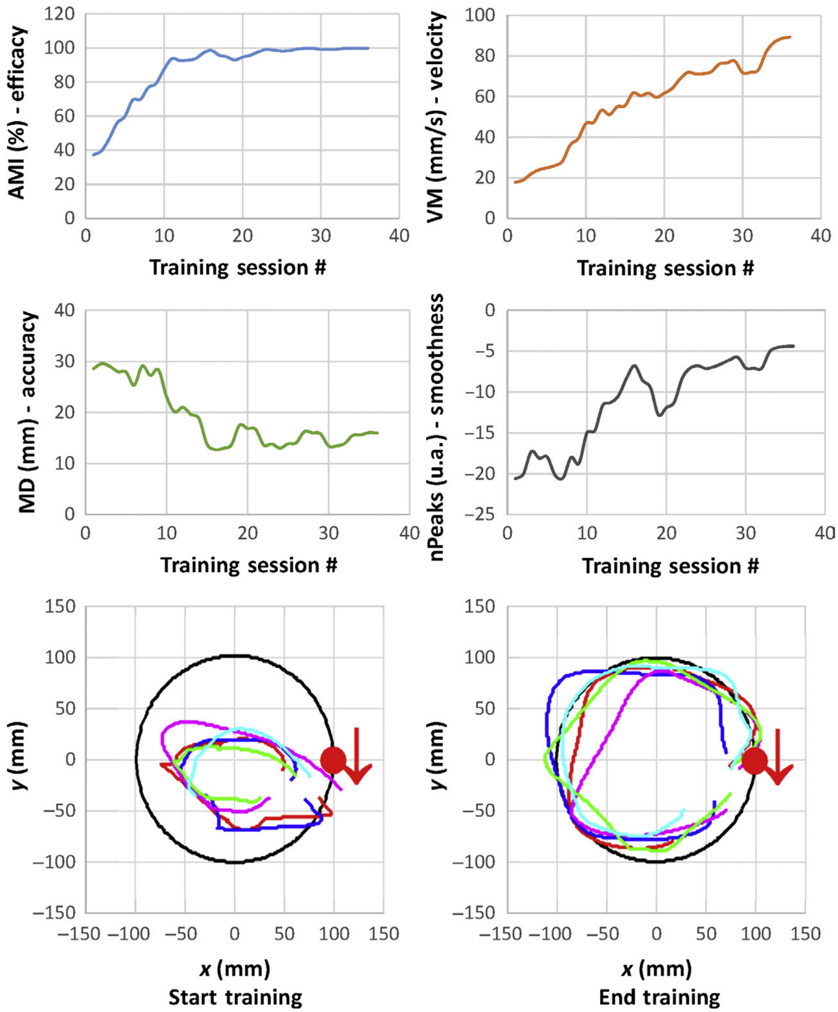

FIG. 1

Time course of recovery of robot-measured parameters. Top and mid panels represent, respectively, the time course of some kinematic measures and specifically the active movement index (AMI), the mean velocity (MV), the mean distance (MD), and the number of peaks of the tangential speed profile that is a measure of smoothness. Bottom panels represent some traces acquired to compute movement coordination indexes at the start and end of training. Note the change from an elliptical to circular shape of the trajectories after training.

are primarily suited for point-to-point reaching tasks and are usually expressed as a percentage. The counterpart of this parameter is the "amount of assistance" provided, that is, the robot's contribution in assisting the subject to perform the assigned task. Depending on the nature of the assistance provided by the robot (end-effector displacement or assistive force), this measure can be classified as kinematic or kinetic.

Force direction error: It describes the ability of a subject to exert force in a desired direction. In order to obtain an effective reaching movement, the patient needs to exert a force on the end effector of adequate magnitude to exceed the robot "stiffness" and orient it in the proper direction. The measure of the discrepancy between the actual and the desired directions can provide quantitative information about the reacquisition of a proper force control in the execution of the assigned motor task. A second mode to compute this parameter compares the pattern of distribution of the patient's exerted force in the workspace plane with that obtained by healthy subjects for the same task. It can be considered as a parameter measuring the amount of error in the orientation of the exerted force during the task execution; therefore, decreasing values during training reflect an improvement in force control [13].

Movement time: It measures the time required to perform a given task successfully. This is a general movement metric that can be associated with different tasks and devices and is strictly related to the mean velocity. In the case of point-to-point reaching movements, it is possible to distinguish between (a) the time required to actually reach the target and (b) the time spent in stabilizing the position once the target is reached. Other time measurements include the reaction time to start and the reaction time to reach the target, but in this case, their reliability depends on the specific instructions given to the subject [6].

Movement coordination indexes: These parameters measure the spatial and/or temporal coordination between different segments of the upper limb during multijoint tasks. A typical example of coordination measure is the interjoint coordination between the shoulder and elbow joint angles and torques obtained during circle-drawing movements. The meaning of this measure and its computation method depends on the specific behavior under consideration. Circle drawing, for example, is often used to assess the "generalization" of recovery, that is, patients get better at drawing circles over the course of a robot therapy program even if they receive no specific training for this task (e.g., because they practiced only point-to-point reaching tasks). In this case, the computed metric includes (1) the axes ratio, that is, the ratio between the minor and major axes of the ellipse best fitting the end-effector path in Cartesian coordinates; (2) the joint angle correlation metric that measures the independence of the subject's shoulder and elbow joint movements—it is obtained by modeling the human arm as a two-link mechanism, the shoulder and the elbow, and the correlation of their joint angles is estimated from the measured end-effector path by inverse kinematic equations; and (3) the "orientation metric," that is, the best-fitting line to the end-effector paths collected during the circle-drawing task—the slope of this line reveals the direction along which most data are distributed [14].

Arm impedance: It is a measure of the viscoelastic properties (intrinsic and reflexes) of the musculoskeletal system in response to stereotyped stimuli, which is related to spasticity. This measure is a characterization of the upper-limb properties at rest and not a motor behavior.

Fig. 1 reports some examples of kinematic parameters measured during the course of training.

MEASURES DESCRIBING SENSORY FUNCTION

Impairment of body sensation following a stroke or incomplete spinal cord injuries is common, with a significant proportion of patients presenting deficits. Sensory function and motor function are important for dexterity. Proprioceptive and haptic feedback and vision contribute to the learning and control of movements necessary to execute a given task. Proprioception on its own is difficult to measure; it is commonly evaluated by clinicians through tests that have poor interrater reliability and sensitivity and give only a qualitative and subjective measure. The recent literature has demonstrated the possibility of using robotic technology for the quantification of sensory impairments. Most of these methods rely on joint position-matching task procedures in a plane or, alternatively, the ipsilateral and contralateral matching of a joint angle in the absence of vision. They provide quantitative measures of the sense of position, kinesthesia (i.e., the sense of limb motion) and proprioceptive acuity (i.e., the sensitivity in discriminating positions and force directions) [15–18].

In order to evaluate the parameters measuring sense of position, the vision of the upper limb is occluded, and the robot moves the paretic arm (passive limb) to different spatial locations of the horizontal workspace in a random order. Subjects are requested to mirror match the geometry of the paretic limb with their nonparetic limb (active limb). The data from the matching arm are mirrored to the midsagittal axis and superimposed on the robotic matching data (Fig. 2), and the following parameters are computed:

Mean error: It is the mean value of the absolute differences between, respectively, the actual and the desired (passive hand) positions for both coordinates. This parameter, in reference to normative data, should indicate the presence of proprioceptive deficits.

Variability: It is obtained by computing the standard deviation of the active-hand positions for each target location and then calculating the mean of the standard deviations for all target locations in the x coordinate (var x), the y coordinate (var y), and the linear variability for both coordinates combined (var xy).

Spatial contraction/expansion: It is the range/area of the workspace matched by the active hand relative to that of the passive one. Values below 1 indicate a spatial contraction, that is, the range of space explored by the active hand is smaller than that obtained by the passive hand. Conversely, spatial expansion is indicated by values above 1. The procedure is usually performed to compute the parameters along both coordinates of the workspace.

Systematic shifts: The systematic shifts for each target are computed for both coordinates, and the mean value is computed. This parameter allows assessment of the presence of a perceived shift in the position estimation of the impaired limb.

Similarly to Rinderknecht et al., we have recently presented a simple test involving wrist flexion/extension of the impaired arm in which the subject is required to estimate the passive hand position [19]. A half-circle graded scale is displayed on a PC screen representing the possible range of displacement during flexion/extension. Wrist sense of position is evaluated by measuring the discrepancy between the actual position of the displaced (flexed/extended) hand and the estimated position, indicated

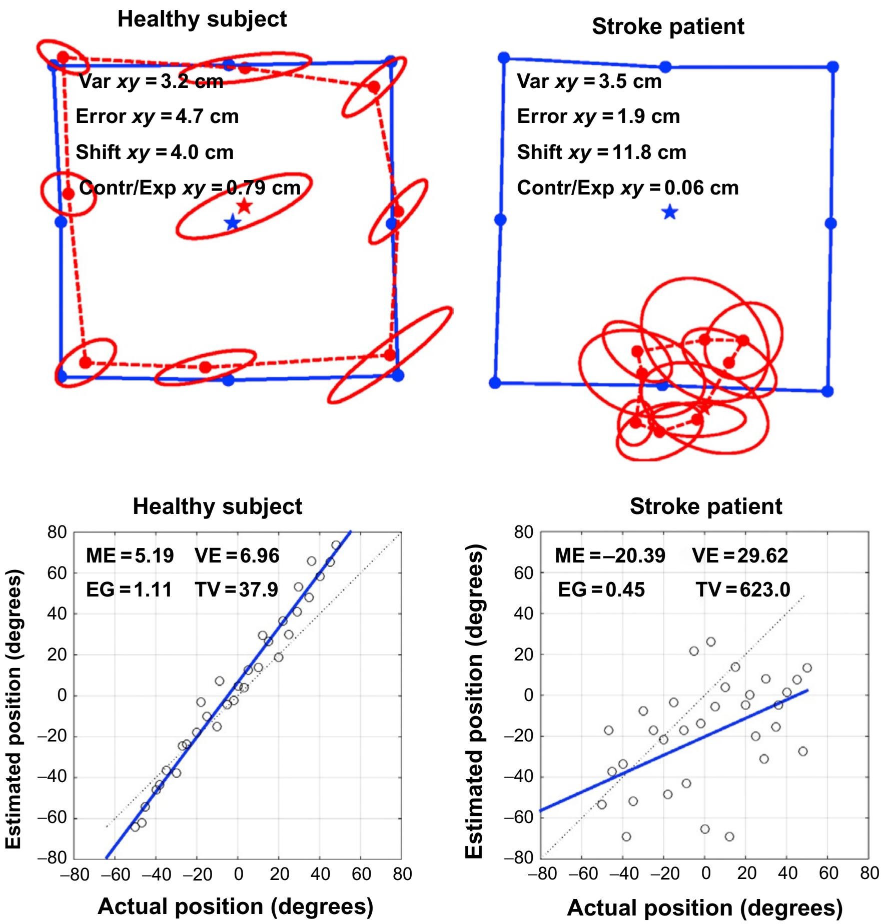

FIG. 2

Example of some parameters describing sensory function. Top panels represent the patient's sense of position pattern and some quantitative parameters evaluated in a healthy subject and in a patient after stroke. Bottom panels represent plot and regression line of the actual versus estimated positions of the wrist joint flexion/extension in a healthy subject and in a patient after stroke with proprioceptive deficits. All measures of the sense of position were carried out without assistance of vision.

by positioning a cursor on the scale through rotation of a potentiometer with the contralateral (healthy) hand. The parameters considered are as follows:

Mean error (ME)—the average value of the differences between actual and estimated position (position error)

Variability (VE)—the standard deviation of the position error

Error gain (EG)—the slope of the regression line between actual (independent variable) and estimated positions (dependent variable)

Total variability (TV)—the mean square of the regression residuals

Fig. 2 reports the performance pattern obtained for the evaluation of the proximal and distal sense of position in healthy subjects and stroke patients.

Other studies have used robotics to document proprioceptive deficits in the upper limb of patients after stroke using an alternative approach that entails the use of two alternative forced choice paradigms to examine the perceptual detection threshold (acuity) for hand perturbations [20].

The subject's arm is moved to a reference position by the robotic manipulandum. Next, the hand is moved away from the reference position through a distractor movement and then brought to a judgment position where it is held until the subject chooses on which side (left or right and forward or backward) the reference position should be. Psychometric function, relating perceived hand position to actual hand position, is estimated by fitting a single subject's set of responses at each judgment position to a binomial model using a cumulative normal distribution function. Proprioceptive acuity is calculated by measuring the range of psychometric function in which the subject is unsure of his hand position (uncertainty range), that is, the range of judgment position between the 25% and 75% probabilities of responding right or forward (as opposed to left or backward). The perceived hand location (bias) corresponds to the judgment position at the 50% probability. A similar method has been applied for the estimation of kinesthetic sense in the force direction discrimination task [17]. Details about the assessment and training of sensory function can be found in Chapter 21.

MEASURES DESCRIBING COGNITIVE FUNCTION

Robot technology in combination with a virtual reality system can be used also to provide an automatic approach for the assessment of mental processes such as attention, perception, memory, decision-making, and judgment that relate to cognitive function [21]. In this case, the upper limb constitutes the way to measure performance of cognitive processes. As an example, robot technology may be very useful to assess a subject's ability to perform rapid decisional processes that cannot usually be examined by the pen-and-paper tests traditionally used in neuropsychological assessments. The quantitative parameters obtained are strictly dependent on the specific behavioral task implemented and generally consist of scores rating the performance obtained during task execution. The number of objects hit, the number of obstacles avoided, the reaction time, etc. are typical examples of performance measures. The tasks are usually implemented in the form of a video game so as to maximize the subject's participation and motivation.

MONITORING COMPONENTS OF MOTOR RECOVERY

Robotic neurorehabilitation, thanks to its capacity to deliver high-dosage and high-intensity training protocols, has the potential for a greater impact on impairment, as demonstrated by the recent literature [22,23]. The observed reduction of motor impairments is generally accompanied by an improvement in the kinematics and kinetics of upper-limb movements. The general pattern of changes can be summarized as follows. With progression of therapy, the movement tends to become faster, more stable (i.e., movements are more accurate, and trajectories are closer to a straight line than at the beginning of training), and smoother (i.e., movements exhibit less oscillations), while the force control ability improves (both in controlling force magnitude and direction), the amount of assistance provided by the robot decreases, and, thanks to motor synergy relaxation, the improvement becomes generalized to movements other than those specifically trained. This continuous improvement of motor performance can be clearly evidenced by using a graphic representation showing the time course of recovery of the robot-measured parameters during the training sessions. In contrast to assessments employing time-consuming clinical scales, this representation monitors the various components of motor recovery without additional effort in that the assessments are automatically carried out by the robotic device. Fig. 1 presents an example of the evolution of kinematic parameters in a patient after stroke who underwent robot therapy. The performance parameters were always measured during the voluntary activity phase (unassisted phase) of each reaching movement and averaged so as to obtain for each parameter one mean value for each training session.

MODELING MOTOR RECOVERY

The time course of recovery of robot-measured parameters can be evaluated through a mathematical model, that is, an equation or a system of equations representing the changes of selected parameters with time. As this topic is dealt with in another chapter, here, only the general principles will be outlined. The recovery after stroke usually displays a nonlinear logarithmic/exponential pattern in which the largest improvements are observed early after stroke onset and then gradually taper off. The concept is that temporal evolution follows a mathematical law that is obtained by a least-square fitting of the various parameters. It has been shown that the models have a moderate to high correlation (0.4–0.8) with the experimental data. What is really important with this computational method is that it is possible to compute a phenomenological model to describe not only single subject behavior but also that of a group.

In a recent study involving a group of subacute and chronic (>6 months from the acute event) stroke patients who underwent robot-assisted neurorehabilitation of the upper limb, we used an exponential model to describe the changes observed in the Fugl-Meyer scale and a set of kinematic variables, demonstrating the effectiveness of the rehabilitation intervention [24]. The model is represented by the following formula:

$$y = B_0 - B_1 e^{\frac{x}{\tau}}$$

where y is the modeled parameter, x is the therapy session number, τ is the time constant related to the exponential increase/decay, and B_0 and B_1 are the model's parameters. Thanks to this model, we demonstrated that the motor improvement of subacute patients was characterized by a time constant that was greater than that found in the chronic patients (Fig. 3).

In actual fact, both groups had a similar rate of improvement at the start of training, but the former required an extra improvement time because the plateau to be reached was higher than that for chronic patients. This result led us to speculate that patients in the subacute phase require longer training programs to maximize outcome and that persistent impairments in patients with chronic stroke may not reflect an exhausted capacity for improvement. Massie et al. recently presented an evolved version of this model that used a two-term exponential function to describe performance recovery [25]. This model revealed two components of learning: a fast component taking into account the changes observed within each training session and a slow one describing the evolution over the whole course of training.

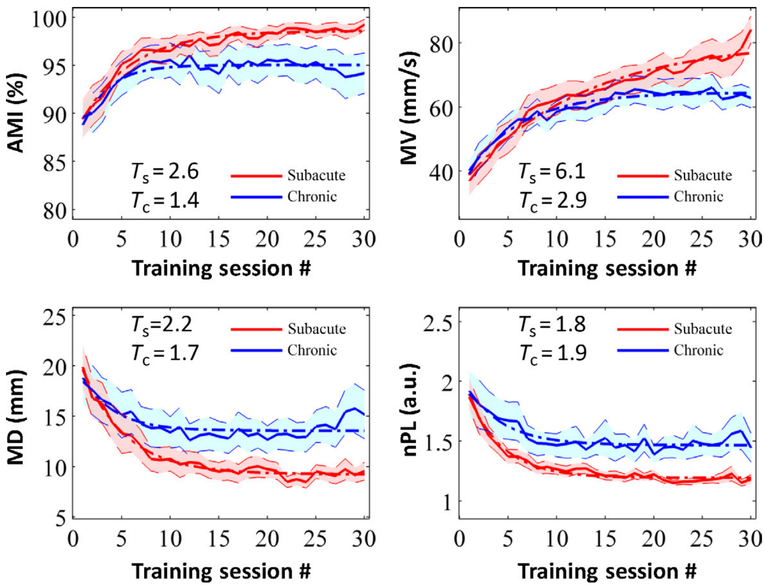

FIG. 3

Models of motor recovery in subacute and chronic stroke. Time course of recovery of the active movement index (AMI), mean velocity (MV), mean distance (MD), and normalized path length (nPL) parameters during 29 exercise sessions in 18 subacute *(red)* and 17 chronic *(blue)* patients. *Solid lines* connect the average value obtained by each group during each training session. The *colored area* represents the standard error. *Dot-dashed lines* represent the exponential increasing/decaying model fitted on the data. T_s and T_c are the time constants of the exponential model of each kinematic parameter, respectively, for subacute and chronic patients.

ADAPTING THERAPY BASED ON MOTOR PERFORMANCE

In robot-assisted neurorehabilitation, matching the task difficulty level to the patient's needs and abilities, both initially and as relearning progresses, can enhance the effectiveness of training and improve patients' motivation and outcome. The patient's performance, evaluated during the course of training through the computation of robot-measured parameters, can be used to guide decisions regarding treatment planning based on rates of motor relearning achieved with the robotic intervention. Specifically, tracking aspects of motor improvement while treatment is being delivered may enable the therapist to dynamically customize practice to boost recovery. In addition, performance-based progressive training schemes have been proposed as a way to gradually reduce the amount of robotic assistance during training or change the task practiced by the patient based on measured abilities. The patient's performance is generally evaluated on a task-level basis at the end of each training session, that is, after each task repetition, but tasks consist of several elementary components, each of which might have a different influence on treatment outcome. Our research group explored the possibility of automatically changing the features of the reaching movements, even during task execution, and also of adapting the difficulty level of the task to the patient's abilities [26–28]. To this end, two different algorithms were developed. First, the time course of motor gains was assessed for each subtask of the practiced exercise. We chose three continuous variables (mean velocity, mean distance, and smoothness) because they showed a significant correlation with a subset of clinical scales and were only moderately intercorrelated, and one discrete variable representing the percentage of successful movements obtained over a whole training session. A statistical algorithm was then tested on simulated data to validate its ability to continuously track improvements and subsequently applied to the recorded data to determine its performance compared with that of a therapist. This algorithm allows differential training on a subtask level, so continuously challenging the neuromuscular system and boosting recovery. A refined version of this algorithm—which we called the progressive task regulation algorithm—was implemented in a robot for upper-limb rehabilitation. In this case, we hypothesized that the performance improvement in stroke patients would be the result of different concurrent optimization processes, including adaptation of both kinematic and effort parameters, starting at the same time but having different time constants. In practice, we used this hypothesis to choose the subset of performance parameters to be included in the algorithm and to design the set of rules to identify the plateau of adaptation in the parameters (steady performance) to optimize training. The algorithm implemented adapts the difficulty level of the motor task to the patient's abilities by selecting different types of assistance (time-triggered, activity-triggered, and negative assistance) and implementing varied therapy practice to promote generalization processes by selecting different reaching sequences with increasing difficulty level. The use of different types of assistance means that our rehabilitation robots can be applied to a wider spectrum of patients. In fact, the adoption of a time-triggered assistance where the assistive force is delivered after a preset time is suitable for more severely impaired patients who exhibit only the ability to initiate movement. The activity-triggered assistance is suitable to adapt the assistive force to patients' needs, while negative assistance, on the other hand, should allow to improve the quality of movement in mildly impaired patients. Both algorithms showed good agreement with the therapist's decisions, so indicating that they could be successfully applied for the implementation of training protocols and allowing individualized and gradual treatment of upper-limb disabilities in patients after stroke.

RELATIONSHIP BETWEEN CLINICAL AND ROBOTIC MEASURES

Robotic measures collected longitudinally in patients after stroke could have a significant relationship to standard clinical outcome measures and, therefore, might represent superior biomarkers. In particular, understanding how the robot-measured parameters relate to their clinical counterparts might be useful for clinicians to associate specific sensorimotor conditions of stroke subjects to the measurements obtained by the robots. The easiest relationship explored is the correlation coefficient. The primary rationale for investigating the correlation between robot-derived measures and clinical scales is to examine the validity of technological metrics as a measure of motor impairment and function. The most explored association in the literature is the correlation between the Fugl-Meyer assessment (FMA) and robot-derived measures. Specifically, it has been found that a weak-to-moderate correlation exists between FMA and robot parameters. Recent studies have further investigated the possibility of developing a model that, through multiple regression analysis, could be used to estimate standard clinical scales from the robot-derived ones. Full models, using up to 20 different parameters, showed a good performance in predicting the FMA ($R=0.802$), motor power score (MP, $R=0.797$), and motor status score (MSS, $R=0.788$) for the training data [9]. The performance for the validation data was weaker for the FMA ($R=0.427$) and MP ($R=0.449$) but not for MSS ($R=0.696$). The use of more complex nonlinear models of the clinical scales, with three-layer artificial neural networks using logistic functions for the hidden and output layers, allowed robotic measures to predict well the clinical measures (FMA $R=0.73$ and MP $R=0.75$) and demonstrated greater sensitivity in measuring the recovery of patients from day 7 to 90 [29]. Recently, Mostafavi et al., using a computational search algorithm known as fast orthogonal search, identified the robotic and clinical biomarkers that best estimated functional independence measures (FIM) [21]. Clinical and robot-based biomarkers were statistically similar at predicting FIM scores at 2 weeks ($R=0.817$ vs 0.774, respectively) and 3 months ($R=0.643$ vs 0.685, respectively).

CONCLUSION

Robotic assessments make it possible to measure and evaluate motor behavior in an objective fashion, under both static and dynamic conditions. These assessments are a good supplement to standard clinical assessments as they provide objective, sensitive, and detailed information about the patient's residual ability. Their semiautomated nature and ease of administration allow for a more frequent assessment of motor performance than is normally possible using clinical assessment tools. Moving from a weekly to a single reaching-time base, robotic measures make it possible to adapt the therapy to the subject's needs so as to optimize training and outcome. The development of robotic assessments has also resulted in novel and interesting data analysis techniques and motor performance measures useful for gaining a better understanding of stroke-affected motor behavior. Although robot-derived measures are objective, sensitive, reliable, and automatic, they cannot be considered as a substitute for standard clinical assessments. Current robot devices are still not so sophisticated at assessing complex movements to the point that they can allow natural movements with minimal interaction, and likely, they catch only some aspects of the complex behavior. However, robots clearly pick up changes that clinical measures for the most part fail to detect. In other words, robots could constitute a new approach to clinical assessment and rehabilitation, making it possible to implement clinical studies based on sensitive measures that can detect meaningful changes due to the rehabilitation intervention. This should improve our understanding of how the brain generates motor, sensory, and cognitive functions and enable the development of more cost-effective training protocols.

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CHAPTER

Computational models of the recovery process in robot-assisted training

9

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INTRODUCTION

A cerebrovascular accident (stroke) elicits in the nervous system a complex series of reorganization processes at molecular, cellular, neural population, behavioral (sensorimotor and cognitive) and social interaction levels, with temporal scales that range from hours, to months, to years [1]; see also Chapter 1. Animal models and human studies suggest that functional recovery after a stroke is mediated by use-dependent reorganization of the preserved neural circuitry. A key to neuromotor recovery and the basis of many neurorehabilitation interventions—including robot-assisted exercise—is the movement associated with a task and with volitional effort [2]. Several studies have modeled the evolution of sensorimotor performance through exercise (motor learning); much fewer studies have specifically addressed the neuromotor recovery process [3]. Models of motor learning focus on a set of variables that summarize task performance within a single trial—for instance, motor error, smoothness, or average speed. The goal of modeling is to describe the trial-by-trial evolution of performance and its underlying mechanisms. Variants of the power law of practice have often been used to describe the trial-by-trial evolution of motor performance. However, these descriptions do not address the underlying mechanisms. Also, they do not consider the effect of exogenous variables—like task difficulty or physical guidance—which likely affect motor performance and/or learning speed. As a consequence, they can only be used to describe spontaneous learning (or recovery).

Here, we use a more general formulation, based on state-space models [4]. These models have been first proposed to describe the temporal evolution and the mechanisms underlying the sensorimotor adaptation and motor learning. Only recently, these same techniques have been used to describe neuromotor recovery.

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COMPUTATIONAL MODELS OF MOTOR LEARNING

MODELS OF SENSORIMOTOR ADAPTATION

The use of the state-space dynamic system models to describe the trial-by-trial dynamics of sensorimotor adaptation [5–8] is now well established. A perturbation during targeted movements induces an adaptation process, consisting of the development of an "internal model" of the perturbation so that future motor commands take this prediction into account. This trial-by-trial process can be described in terms of a dynamic model. Model formulation requires specific assumptions on the signal or signals that drive adaptation. To identify the actual adaptation mechanism, alternative models of the same process may be compared [8] to select which model best describes the data.

Most trial-by-trial models of adaptation assume that hand position on the tth trial, $h(t)$, is determined by the movement (motor command) $u(t)$, plus a force perturbation $f(t)$:

$$h(t) = u(t) + D \cdot f(t) \tag{1}$$

In many studies, the perturbation $f(t)$ is a velocity-dependent force field [9]. Parameter D can be interpreted as the arm compliance (the inverse of arm stiffness, $K = 1/D$) [5]. Note that we are only interested in modeling the component of the motor command and of hand position that relates to perturbations, whereas the components that are supposed to be responsible for reaching the target are assumed to be unaffected by the perturbation. In velocity-dependent force fields, the perturbation is always orthogonal to the movement, so that $h(t)$ is a measure of lateral deviation of the movement with respect to the straight line from starting point to target. The "motor command," $u(t)$, can be interpreted as the lateral deviation observed when the perturbation is removed ($f = 0$). We also assume that the perceived hand position, $y(t)$, is modeled as the actual hand position, plus some sensory (e.g., visual) noise, $n_v(t)$:

$$y(t) = h(t) + n_v(t) = D \cdot f(t) + u(t) + n_v(t) \tag{2}$$

In case the perturbation is visual, that is, it affects the way the hand is displayed (e.g., a rotation), the displayed ("cursor") position of the hand on the tth trial, $c(t)$, is obtained as the hand position $h(t)$ plus the visual perturbation $r(t)$:

$$c(t) = h(t) + r(t) \tag{3}$$

Again, we assume that the visually perceived position, $y_v(t)$, is equal to the actual visual (cursor) position plus some sensory (e.g., "visual") noise $n_v(t)$:

$$y_v(t) = c(t) + n_v(t) = h(t) + r(t) + n_v(t) = r(t) + u(t) + n_v(t) \tag{4}$$

where the motor command $u(t)$ denotes the hand position without perturbation.

Both models may incorporate proprioception-based information on hand position, $y_p(t)$, expressed as the true hand position $h(t)$, plus sensory (proprioceptive) noise, $n_p(t)$:

$$y_p(t) = h(t) + n_p(t) \tag{5}$$

Proprioception is affected by force perturbations but not visual perturbations. In this case, the overall sensory information available to the nervous system would include both vision and proprioception, so that $y(t)=[y_v(t)y_p(t)]^T$. Proprioceptive perturbations could be also provided, for instance, by muscle vibration. In this case, the extension of the model would be straightforward. Both dynamic and kinematic perturbations might be applied at the same time [10]. In this case, the overall disturbance would be denoted as $x=[fr]^T$ and the overall execution noise term as $n_y=[n_v\, n_p]^T$ with $n_y \sim N(0,R)$. We would end up with

$$y(t) = H \cdot x(t) + G \cdot u(t) + n_y(t) \tag{6}$$

where H and G combine Eqs. 2, 4.

A "controller" is assumed to determine the motor command $u(t)$ on the basis of the dynamic and/or kinematic perturbations, that is, $x(t)$. The nervous system does not have a direct access to perturbations, but may estimate their effects adaptively based on the available evidence, that is, the sensory information $y(t)$.

Estimation of the disturbance is a dynamic process, which can be described by a state-space equation

$$\hat{x}(t+1) = A \cdot \hat{x}(t) + B \cdot e(t) + n_x(t) \tag{7}$$

where $\hat{x}(t)$ denotes the estimated disturbance. Eq. (7) indicates that the predicted disturbance at the next trial is a combination of the current estimate and an "adaptation" term proportional to a "driving" signal, $e(t)$. A noise term, $n_x(t) \sim N(0,Q)$, or process noise models the extent to which perturbation can be predicted. Coefficients A and B denote, respectively, the "retention rate," the extent to which a given estimate is retained at the next trial (for stability, A should be $0<A<1$), and the "learning rate," the extent to which the estimated perturbation is sensitive to the driving signal. Different hypotheses have been formulated on the nature of $e(t)$. Empirical studies [11] have suggested that adaptation is driven by the mismatch between actual and predicted perturbation, that is, $e(t)=x(t)-\hat{x}(t)$. A Bayesian approach, optimally combining all the available evidence, can be used to identify the ideal adaptation mechanism. In this way, a model of adaptation can be derived from general principles, with no need to make specific hypotheses on the driving signals, and then compared with empirical evidence. Haith et al. [12] first proposed a Bayesian approach to model the adaptation to a velocity-dependent force field. In a Bayesian framework, an optimal estimate of the perturbations, $\hat{x}(t)$, can be derived by combining prior belief and the available measures, that is, $y(t)$ and $u(t)$. We denote prior belief as $\hat{x}^-(t)$ and model it as

$$\hat{x}^-(t+1) = A \cdot \hat{x}^-(t) + n_x(t) \tag{8}$$

where $0<A<1$ is a decay parameter. Basically, we are assuming that the best we can do in absence of new information is to predict the future perturbation in terms of the current estimate. Sensory information, that is, $y(t)$, is a potential source of information on the perturbation. To make sense of it, we need to quantify the sensory consequence $\hat{y}^-(t)$, of the predicted state, $\hat{x}^-(t)$: $\hat{y}^-(t) = H \cdot \hat{x}^-(t) + G \cdot u(t)$

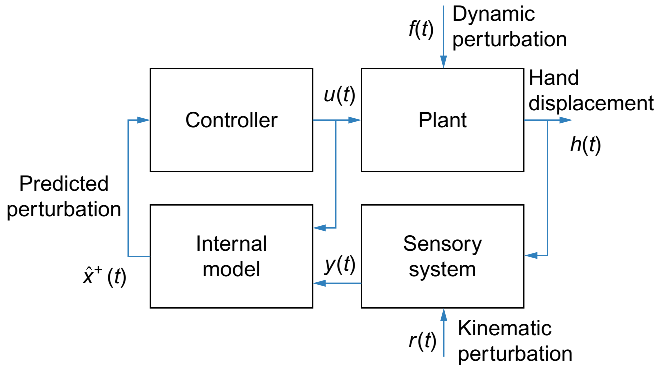

FIG. 1

Computational model of sensorimotor adaptation.

An unbiased minimum-variance posterior estimate of the state, $\hat{x}^+(t)$, would take the form of a combination of prior belief and error correction based on sensory information:

$$\hat{x}^+(t+1) = \hat{x}^-(t+1) + K(t)\cdot\left[y(t) - \hat{y}^-(t)\right] = A\cdot\hat{x}^+(t) + K(t)\cdot\left[y(t) - \hat{y}^-(t)\right] \qquad (9)$$

The gain $K(t)$ is computed iteratively through the Kalman algorithm. The overall computational model is depicted in Fig. 1.

In the case of force or visual perturbation alone, motor commands are simply calculated as the opposite of the predicted perturbation, that is, $u(t) = -\hat{x}(t)$. Other control schemes may be plausible, for instance, involving a combination of prediction (of the perturbation) and resistance to it (achieved, for instance, by increasing arm stiffness) or a trade-off between error and effort [13].

In all cases, the model predicts that asymptotic cancelation of the perturbation is not complete because the forgetting term, A, counteracts adaptation. Large values of A lead to slower forgetting and more adaptation; lower values of A result in fast forgetting and less adaptation. If both visual and proprioceptive modalities are taken into account, the Bayesian model of adaptation also predicts that force-field adaptation would introduce not only a change in the motor commands that incorporate a prediction of the perturbation but also a sensory bias in proprioception [12]. This prediction has been confirmed experimentally [14], thus emphasizing the interplay between motor and sensory (proprioceptive) adaptation. The Kalman framework confirms the empirical finding that sensorimotor adaptation is optimally driven by the discrepancy between actual and predicted perturbation, which is equivalent to the discrepancy between actual and predicted sensory output; see Eq. (9).

Multirate adaptation

Empirical findings [15] have suggested that the nervous system may keep multiple internal representations of the perturbations, each with their own time constant. The basic model (Eqs. 3, 9) is easily extended to account for multiple internal representations if we posit more internal models, each with their own dynamics equation. Specifically, Smith et al. [15] suggested that two internal representations, with different time constants ("fast" and "slow," i.e., $B_f > B_s$ and $A_f < A_s$)

$$\begin{aligned}\hat{x}_f(t+1) &= A_f \cdot \hat{x}_f(t) + B_f \cdot y(t)\\ \hat{x}_s(t+1) &= A_s \cdot \hat{x}_s(t) + B_s \cdot y(t)\\ y(t) &= D \cdot f(t) + u(t)\end{aligned} \tag{10}$$

with $u(t) = -\hat{x}_f(t) - \hat{x}_s(t)$, account for the observation that in repeated adaptation-washout cycles, subsequent adaptations tend to be faster and more persistent than those observed in naive subjects—the so-called "savings" property. Adaptation mostly relies on implicit mechanisms, which do not need voluntary control to take place. More recently, explicit [16] and reward-based (see [17] and below) components of adaptation have been identified. Specifically, explicit and implicit components of adaptation have been related [18] to the fast and slow components above.

Spatial generalization

Movements during an adaptation trial may differ in terms of starting position, amplitude, and/or direction. In particular, many studies have been focusing on movements with the same starting position and amplitude, but different directions. An important issue is whether and to what extent adaptation to perturbations in a specific movement generalizes, that is, affects the adaptation to perturbations applied to similar movements. Models of adaptation often assume that movements in each direction $\theta_1, \ldots, \theta_D$ are specified by a different "motor memory" or motor commands. In other words, there is a different $\hat{x}_d$ for each movement direction, $d = 1, \ldots, D$, and making one movement is assumed to affect the motor memories of similar movements (directional generalization). In principle, all model parameters may be direction-dependent. Arm compliance is known to depend on direction [19]. Similarly, learning and retention rate may differ in the different motor memories. Taking $x = [x_1 \ldots x_D]^T$, for a movement in direction θ, for a force-field adaptation experiment, we have the following:

$$\begin{aligned}\hat{x}_d(t+1) &= A(d,\theta) \cdot \hat{x}_d(t) + B(d,\theta) \cdot y(t)\\ y(t) &= D(\theta) \cdot f(t) + u(t)\end{aligned} \tag{11}$$

We tentatively assume that learning rate is maximum for the direction at which the movement is made and gradually decays for positions that are further away. A way to model this is to assume that the learning rate for the dth motor memory is given by $B(d,\theta) = B_d \cdot \varphi_d(\theta)$, where B_d denotes the learning rate of the dth motor memory. The function $\varphi_d(\theta)$ has a unit peak when $\theta = \theta_d$; it is often modeled as a von Mises function—the circular analogue of the Gaussian distribution [20], which implies that training is always beneficial on motor memories, that is, $B(d,\theta)$ is positive for all d. This may not always be the case. In some studies, for example, [5,19,21], no specific shape is assumed for $B(d,\theta)$, and a nonparametric model is used. Similarly, the retention rate $A(d,\theta)$ may depend on movement direction. It has been suggested [22] that for a given motor memory, retention may be minimum for nearby movement directions and maximum for directions that are less relevant (i.e., further away). In other words, motor memories in irrelevant positions do not change and do not decay. In contrast, motor memories in the direction of the actual movements exhibit the maximum change. The predicted perturbation in the direction $\theta(t)$ is calculated as follows:

$$\hat{x}(t,\theta) = \frac{\sum_d \varphi_d(\theta) \cdot \hat{x}_d(t)}{\sum_d \varphi_d(\theta)} \tag{12}$$

This expression is used in Eq. (11) to determine the motor command, that is, $u(t) = -\hat{x}(t,\theta)$.

Sensorimotor adaptation is widely used as experimental model for exercise-driven motor plasticity. Robot-assisted neuromotor recovery cannot be simply reduced to a form of adaptation, but adaptation paradigms are often used in rehabilitation to clarify how neurological diseases affect motor plasticity. Robots are essential tools to study the adaptation to perturbations, and models can be used to draw specific conclusions. For instance, empirical studies using adaptation models have suggested that persons with cerebellar atrophy, but not Huntington's disease, exhibit a near-zero learning rate, B, and are therefore unable to adapt to a force field [19]. Persons with multiple sclerosis and little or no disability have intact adaptation capabilities but defective motor performance, as shown by the large variance of the output noise, R [21].

MODELS OF MOTOR SKILL LEARNING

Sensorimotor adaptation is a specific form of learning, driven by the discrepancy between a perturbation and its internal representation. The goal of motor skill learning is to develop a "motor command" or action that maximizes its long-term benefit or "value" in relation to a specific task. To quantify the compliance of actions to the task, there is no available motor error. Rather, the environment provides a scalar or even binary "reward" signal, and the long-term benefit is expressed in terms of the expected future rewards. Different from sensorimotor adaptation, this creates the need for active exploration of the action space, that is, an explicit trial-and-error search for "good" behaviors.

Learning of actions based on a reward is usually referred as reinforcement learning (RL); see [23] for a comprehensive presentation. RL models have been largely used in modeling cognitive tasks, in which the "action" consists of a decision among a discrete number of options. Much less often, these models have been applied to describe the trial-by-trial dynamics of learning a motor skill. Here, we only summarize the main concepts and the formulations that are most relevant to the development of state-space models of motor skill learning. In an RL scenario, the environment responds to each motor command $u(t)$ with a scalar reward signal, $r = r(u)$. The agent's goal is to gradually develop a policy that maximizes the long-term benefit or action "value," defined as the weighted sum of the rewards obtained in the current and future trials—the expected cost to go:

$$V(t) = E\left\{r(t) + \gamma \cdot r(t+1) + \gamma^2 \cdot r(t+2) + \ldots + \gamma^{T-t} \cdot r(T)\right\} \tag{13}$$

where parameter γ is the discount rate, quantifying the relevance of future rewards ($\gamma = 0$ indicates that only the current reward matters), and T is the total number of trials. If T is sufficiently large, the following property holds $V(t) = r(t) + \gamma \cdot V(t+1)$. We assume that the learning agent maintains a model of the action value, $\hat{V}(t)$—usually referred as the "critic." The quantity $\hat{V}(t) - \gamma \cdot \hat{V}(t+1)$ can be interpreted as the expected reward at time t, so that we can define a reward prediction error (RPE) at the tth trial: $\delta(t) = r(t) - \hat{V}(t) + \gamma \cdot \hat{V}(t+1)$. The critic can be learned through the temporal difference (TD) learning rule [23]:

$$\hat{V}(t+1) = \hat{V}(t) + \alpha_c \cdot \delta(t) \tag{14}$$

where α_c is the critic's learning rate. As regards the selection of the next action, we can assume that the agent develops a separate representation of the next action (an "actor" in RL terminology). This is called the actor-critic (AC) model. Similar to the critic, optimal action may be developed in terms of a TD learning rule. Various rules are possible; for instance, Izawa et al. [17] assumed that the motor command $u(t)$ is a combination of an "action" $a(t)$ and an "active search" or "exploration" noise, that is, $u(t) = a(t) + n_a(t)$. The action update in the "actor" learning rule was assumed to be proportional to the exploration noise [17]—more exploration leads to a greater change:

$$a(t+1) = a(t) + \alpha_a \cdot \delta(t) \cdot n_a(t) = a(t) + \alpha_a \cdot \delta(t) \cdot \left[u(t) - a(t)\right] \tag{15}$$

where α_a is the actor's learning rate. Izawa et al. [17] used this formulation to identify the relative contributions of error-based and reward-based learning in the adaptation to visual rotations.

The above formulations are suitable in stationary situations, in which there is one action to learn and the environment is stable. In more general situations, the environment may change—this includes, for instance, perturbations or changes in task parameters, for example, task difficulty. If the environment state is denoted by $x(t)$, the long-term benefit is denoted by an action-value function, $Q(u,x)$. The critic's goal is to learn a model of this function, $\hat{Q}(u,x)$, which may depend on a number of parameters. At each time step, an action is selected as a trade-off between exploitation (maximizing $\hat{Q}(u,x)$) and exploration of the action space. The Gibbs softmax procedure is often used:

$$p(u|x) \propto e^{\hat{Q}(u,x)/\lambda} \tag{16}$$

where λ is a "temperature" parameter that regulates the amount of exploration (greater λ implies more variability and therefore more exploration). RL models are appropriate for describing situations in which learning occurs through trials and errors and is driven by reward. This is the case, for instance, of many of the exercise games (exergames) used in neuromotor rehabilitation. RL models based on TD learning can be expressed as state-space linear or nonlinear models; therefore, they fit well in this general framework.

MODELS OF NEUROMOTOR RECOVERY

Similar to motor skill learning, exercise-based neurorehabilitation aims at gradually improving performance through repeated exercise. However, different from motor learning, poor performance depends not only on insufficient skill but also, first and foremost, on the presence of an impairment. Therefore, the problem is not primarily to learn a skill but, rather, to achieve satisfactory performance despite the existing impairment. Redundancy in the musculoskeletal system plays a key role in recovery: as the motor system has more degrees of freedom than task variables, the same functional behavior may be achieved with different movements. The pressure toward regaining functional independence may lead to the development of compensatory strategies that, although adequate for carrying out activities of daily life (ADLs), may be energetically inefficient and may ultimately prevent true recovery [24,25]. For instance, an excess use of the nonparetic limb may have a negative influence on the process of cortical reorganization [26] by further reinforcing the imbalance between the impaired and nonimpaired hemispheres. Understanding the complex set of interactions among the neural structures that underlie voluntary movements is of paramount importance to understand neuromotor impairments and to identify treatments that facilitate recovery [3]. A model of neuromotor recovery must build on specific assumptions on the nature of the impairment and on the way it affects performance. In other words, to model motor recovery, we need to account for both motor learning and neural plasticity (and recovery) mechanisms [27].

MODELS OF RECOVERY AT NEURAL LEVEL

Reinkensmeyer et al. [28] developed a model of cortical damage and its consequences on arm-reaching movements. Based on experiments on nonhuman primates [29], neurons in the motor cortex are assumed to collectively encode the initial direction of the movement (population vector coding). Specifically, each neuron's firing rate is assumed to be a function (truncated cosine) of the difference between the actual movement direction and the "preferred direction" for that neuron plus a noise term, whose standard deviation is proportional to the deterministic part of the cell response (signal-dependent noise). The overall encoded (i.e., internally represented) movement direction is the sum of the preferred directions of each individual neuron, weighted by their activity levels. Cortical lesions were simulated by eliminating a fraction of the neurons (cell death)—hence resulting in underrepresented or non-represented preferred directions. Movement performance was measured in terms of the discrepancy between intended and encoded movement direction. These authors specifically looked at the variability of the directional error within the same intended direction and across directions and how these quantities are affected by cell death. They found that both error measures are inversely correlated to the fraction of surviving cells. In a number of experimental studies with stroke survivors, the same indicators exhibit similar relationships with the subjects' clinical impairment measures [30–32].

The above study addresses how cortical damage results in impaired movements, but does not address the mechanisms of recovery. Han et al. [33] used the same model of lesions in cortical motor areas to understand how lesions affect the mechanisms of arm selection to achieve a goal (reaching a target) and how impairment evolves through spontaneous arm use. Therefore, the model accounts for both motor cortical dynamics (both hemispheres) and action selection; see Fig. 2.

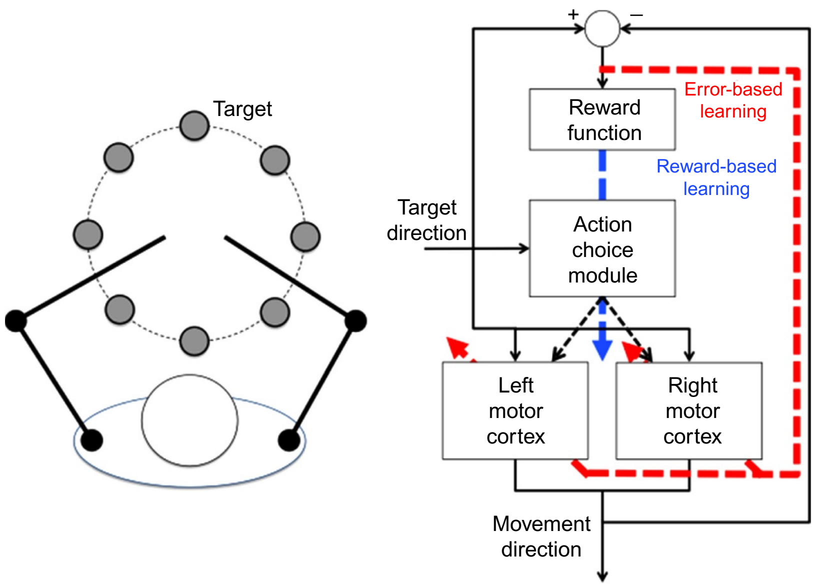

FIG. 2

Model of spontaneous recovery after stroke. The model focuses on reaching movements (left), for which subjects spontaneously select what arm to use. The model (right) includes a model of the motor cortex (both hemispheres) and an action selection module.

Modified from Han CE, Arbib MA, Schweighofer N. Stroke rehabilitation reaches a threshold. PLoS Comput Biol 2008;4(8):e1000133.

The effect of a stroke was modeled by eliminating part of the neurons within one hemisphere's motor cortex. Activity-dependent cortical reorganization is modeled by a Hebbian mechanism, in which the preferred directions of each neuron are assumed to adapt as a function of activity. Adaptation has two aims: (i) shifting the actual encoded direction closer to the desired direction (supervised component) and (ii) shifting the preferred directions of the individual neurons toward the desired direction (self-organizing component). The process of deciding which arm to use is modeled in terms of the RL framework. An action selection module accounts for the process of selecting the hand that will actually make the movement. After every movement, a reward signal is provided, defined as the sum of two terms, respectively, reflecting (i) how close the cortex's encoded direction is to the desired movement direction and (ii) the fact that the left hand is more likely chosen for leftward movements, whereas the right hand is more likely selected for rightward movements. A model of the action-value mapping, based on radial basis functions, generates the expected reward as a function of the direction of the actual movement. The hand corresponding to the maximum expected reward is selected to execute the movement. After each trial, the action-value model is updated to minimize the difference between actual and expected reward (TD learning).

The impaired side is initially unlikely to be selected for movements on that side, and the lack of use makes its selection even less likely. Forced use of the impaired side induces reorganization, so that the intact portion of that hemisphere gradually shifts its preferred directions toward those that were once covered by the impaired portion. In summary, the model addresses the mechanisms of interaction between activity-driven cortical reorganization and functional compensation, that is, the change in the motor strategy (in this case, from the impaired to intact arm) that is driven by the need to preserve functional performance (e.g., a high reward). The model predicts that recovery will self-sustain if the amount of spontaneous use of the impaired arm reaches a certain threshold. If this is not the case, the impaired arm will be less likely selected, and recovery (if any) will gradually wash out. The model makes an important qualitative prediction—an activity threshold is a necessary condition for recovery to self-sustain. This may explain the mechanisms of action of rehabilitation strategies that rely on forced use of the impaired arm. Observations from a rehabilitation trial based on constraint-induced movement therapy (CIMT) are indeed consistent with the "threshold" notion [34]. The model also suggests a criterion to personalize the therapy—aiming to achieve an "activity threshold" rather than providing a fixed amount of training. This model is important, because it is a first attempt to address the interplay between the cortical reorganization and the development of compensatory strategies.

Unilateral spatial neglect (USN) is a neuropsychological syndrome described as a "failure to report, orient toward, or respond to stimuli in contralesional space, which cannot be attributed to primary motor or sensory dysfunction" [35], which is often observed in right-hemisphere stroke patients. Recently, Leigh et al. [36] proposed a neural model that qualitatively describes cortical lesions and predicts the resulting neglect symptoms. The model reproduced a few symptoms of neglect, like the line bisection behavior and the beneficial effect of prism adaptation [37]. However, model predictions are qualitative and cannot be used to explain individual behaviors.

MODELS OF RECOVERY AT FUNCTION LEVEL

Models of recovery at neural level may qualitatively predict the mechanisms and the determinants of recovery, but cannot be used as analytic tools to understand the recovery process of individual subjects. To do so, we need models of recovery that capture the main processes occurring at cortical level, but are expressed in terms of quantities that are directly observable, for example, sensorimotor performance. Hidaka et al. [38] redefined Han's recovery model in terms of quantities that either are directly observable or can be estimated from observations. The functionality of the affected (A) and nonaffected (N) arm at time t is summarized into two variables, $u_A(t)$ and $u_N(t)$. A binary variable, $y(t)$, encodes the arm selected ($y=1$, affected arm; $y=0$ nonaffected arm). The probability of selecting the affected arm is modeled as a logistic function of u_A:

$$\Pr(y(t)=1|u_A)=\frac{1}{1+e^{-\left[H\cdot u_A(t)+G\right]}} \tag{17}$$

where parameter H denotes the effect of function on arm use. The functionality of the nonaffected arm is assumed to be constant, and its effect on arm use is accounted by parameter G. The functionality of the affected arm is assumed to improve with use ($y=1$) and to decline with nonuse ($y=0$)—in Hidaka et al.'s words, "use it and improve it, or lose it":

$$u_A(t+1)=A\cdot u_A(t)+B\cdot y(t) \tag{18}$$

where parameter B (recovery rate) captures the effect of arm use on arm function. To minimize the number of parameters, the decay time constant (retention rate, A) was assumed to be the complement of B, that is, $A=1-B$. The model was used to interpret the arm selection time series from the EXCITE trial [34], in which stroke patients underwent constraint-induced movement therapy (CIMT)—subjects were forced to use their nonaffected arm for a fraction of their time. The available data were a questionnaire-based normalized arm use score and a measure of arm functionality based on movement time, assessed every 4 months during the 24-month trial. In two groups, a 2-week CIMT protocol was administered either at the beginning (immediate group) or at the end of the trial (delayed group). Model simulations suggested that the effect of function on arm use (parameter H) is the main determinant of the long-term increase of arm use. Comparisons with data before and after treatment also suggest that the main effect of CIMT therapy is to increase H.

Likewise, starting from Leigh's model of neglect [36], Sedda et al. [39] derived a computational model of recovery from neglect through exercise. The model reproduces the main observations of prism adaptation experiments and was fitted to data from a rehabilitation trial based on a novel VR-based rehabilitation approach, involving reaching movements within an adaptive environment.

MODELING THE ROLE OF ROBOT ASSISTANCE

Robots can be used in many different ways to promote recovery; see Chapter 5 for an overview of possible approaches. Robots may help completing the movement when the subject is unable to do it alone, thus increasing the administered exercise dose and/or intensity. In this case, the robot only plays an indirect role in the recovery process. Robots can also be used to increase movement variability, thus increasing the amount of exploration. More exploration leads to more accurate control in later movements [40]. In other scenarios, robots continuously assist movements, very much like human therapists. Only few modeling studies have addressed how continuous robot assistance affects recovery. Emken et al. [13] looked at adaptive changes in gait movements in the presence of assistive forces. The model specifically addresses the trial-by-trial evolution of performance. As in Fig. 1 and similar to force-field adaptation experiments, a controller receives the desired trajectory as input and generated the motor command. One main assumption is that the motor system behaves as a "greedy" optimizer, that is, the motor command is generated through an optimization process, which accounts for a combination of motor error and effort. As the assistive force aims at reducing the error, it is gradually incorporated into the motor plan so that the motor command gradually reduces its magnitude while the performance level (e.g., a small error) is maintained. This decay mechanism has been termed "slacking" and is a consequence of the forgetting term in the adaptation equation.

Emken et al. [13] also suggested that slacking may have adverse effects on recovery (the "slacking" hypothesis). As a consequence, in robot-assisted rehabilitation, assistance should be kept to a minimum (assist as needed). Furthermore, it has to be decreased—manually or automatically—as performance improves. A variety of techniques have been proposed to adaptively regulate the magnitude of assistive force as a function of the observed outcome; see the Chapter 5 for an overview. The "greedy optimizer" model has been highly influential to rehabilitation, but does not explicitly address the recovery mechanisms. In fact, it has been derived from studies on healthy subjects, and its implications for recovery are largely speculative. The slacking hypothesis has never been directly tested in clinical rehabilitation trials.

Casadio and Sanguineti [41] developed a dynamic model to describe the trial-by-trial evolution of the motor performance in chronic stroke survivors who underwent a rehabilitation protocol based on a robot-assisted arm extension task. Similar to [13], the model assumed that in robot-assisted exercise, the robot and the subject cooperate toward a common goal—a form of shared control. Specifically, the model assumes that task performance, $y(t)$, is a function of a voluntary, human-generated command, $u(t)$, (taken as the model's state variable) and of a robot-generated assistive force, $x(t)$:

$$y(t) = u(t) + D \cdot x(t) \tag{19}$$

Average speed was taken as the task performance measure. Therefore, parameter D can be interpreted as hand mobility (the inverse of viscosity); see Fig. 3, top right.

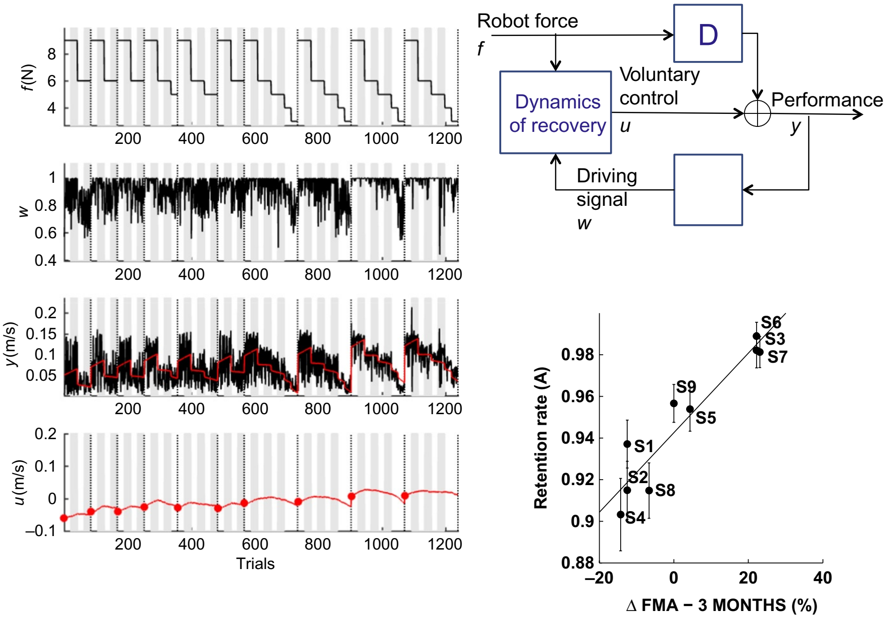

FIG. 3

State-space model of stroke recovery through robot assistance. Left: fitting performance. Right: model schematic (top) and the main result that the model's rate of retention parameter predicts the long-term outcome—change in the Fugl-Meyer assessment (FMA) score in the 3 months following the end of the treatment (bottom).

Modified from Casadio M, Sanguineti V. Learning, retention and slacking: a model of the dynamics of recovery in robot therapy. IEEE Trans Neural Syst Rehabil Eng 2012;20(3):286–296.

As regards the recovery process, the model assumes that the amount of voluntary control on the next trial is the sum of three components: (i) a "memory" or "retention" term, a fraction of the current amount of voluntary control; (ii) a "learning" component, proportional to a "driving" signal, a function $w(t)$ of movement performance that can be interpreted as a reward; and (iii) an assistance-related component, proportional to the magnitude of the assistive force:

$$u(t+1) = A \cdot u(t) + B \cdot w(t) - S \cdot x(t) \tag{20}$$

The three parameters denote, respectively, the retention rate (A), the learning rate (B), and the "slacking" rate, S. Therefore, this model posits separate mechanisms for "retention" and for the effect of assistance, that is, the actual "slacking." These terms have often been used interchangeably; see [42] for a review that specifically covers slacking models. The model was used to analyze the trial-by-trial time series of performance in nine chronic stroke survivors, who underwent a 10-session training protocol; see Fig. 3, left.

As performance measure and driving signal, they took, respectively, the average speed and the fraction of amplitude covered by the first assisted submovement. The estimates of the model parameters for each subject suggested that recovery is determined by a complex interplay of memory (retention), performance, and slacking. One specific finding was that in severely impaired subjects, recovery is greater when the driving (reward) signal is greater; hence, recovery improves when the performance—not the motor error—is greater. Another finding was that a greater assistive force has a negative impact on recovery (slacking). However, only a few subjects—the least impaired—exhibited a significant "slacking" effect. The single most important finding was that the retention rate (memory decay) parameter accurately predicts the long-term outcome of the rehabilitation trial (see Fig. 3, bottom right). This finding is consistent with [33]: the hypothesis that recovery must reach a threshold in order to self-sustain implies a buildup mechanism that integrates the effect of repeated motor activities. High retention is an essential prerequisite of this mechanism. The mechanisms of recovery may differ in different subjects; see Fig. 4.

Specifically, some subjects turned out to be little sensitive to assistive force, whereas their performance was much more affected by the presence or the absence of vision of the hand; see Fig. 4 (left). Other subjects exhibited a large forgetting rate, so that the intertrial improvement in performance did not build up into a massive improvement; see Fig. 4 (right). Intersubject differences call for an adaptive regulation of assistance, in which peculiarities of the individual subjects are to be taken into account. Again, this calls for an adaptive regulation of assistance, in which peculiarities of the individual subjects are to be taken into account.

MULTIRATE AND SPATIAL GENERALIZATION MODELS OF RECOVERY

As noted in the introduction, neuromotor recovery results from the combination of various processes, each with their own timescale [43,44]. Models involving multiple recovery processes, with different time constants, like those used in sensorimotor adaptation, could capture these effects.

Neuromotor impairment is highly dependent on arm configuration and varies with movement direction [45]. Likewise, the dynamics of recovery may be direction-dependent, because the arm moving in different directions may exhibit a different sensitivity to assistance. These effects must be accounted for while analyzing the temporal evolution of the subjects' voluntary control in tasks that involve submovements in different directions. A way to do this is to use the same approaches used to account for spatial generalization in models of sensorimotor adaptation (see above).

SYSTEM IDENTIFICATION TECHNIQUES

All the recovery models presented here take the form of state-space dynamic systems, either linear or nonlinear. Given reasonable values for the parameters, these models can be used to simulate the dynamics of the recovery process. However,

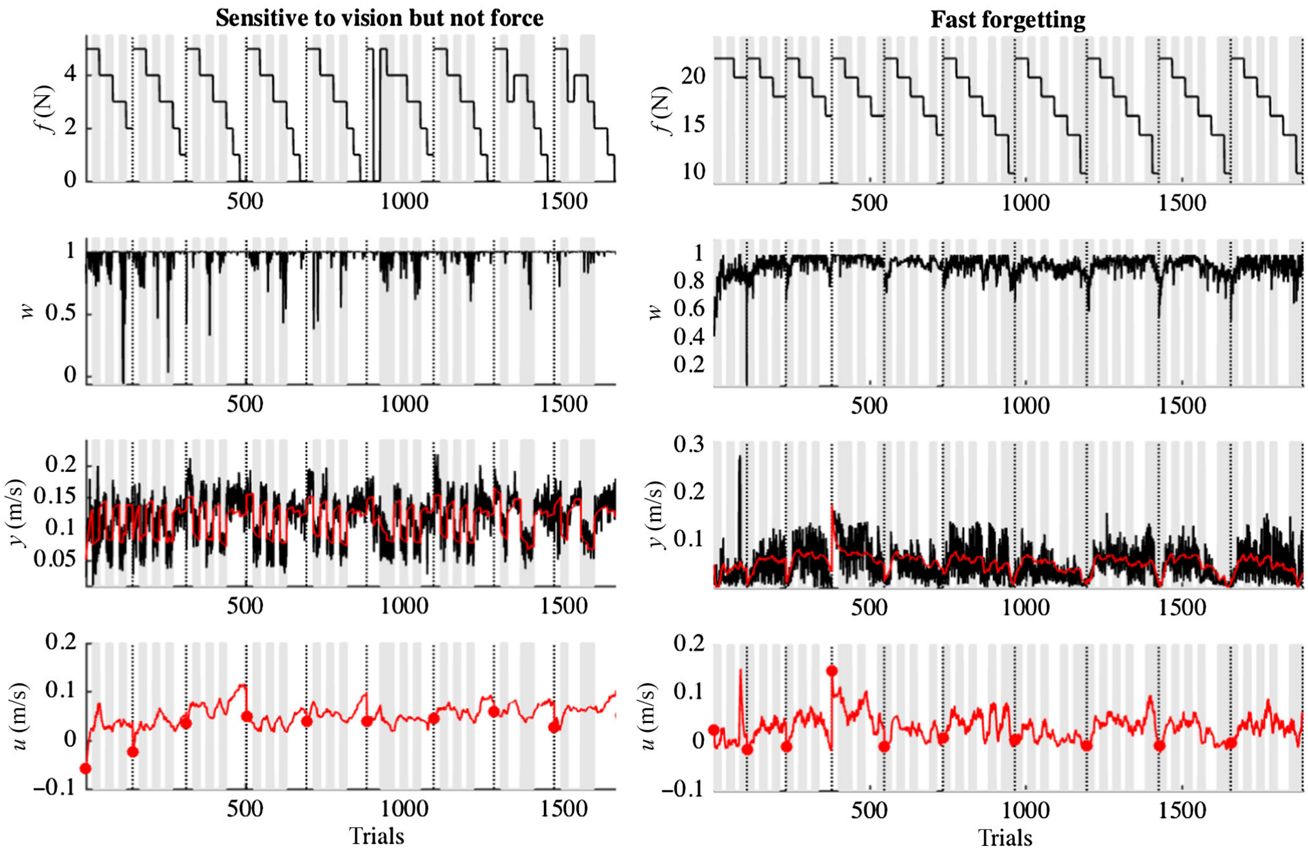

FIG. 4

Fitting examples from the state-space model. Left: performance and model fitting in a subject who is a little sensitive to assistive force and is more sensitive to the presence/absence of arm vision (white and shaded areas). Right: performance and model fitting in a fast-forgetting (low retention) subject, who is unable to build up performance from trial to trial.

Data from Casadio M, Sanguineti V. Learning, retention and slacking: a model of the dynamics of recovery in robot therapy. IEEE Trans Neural Syst Rehabil Eng 2012;20(3):286–296.

if suitable data are available, we can estimate the model parameters for a specific recovery process. The available data may include the following: (i) one or more measures of performance, these are the system outputs, denoted as $y(t)$; (ii) one or more external inputs or environmental states, for instance, the amount of robot assistance or measures of task difficulty or other task parameters, denoted as $x(t)$; and (iii) the reward $r(t)$ provided at the end of each movement. The "motor command" $u(t)$ that changes with exercise may be one of the performance variables or may not be directly observable—for instance, movement speed when no assistance is provided. In this case, it constitutes a "latent" model variable.

Most rehabilitation trials are organized into multiple training sessions. Each session is described by a specific time series. If we assume a stationary recovery process, the model parameters will be constant over sessions. Alternatively, model parameters may be separately identified within each session. The identification of parameters from data in state-space models can be formulated in Bayesian terms, as the maximization of a posterior probability or a model likelihood [38]. If the state variables are not observable, model identification can be carried out through an expectation maximization (EM) algorithm, which alternates estimates of the state given the parameters (expectation or E-step) and estimates of the parameters given the state, through maximization of a quasilikelihood (maximization or M-step) [8,46]. Alternative approaches involve prediction error methods (PEM) that rely on more general formulations, also suitable for nonlinear models [47].

Not all models guarantee reliable identification of the model parameters. For instance, in a linear state-space model, stable parameter identification is problematic if the variance of the process (state) noise is large with respect to the variance of the sensory (output) noise [8]. A number of software tools are available for the identification of state-space models. MATLAB's System Identification Toolbox uses PEM for identification of various classes of linear and nonlinear state-space models. An EM identification algorithm is available as supplementary material of [8]. In many rehabilitation trials, robot assistance or task difficulty are adjusted to the actual subject's performance, on a trial-by-trial basis. In this case, recovery process and assistance control indeed constitute one single dynamic system. Identification must take both into account.

Finally, analytic tools are necessary to quantify the performance of one model, to compare multiple models, and in order to decide which one is best for our data. The variance accounted for (VAF)—or coefficient of determination (R^2)—is widely used. Comparing different models may require to correct the performance measure to account for different numbers of model parameters—Akaike information criterion (AIC) is an example of these techniques.

CONCLUSIONS

A deeper understanding of the functional and physiological mechanisms underlying recovery would likely have a strong impact on neuromotor rehabilitation. Computational models may greatly contribute to this understanding [27,48].

As a future development, adaptively estimated computational models of recovery might be incorporated into patient-specific interaction strategies with the robot. This would lead to more effective ways to maximize recovery, resembling a therapist who keeps an "internal model" of how the patient reacts to his manipulations and on this basis continuously adapts his/her actions.

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CHAPTER

Interactive robot assistance for upper-limb training

10

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INTRODUCTION

An increasing number of individuals are affected by neurological diseases worldwide, due in particular to an ever increasing aging population. For instance, typically, 1/500 people are affected by a stroke every year in developed countries. Therefore, dedicated robotic interfaces have been developed in the last three decades as an attempt to provide neurologically affected individuals with sufficient physical training despite the limited human and financial resources of health systems (Fig. 1). Importantly, the *interactive control* of such rehabilitation robots with the trainee is critical to motor recovery. For instance, clinical trials have demonstrated that passive training is not an efficient strategy, and successful rehabilitation requires the trainee to actively engage in motor task execution [2,3].

Chapter 5 describes various interactive control strategies that have been implemented on rehabilitation robots [4,5] and tested in clinical trials [2,3]. These strategies have generally been developed in an ad hoc way and have not been proved to provide a stable interaction. Furthermore, the control generally constrains the user's hand movement to a straight haptic channel, whereas variability in repeated movements is inherent to reaching learning [6,7], and preventing this variability can deteriorate learning [8].

This chapter introduces a systematic interaction control framework to address these issues. In order to develop suitable control strategies, let us first list the properties that promote efficient robot-assisted neurorehabilitation:

1. The interactive control should be *safe*.
2. It should be *smooth*, so as not to disrupt natural movements of the trainee.
3. *But* it should be *able to forcefully pull the trainees*' *limb*, as neurological diseases such as stroke or spinal cord injury can increase limb resistance due to spasticity or dystonia.

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(A) (B)

FIG. 1

Interactive control concept and experiments. (A) One-on-one physical training with a physiotherapist. (B) A subject training arm movements with the HMan robotic interface [1].

4. Furthermore, *the control should guide yet not constrain the limb movement* so as to not interfere with the large variability in repeated movements.
5. It should *consider the current movement of the trainee and be able to react to it* adequately.
6. Finally, the control should *be adapted to the motor capabilities of the trainee*, so that she/he can succeed in the task but is challenged by it.

Let us briefly comment on these desired properties. Various measures can be taken to ensure a safe interaction of a trainee with a rehabilitation robot (property 1), including mechanical and electronic stops, torque/force, acceleration, and velocity bounds in addition to power interrupters for the robot user and their carer [9]. A stable and smooth control will also contribute to safety. On the other hand, most existing control modes constrain the limb movement along a path and also temporally [4]. However, humans never use the same trajectory or muscle activation when they repeat a task, and repeated movements exhibit a large variability [10]. Not interfering with the natural movement variability (property 4) may improve training and the transfer to real tasks. In particular, constraining the movement temporally through trajectory control is generally felt by trainees as disturbing [11,12] and can disrupt their movement. Furthermore, similar to human physiotherapists, the rehabilitation robot should analyze the trainee's actual performance and adapt its control correspondingly during the movement (property 5). Finally, many authors have documented the need for assist-as-needed control that orients to each trainee's sensorimotor capabilities and enables them to succeed in the task [4], which should motivate training and let them complete the assigned motor task (property 6). Furthermore, when a trainee improves their motor skill, it is important to continuously increase the task difficulty correspondingly, thus keeping them in the "challenge point" [13].

In order to design an interactive control framework with these properties, we propose that the physical interaction with the trainee is regulated by the robot as in one-on-one training with a human physiotherapist (Fig. 1A). In this purpose, we assume that the trainee and the robot or the human therapist can be modeled as two agents with a task and a behavior specified by a quadratic cost function [14]. By developing a control that guides the user movement through minimizing the resulting cost, the robot therapist will provide smooth guidance toward the target during reaching movements (property 2) without any other constraints such as using a specific path or trajectory (property 4).

How to regulate the interaction? Recent neuroscience studies have provided evidence that human motor control corresponds to the minimization of effort and error [15]. Similarly, we use a quadratic function of error and effort to compute the robot motor command [14]. Robotic control strength (property 3) is adapted trial after trial by tuning the effort cost term to provide just enough assistance for the trainee to succeed in the task (property 6), in an assist-as-needed adaptation scheme. The iterative adaptation of control strength is based on the human user control, which can be inferred directly from the motion or indirectly from the deviation [15] or from motion smoothness [16] in consecutive trials. Finally, control theory tools are used to ensure a stable and efficient interaction. In particular, game theory is used to design a reactive control depending directly on the trainee's movement (property 5).

In this chapter, we focus on point-to-point arm movements in Cartesian space, which is the most popular protocol for upper-limb physical neurorehabilitation. Section "Optimal Control Interaction Framework" presents the optimal control framework with two agents to describe the interaction of a rehabilitation robot with a trainee and then illustrates its effect on the movements of stroke survivors interacting with the HMan rehabilitation robot (Fig. 1B). An extension to a reactive controller based on differential game theory is then presented in Section "Stable, Reactive and Adaptive Interaction Control Based on Game Theory," followed by a discussion on the scope of the interaction control framework presented in this chapter.

OPTIMAL CONTROL INTERACTION FRAMEWORK

We want to analyze how a physiotherapist or a robot can assist a neurologically impaired individual to train *arm reaching from a start position to a target*. Let $x_h \equiv x$ represent the position difference to the target for both the human trainee and the therapist, respectively. Let v be the force exerted on the trainee's arm at x by the human/robot therapist and u_h the force provided by the trainee. These two forces move the trainee's arm according to

$$M\ddot{x} + C\dot{x} + G = u_h + v. \tag{1}$$

Setting $v \equiv G + u$ then yields

$$\dot{z} = Az + B(u_h + u), \quad z \equiv \begin{bmatrix} x \\ \dot{x} \end{bmatrix}, \quad A \equiv \begin{bmatrix} 0 & 1 \\ 0 & -M^{-1}C \end{bmatrix}, \quad B \equiv \begin{bmatrix} 0 \\ M^{-1} \end{bmatrix}, \tag{2}$$

where M, C, and G are nearly constant for the small amplitude movements typically trained during neurorehabilitation.

According to which strategies should the trainee and the therapist control the arm movement? The framework of [14] can be used to characterize and implement various control strategies between interacting agents, by generating the motor commands (u_h and u) of the two agents according to their individual cost functions (V_h and V). In this section, we describe interactive control strategies from this framework relevant to physical training.

MASTER-SLAVE INTERACTION FOR PASSIVE TRAINING

For the arm of an impaired individual unable to move it by themselves $u_h \equiv 0$, the power to move the arm is provided by the therapist's force u, yielding a *master-slave relationship* as described in [14]. Furthermore, we can assume that the therapist's command u corresponds to the concurrent minimization of error and effort as observed in [10,15]

$$u^* = \min_u \{W(u)\}, \quad W = \int_0^\infty V dt, \quad V \equiv z^T Q z + u^T R u, \quad z \equiv \begin{bmatrix} x \\ \dot{x} \end{bmatrix} \tag{3}$$

where Q and R are appropriate (respectively, positive semidefinite and positive definite) weighting matrices such as diagonal matrices with positive numbers. The linear quadratic regulator (LQR) corresponding to the solution of Eq. (3) is then computed from

$$\begin{aligned} &u = -L(A,B,Q,R)z \equiv -[L_x L_{\dot{x}}]z, \\ &L = R^{-1}B^T P, \quad A^T P + PA - PBR^{-1}B^T P + Q = 0 \end{aligned} \tag{4}$$

where one recognizes in the last term a *Riccati equation* [17]. Note that in the cost function V of Eq. (3), Q and R typically are diagonal matrices, corresponding to straight-line movements typically followed by the hand in point-to-point arm movements [18]. Curved geometries corresponding to different tasks could be described by different cost functions obtained, for example, from inverse optimal control [19].

The force u is provided by the human therapist or by a rehabilitation robot, in which case the actuators' torque vector τ can be computed via the Jacobian J (defined through $\dot{x} \equiv J(q)\dot{q}$, where q denotes the joints' vector) [20]:

$$\tau = J^T u. \tag{5}$$

This solution can be implemented on nonredundant endpoint-based rehabilitation robots such as MIT-Manus [21], Gentle [22], or EMU [23]. It can be generalized to redundant robotic interfaces, including arm exoskeletons affixed to the body with the joint coinciding with the anatomical joints such as the CEA's ABLE [24]. In this case additional constraints must be added to solve $\dot{x} = J\dot{q}$ for $\dot{q}$ [20], which affects Eq. (1). One such condition is to minimize the square joint velocity:

$$\dot{q}^T N \dot{q} \tag{6}$$

where N is a positive definite weighting matrix. As the exoskeleton joint space $\{q\}$ corresponds to the arm trainee's joint space, N's components can be selected to target a treatment's purpose, for example, to focus training on a specific joint [25].

EDUCATION-TYPE INTERACTION FOR PHYSICAL REHABILITATION

Particularly relevant to physical rehabilitation is the *education relationship* of [14]. By contrast to the above master-slave relationship, in the education relationship, it is the patient who carries out the movement as they wish (they themselves are the "master"), which is expressed through the cost function

$$V_h \equiv z_h^T Q_h z_h + u_h^T R_h u_h. \tag{7}$$

The physiotherapist assists the patient in carrying out the task as specified in Eq. (3), where $z \equiv z_h$ is the difference to the target for the patient. Importantly, in the cost function V of Eq. (3), the therapist minimizes their own effort, which keeps the patient engaged in training and thus prevents a passive behavior that is known to limit motor recovery [2,3]. The two cost functions (Eqs. 7, 3), characterizing the education relationship [14], can thus be used to describe the trainee-physiotherapist interaction, with two independent solutions as described in Eq. (4) for the robot and similarly for the trainee.

INTERACTION WITH POSTSTROKE INDIVIDUALS

The above interactive controller in education control mode was implemented on the HMan [1], which is a dedicated robotic interface for planar arm movements. This system has been used in a clinical trial involving chronic stroke survivors at Tan Tock Seng Hospital in Singapore [26]. We present here only results to illustrate the effect of the interaction control.

Ethical approval for the trial was obtained from the institutional committee, and all sessions were supervised by a bioengineer and a trained occupational therapist. Subjects included in the trial had suffered a stroke 3 months to 2 years before the experiment and were considered at a chronic state of motor recovery. They had shoulder abduction and elbow flexion >3/5 on the Medical Research Council scale for muscle strength and a Fugl-Meyer Upper Extremity Motor Assessment (FMA) score in the 20–50 range.

Fig. 2 shows point-to-point movements without assistance (A) and with assistance using stiffness in the range 32–50 N/m (B). We see that the controller neither disrupts arm motion nor prevents deviation from the straight line to the target in repeated movements, which is likely to favor learning [8].

CHALLENGING PHYSICAL REHABILITATION THROUGH COMPETITION

Another type of interaction that may promote motor recovery in neurologically impaired individuals is *competition*, where the robot or the human therapist challenges the trainee by using a conflicting goal. The competition interaction strategy, which may motivate patients to maximally engage in the physical task, can be represented by the cost functions

$$\begin{aligned} V_h &= z_h^T Q_h z_h + u_h^T R_h u_h + z^T Q_h^p z + u^T R_h^p u \\ V &= z^T Q z + u^T R u + z_h^T Q^p z_h + u_h^T R^p u_h \end{aligned} \tag{8}$$

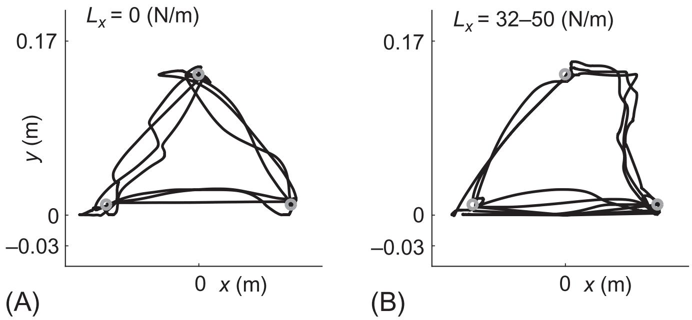

FIG. 2

Performance of a typical stroke survivor in robot-aided training. Point-to-point movements without (A) and with (B) motion assistance. The subject had to move the arm point to point, with targets placed in a triangle, one at a time, in the counterclockwise direction.

where z_h is again the difference to the target for the patient and $z_h \equiv z$ [14]. Q_h and Q are positive semidefinite matrices, R_h and R are positive definite, Q_h^p and Q^p are negative semidefinite, and R_h^p and R_p are negative semidefinite. These equations mean that the two agents favor their own goal and minimize their own effort while maximizing the partner's effort and preventing them from reaching their goal. Note that this relationship can lead to instability, for example, when the two agents have distinct targets.

STABLE, REACTIVE AND ADAPTIVE INTERACTION CONTROL BASED ON GAME THEORY

The above implementation relies on cost functions as in Eq. (7) or (8), corresponding to the situation that each agent carries out their own action without considering the partner's action. However, human therapists likely consider the patient's ongoing movement to react in an appropriate way during training. In fact, recent studies on physical interaction between humans demonstrated that one automatically considers a partner's movements to improve joint action while forming a model of the partner's control [27–29].

Similarly, we recently used *differential game theory* [30] to create a reactive robot behavior considering the control behavior of the human user and adapting to it online. Since each agent's controller affects the partner's performance, the two agents may not be able to minimize their own cost functions (Eqs. 7, 3) even if they have the same goal. In game theory, this can be resolved by determining an equilibrium between two agents' behaviors. Here, we consider the *Nash equilibrium* that indicates that both agents best respond to the partner while considering their own cost function.

Differential game theory for linear systems [30] has shown that the control inputs of the robot u and the human u_h minimize the cost functions (Eqs. 7, 3) in the sense of the Nash equilibrium when P and P_h are computed from the following *coupled* Riccati equations:

$$\begin{aligned} &A_r^T P + PA_r + Q - PBB^T P = 0, \quad A_r \equiv A - BL_h \\ &A_h^T P_h + P_h A_h + Q_h - P_h BB^T P_h = 0, \quad A_h \equiv A - BL \end{aligned} \tag{9}$$

where A_r and A_h are the closed-loop system matrices for the robot and the human, respectively. R and R_h in Eqs. (7), (3) are assumed to be unit matrices and thus do not appear in Eq. (9). In these coupled equations, A_h (thus also L) is needed to solve P_h, and similarly, A_r (thus L_h) is needed to solve P. This illustrates how game theory works: both agents update their own controller based on the partner's controller in order to minimize their own cost function. In contrast, in the LQR solution of Eq. (4) for the robot and the similar solution for the human trainee, the optimal gains are solved independently, without considering the partner's effect.

Since the robot and human control gains L and L_h are unknown to each other, it is necessary to estimate the partner's controller. Let us explain how this can be realized. Let the robot use the following model to observe the system state:

$$\dot{\hat{z}} = A\hat{z} + B\left(u + \hat{u}_h\right) - \Gamma\Delta z, \quad \Delta z \equiv \hat{z} - z \tag{10}$$

where Γ is a positive definite matrix, $\hat{z}$ is the estimate of z, Δz is the state estimation error, and $\hat{u}_h$ is the estimate of an unknown human control. Ensuring that a suitable Lyapunov function has a negative gradient results in the following update law that minimizes Δz and yields a stable interaction:

$$\dot{P}_h = -\alpha \frac{\partial P_h}{\partial Q_h} \bullet \left(A_{rh}^T + A_{rh}\right)\Delta z z^T, \quad \alpha > 0, \quad A_{rh} \equiv A - BL - BL_h, \tag{11}$$

where $\bullet$ stands for elementwise multiplication and $\frac{\partial P_h}{\partial Q_h}$ is computed by solving

$$-A_{rh}^T \frac{\partial P_h}{\partial Q_h} - \frac{\partial P_h}{\partial Q_h} A_{rh} = I. \tag{12}$$

The estimate of the human trainee's control gain can be obtained as $L_h = B^T P_h$, using P_h as updated in Eq. (11). Furthermore, based on the estimation of the trainee's control gain L_h, the robot's controller is obtained as u in Eq. (4), where P is solved from the robot's coupled Riccati equation (9).

The framework of interactive game theory control is completed when we suppose that the trainee uses a process similar to Eqs. (10)–(12) for estimating the robot's controller and that it develops its own controller u_h. The proposed framework enables the robot to (i) estimate the trainee's controller during interaction and (ii) adapt to the trainee in order to guarantee a certain desired interactive behavior.

We have carried out simulations to examine how the estimation of the partner's controller and the game-theory-based controller induces an adaptive control strategy guaranteeing stability of the interaction and successful reaching. We compared the game theory controller with an LQR controller not considering the partner's behavior in two typical scenarios of robot-assisted reaching. We simulated 10 forth and back reaching movements between −0.1 and 0.1 m during a total time of 40 s, with parameters of the point-mass robot dynamics set as mass = 6 kg, observer gain in Eq. (10) $\Gamma \equiv \mathrm{diag}(10, 1)$, and learning rate in Eq. (11) $\alpha \equiv 10^4$ and human's parameters as observer gain $\Gamma_h \equiv \mathrm{diag}(10, 1)$ and learning rate $\alpha_h \equiv 10^4$.

The first scenario emulates the situation where the robot and the human compete against each other, by assigning cost functions with opposite signs, $Q = \mathrm{diag}(200, 2)$ and $Q_h = -\mathrm{diag}(180, 1.8)$. Note that setting a negative definite Q_h leads to a controller that destabilizes the system, which is unusual from the point of view of control design, but expresses the situation of a robot therapist challenging its human user to promote learning. Fig. 3A illustrates the position profile during the reaching movement: the reaching task is successfully completed with the game theory controller,

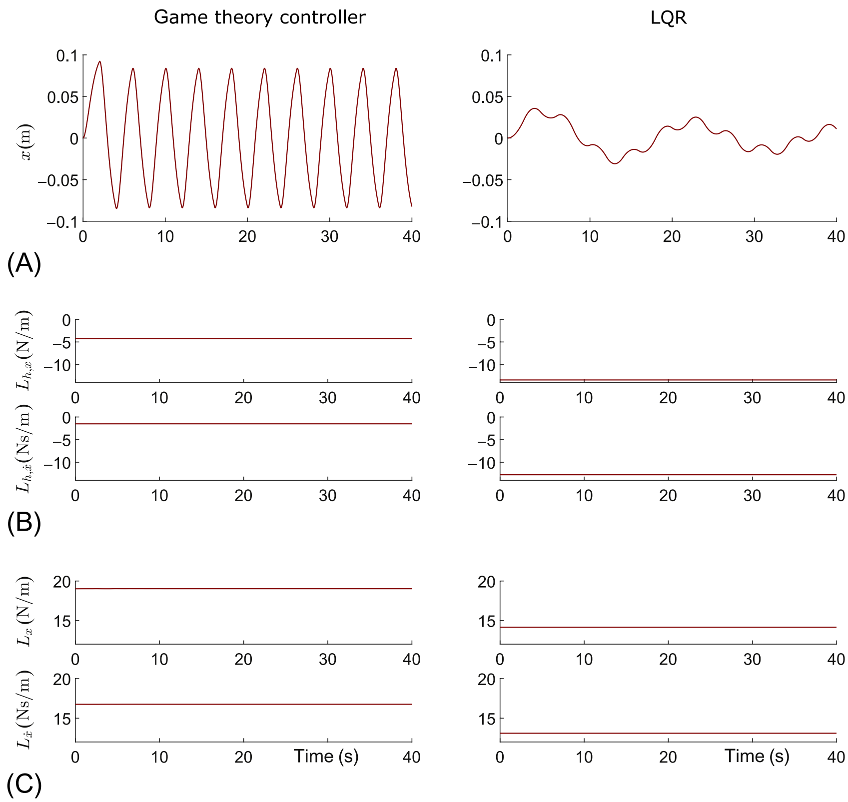

FIG. 3

Competition in robot-assisted reaching simulated with game theory controller (left panels) and LQR (right panels). (A) The position profile during the reaching movement shows that the reaching task is completed under the game theory controller but is unstable and fails under the LQR. (B, C) They show the human and robot controller gains, respectively.

but fails under the LQR. In the case of the LQR controller, since neither the robot nor the human considers the partner, both try to minimize their own cost function, and overall system behavior trades off the two individual goals. This can be observed in Fig. 3B and C, where the robot and the human have controller gains with similar magnitude but opposite signs. Fig. 3B and C also show why the game theory controller achieves the objective of reaching: the robot generates a higher controller gain to compensate for the human's controller. This simulation demonstrates the value of estimating the partner's controller and illustrates the advantage of the game theory controller.

In the second scenario, the robot and human partners have the same cost function with $Q = Q_h = \mathrm{diag}(200, 2)$ to participate to the same redundant task. Fig. 4A shows the position profile during the reaching movement. The reaching task is completed with a small tracking error, using either the LQR or the game theory controller. Fig. 4B

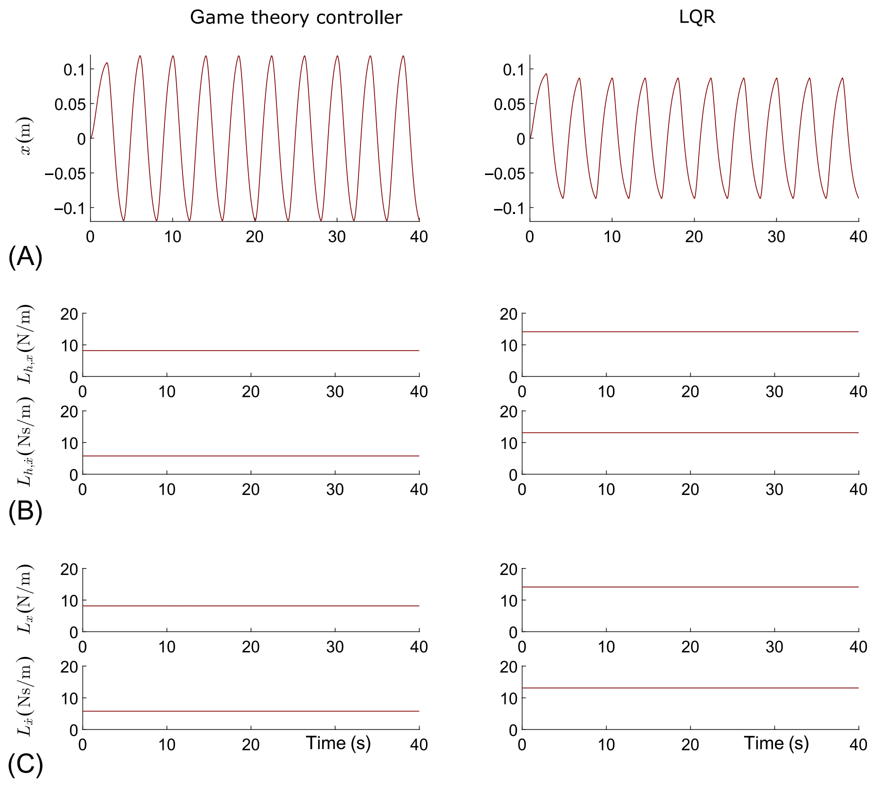

FIG. 4

Effort minimization in simulated robot-assisted reaching under game theory controller (left panels) and LQR (right panels). (A) The position profile during the reaching task is completed under both game theory controller and LQR, while there is a small tracking error in the two cases. (B, C) They show the human and robot controller gains, respectively.

and C show that reaching is realized through different control efforts: comparatively smaller for game theory controller as with the LQR. This is due to the fact that with the game theory controller, both the robot and the human consider that the partner contributes to the task, so know that they can decrease their own effort. In contrast, using LQR, the human and the robot only minimize their own cost function without considering the partner's behavior and may therefore provide a too large an effort.

In summary, these simulations demonstrate the stability and the optimality provided by the game theory controller considering the dynamics of both partners during their interaction.

CONCLUSION

In this chapter, we presented a consistent framework for the interaction control of rehabilitation robots. The main idea is to specify the control of the rehabilitation robot and its human user through designing respective cost functions. Using this framework, different types of interaction strategies can be analyzed, implemented, and tested. In particular, the education type of interaction control provides just enough assistance to succeed in the reaching task, by sharing the trainee's task specification while minimizing the guidance effort. The competition type of interaction control, where the two agents have conflicting goals, can be used to challenge trainees with sufficiently good control capabilities, thus keeping them engaged in training. Results from a pilot experiment with stroke survivors showed that the resulting control enables smooth interaction and does not disrupt movement nor restrict the inter-trial variability, which is likely important for learning.

Furthermore, recent works have revealed the sensorimotor exchange taking place through physical contact when two partners are collaborating on a physical task [28,29], relying on a model of the partner's control automatically acquired during interaction. The advantages of this haptic communication for joint performance and learning motivated us to develop a game theory version of the interaction framework, which enables the robot to adapt the guidance control strategy online to the trainee's performance and react adequately. A critical part of the algorithm consists of identifying the human users' control, which is necessary in order to consider it adequately. Simulations demonstrated the stability this game theory robot control provides to even a catastrophic action of the trainee, its reactivity, and the behavior adaptation to the partner's control dynamics.

While these results present important advantages for a successful physical interaction and promise good rehabilitation outcomes, the framework has been formulated here only for training point-to-point arm movements in Cartesian space. Consideration of curved geometries corresponding to different tasks could extend the formulation by considering different cost functions extracted through experiments and inverse optimal control [19]. Furthermore, the interaction control framework should be extended to other tasks, in particular to continuous tasks, for example, tracking, based on the intrinsic compatibility of optimal control to such tasks [17].

We would like to note that while we used optimal control to develop this motion assistance framework, our interest is not to induce optimal movements of the rehabilitation robot or of its human user. In fact, such optimality is not necessarily desirable for neurorehabilitation, and it is unclear which optimality should be sought for the trainee's movements. In contrast, optimal control and differential game theory were used to induce a safe, smooth, reactive, and adaptable interaction and as a tool to implement different interaction behaviors such as education or competition. The presented framework can also be used to analyze whether therapists adapt their control to the impaired sensorimotor system of specific individuals and which aspects of haptic communication is favorable to physical neurorehabilitation.

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CHAPTER

Promoting motivation during robot-assisted rehabilitation

11

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INTRODUCTION: WHY IS MOTIVATION IMPORTANT?

Numerous robotic technologies have been developed for motor rehabilitation, from low-cost home rehabilitation devices [1,2] to expensive robots with multiple actuated degrees of freedom [3]. Such robots have shown favorable results when compared with equivalent doses of usual clinical therapy [4,5] and are thus likely to become increasingly widespread in motor rehabilitation. To take full advantage of rehabilitation robots, however, we should not just deliver the same dose of exercises that patients would normally get—as rehabilitation robots can work with patients for hours without getting tired, they could potentially deliver longer and more intensive therapy to each patient. This could have great benefits for rehabilitation, as patients who receive additional hours of therapy are likely to have a better final rehabilitation outcome [6,7].

Longer and more intensive therapy can, however, only be achieved if the patient wants to participate in it. The lack of motivation is often a problem, particularly in home rehabilitation: for example, a recent study found that, if a therapist prescribes a home rehabilitation regimen, only 30% of unsupervised patients comply with the regimen [8]. It is thus critical to find ways to increase patient motivation, as studies in other fields of physical training have repeatedly shown that increased motivation results in better compliance and higher exercise intensity [9,10]. Furthermore, recent studies have indicated that higher motivation may also lead to better motor learning [11,12]. As the amount and intensity of exercise and the quality of motor learning are positively correlated with rehabilitation outcome [7,13], promoting motivation would thus allow us to maximize the benefits of robot-assisted rehabilitation.

VIRTUAL REALITY IN ROBOT-AIDED REHABILITATION

The primary way to increase motivation in robot-assisted rehabilitation has been through virtual environments (VEs) or serious games. These two terms have a large degree of overlap, and serious games can be thought of as relatively simple VEs.

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Historically, perhaps the most famous example of VEs in robot-aided rehabilitation was the MIT-MANUS, which featured several "video games" such as drawing shapes and navigating around obstacles [14]. The stated goal of these games was to maximize sensory feedback, though the design principles of the games were not explored in detail.

Soon afterward, several authors began to explicitly explore ways to increase patient motivation through VEs [15–17]. Much of this work has been based on self-determination theory [18], which divides motivation into extrinsic and intrinsic. Extrinsic motivation is characterized by factors external to the activity performed, such as threats or monetary rewards; conversely, intrinsic motivation is characterized by engaging in the activity out of interest in the activity itself [18]. By making rehabilitation more interesting, VEs thus attempt to promote intrinsic motivation.

In recent literature, long-term use of VEs has been found to result in positive rehabilitation outcome, and training with a combination of VE and rehabilitation robot is generally more effective than training with only a robot [19,20]. However, it has been emphasized that it is not clear which elements of VEs contribute to positive rehabilitation outcome [19]. Nonetheless, this chapter will explore different elements of VEs, explaining the justifications for their use and design concerns that should be considered.

DETERMINING THE PATIENT'S GOAL IN A VIRTUAL ENVIRONMENT

When designing a motivational VE, we must first decide what patients will need to do within the VE. According to a classic paper on motivation in serious games [21], each game should have a series of goals that can be either personally meaningful to the player and/or may be generated by the game to keep the player engaged.

Rehabilitation VEs can be broadly divided into two categories according to the patient's goals: simulated activities of daily living (ADLs) and gamelike VEs. In ADLs, the goal is to complete activities such as cooking (Fig. 1), cleaning, and shopping [23,24]. As these activities are similar to those that patients perform in the real world, they should be meaningful and relatable; furthermore, training with such VEs should be relatively easily transferrable to real-world activities [25].

Conversely, gamelike VEs present patients with more fun and/or exotic goals: exploring distant lands [26,27], racing [28], and sports [29] (Fig. 2). While such goals are not as relatable as ADLs, they have another important purpose: stimulating a patient's sense of fantasy. Fantasy is a major element of intrinsic motivation [21] and can be most effectively stimulated by tailoring the goals of a gamelike VE to specific patient populations. For example, gamelike VEs for pediatric rehabilitation often include elements such as wizards, jetpacks, and bioluminescent flowers [27]. However, there are currently no strong guidelines for what goals are appropriate in gamelike VEs, while studies with small sample sizes have shown that some goals are more appropriate than others and that different types of patients prefer different goals [28,30]; knowledge on this topic is limited.

FIG. 1

A virtual environment that simulates an activity of daily living—in this case, cooking. The environment was used in Novak et al. [22].

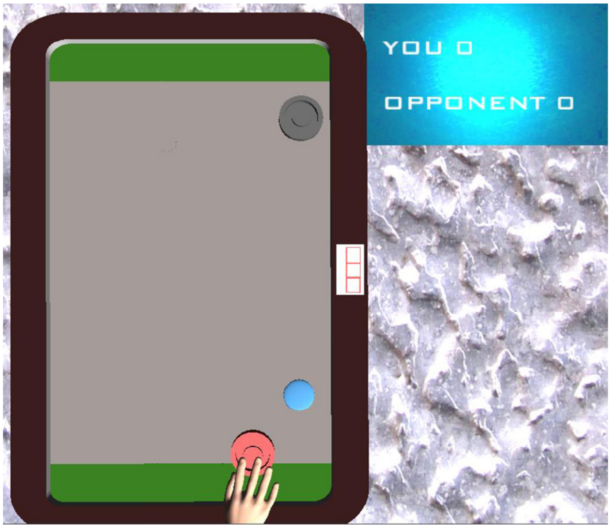

FIG. 2

A virtual environment that consists of a gamelike task—in this case, air hockey. Figure originally appeared in Novak et al. [30].

To ensure a more structured and motivating experience for the patient, we can also present goals in multiple tiers. For example, Mihelj [26] proposed three tiers for a gamelike VE involving exploration: short-term (complete the current motion), medium-term (complete a level of the game), and long-term goals (complete all levels and find the treasure). A similar approach can be taken for an ADL such as cooking: short-term goals would involve adding one ingredient to the dish, medium-term goals would invite preparing an entire dish, and long-term goals would involve gaining access to more advanced recipes [22]. This would provide a more structured, focused experience for the patient.

Finally, there is currently a growing interest in interpersonal VEs: VEs where the goal is for patients to perform a task while competing or cooperating with another person [30,31]. The other person could be another patient, the therapist, or even a friend or relative of the patient. As both competition and cooperation are important contributors to intrinsic motivation [21], they could result in higher motivation than exercising alone. However, such interpersonal VEs have only been tested in brief single sessions and must be more closely studied to determine whether they are beneficial over a longer period.

DESIGNING THE APPEARANCE OF THE VIRTUAL ENVIRONMENT

Once the patient's tasks in the VE have been defined, we can implement the audiovisual and haptic aspects of the VE. The appearance has a potentially huge impact, as sensory curiosity (which is activated by the aesthetics of a VE) is one of the three major contributors to intrinsic motivation [21]. However, several factors should be considered when designing a rehabilitation VE: the hardware, the labor required, the patients' characteristics, and goal-related feedback.

A VE could in principle be displayed on extremely complex devices, such as a 3D projection system with multiple projectors or an augmented reality headset. However, most state-of-the-art rehabilitation robots use either a standard computer monitor or a single 2D projector. As noted in our own studies with three-dimensional VEs [26], patients often have trouble perceiving or working with depth on a standard monitor, and many rehabilitation VEs (particularly those for home use) are thus simply limited to two dimensions. Furthermore, programming a 3D VE can be significantly more complex than a 2D one, requiring additional development time. While three-dimensional environments are useful for many exercises (e.g., three-dimensional reaching), we should thus consider whether the benefits justify the additional labor and possible costs of more complex display hardware.

In addition, while a rich audiovisual environment can be beneficial from the perspective of intrinsic motivation [21], we must make sure not to overwhelm the patient. As a simple example, one of our previous VEs included a quiz (similar to a game show) that patients could play using arm motions, augmenting the physical exercise with cognitive challenges [26]. However, while mildly impaired patients were intrigued by this element [26], a follow-up study with more severely impaired patients found that the cognitive challenge would distract them from the physical exercise [32]. Instead of overloading patients with multiple audiovisual elements at once, we could instead gradually change the appearance of the VE over time, motivating patients by providing constant novelty [33]. Furthermore, patients with certain visual impairments (e.g., neglect) may have trouble perceiving part of the VE, and we should thus always consider whether certain elements of the VE will be beneficial, ignored, or detrimental.

Finally, we must ensure that the VE can effectively provide the patient with feedback about their performance. When interacting with a VE, patients immediately obtain some feedback by way of current performance. However, the VE could also keep track of the patients' performance and provide comparisons of current and past performance to help patients determine how their skills have improved over time. The VE could even deliberately provide false feedback to motivate patients. For example, in reinforcement-induced movement therapy [34], hemiparetic patients are allowed to perform motions with either the impaired or unimpaired arm, but the VE artificially increases the success rate of motions performed with the impaired arm (without telling the patient), encouraging the use of that arm.

ENSURING APPROPRIATE CHALLENGE

According to intrinsic motivation theory [21], motivation is highest when a person is challenged and nonetheless achieves their goal, with the optimal challenge being neither too difficult nor too easy. The need to provide an optimal challenge level is also described by two other theories. The theory of "flow" requires players to be provided with a sense of control and a challenging activity that requires skill and concentration, thus keeping players in a state of deep enjoyment and creativity [35,36]. Similarly, the optimal challenge point framework (which is specific to motor learning) requires patients to be kept at an optimal challenge level where they are neither bored or frustrated with the exercise and can exercise at a high intensity without tiring too quickly [37].

In robot-aided rehabilitation, the optimal challenge level is generally ensured by automated difficulty adaptation algorithms, which regularly adjust characteristics of the VE (e.g., the speed of incoming balls [29]) based on the patient's performance. The performance level can be quantified using a general metric such as the patient's range of motion or a VE-specific metric such as the percentage of incoming balls successfully caught by the patient [29,38]. The adaptation is usually done with if-then rules such as "if performance is high in the last minute, increase difficulty by one level," with the performance threshold set so that the patient successfully performs most of the required motions. By adapting the exercise difficulty, such algorithms both increase motivation and optimize exercise intensity, providing two important benefits to rehabilitation. They can be thought of as a useful complement to assist-as-needed robot control: assist-as-needed control helps patients perform the currently assigned motion [39,40] while difficulty adaptation determines the difficulty of motions that are assigned to the patient.

A less common approach is adaptation based on the patient's physiological responses. The reasoning behind such physiology-based adaptation is that performance metrics may not accurately capture the workload put in by the patient: for example, a patient may be successfully completing motions but at the cost of extremely high physical workload and mental stress. Several studies have demonstrated that including physiological measurements such as heart rate in the adaptation process results in more accurate difficulty adaptation [41–43]. However, no long-term evaluations of this approach have been performed, and it is not yet clear whether the improved difficulty adaptation leads to long-term benefits that outweigh the cost and complexity of physiological sensors.

MEASURING MOTIVATION

The design elements described in the previous section allow us to promote patient motivation in rehabilitation. However, once we have implemented these elements into a rehabilitation VE, how can we be sure that motivation has been improved?

The most common motivation measure in rehabilitation is the intrinsic motivation inventory (IMI) [44], a questionnaire that measures four factors: interest/enjoyment, effort/importance, perceived competence, and pressure/tension. Each factor is measured with multiple statements that the subject can agree or disagree with on a seven-point scale. The IMI was first used for motor rehabilitation in 2007 [15] and has become very common since then—both for evaluations of a single VE [1,15] and for comparisons of multiple VEs [26,30]. However, in the author's experience, it also has multiple weaknesses. First, it contains several negative statements (e.g., “I couldn't play the game very well”) that can be confusing for patients with brain injuries, as it is not always clear what disagreeing with a negative statement implies. Second, there is no clear knowledge of what IMI scores constitute a “high” or “low” motivation, and it is unclear how big a change should be in order to be considered meaningful.

A more objective alternative to questionnaires is to compare how different versions of a VE (with and without motivating elements) affect quantities important for rehabilitation: exercise intensity, exercise duration, or motor learning effectiveness. For example, a recent study found that a VE with motivating elements resulted in better motor learning outcome over a 1-week interval than a version of the VE without the motivating elements [11]. Since motor learning is an important aspect of rehabilitation, we can then predict that the motivating elements would improve rehabilitation outcome over the 4- to 6-week period that is common in rehabilitation [4,5]. Similarly, our own study of cognitive rehabilitation games found that adding motivating elements to a game increased the total gameplay duration over four sessions [33], which allows us to predict that these motivating elements would result in longer exercise duration and consequently better long-term rehabilitation outcome.

As questionnaires and objective measures such as exercise duration can be used simultaneously, perhaps the best way to validate motivating elements in robot-aided rehabilitation is to compare an exercise with the motivating elements with an equivalent exercise without these elements over 3–4 sessions. Depending on subject availability, this could involve two subject groups (each group exercises with one variant) or a single group (all subjects try both variants). Both the IMI and objective measures (e.g., exercise intensity and duration) should then be compared between the two exercise variants to determine whether the motivating elements increase self-reported motivation and/or objective measures. Such an evaluation might not capture long-term factors, but would allow researchers to predict whether the motivating elements are likely to improve rehabilitation without carrying out a full clinical trial.

CONCLUSION

Motivation is a critical aspect of motor rehabilitation, and this chapter presents an overview of ways to increase and measure patient motivation. However, it should be emphasized that motivation research in robot-aided rehabilitation is still in its infancy; while many different motivational virtual environments have been developed, the contribution of different elements is not yet clear, and most of the guidelines presented here are based on studies with a relatively small number of subjects. Nonetheless, as psychologists and computer scientists become increasingly involved in rehabilitation research, the body of knowledge on motivational rehabilitation interventions will continue to grow. By improving patient compliance and increasing exercise intensity, motivational virtual environments have the potential to greatly improve the outcome of robot-aided rehabilitation and improve the lives of millions of people living with chronic motor impairment.

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CHAPTER

Software platforms for integrating robots and virtual environments

12

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INTRODUCTION

The field of development environments for robotics suffers from a lack of standardization. Hence, it is not surprising that even in the specific context of rehabilitation robotics, there is not yet consensus on which software platform is most suitable to this purpose.

In a typical rehab robotics scenario, the patient performs a task on a haptic workstation while receiving visual and auditory cues (Fig. 1). Eventually, additional equipment may be present in order to detect the patient's activity, as, for instance, electromyography (EMG) or brain-computer interfaces. The different system units can be controlled either by a single machine or by separate dedicated computing equipment. Regardless of the system architecture, there is a variety of required tasks that the software should be able to accomplish. These include

- robot control: at low level, a real-time loop is responsible for reading data and status from the robotic device and sending commands;
- haptic rendering: commands sent to the robot are elaborated based on the updated status. Such processing depends on the chosen training paradigm (e.g., assistance and resistance), the phase of the task, and the virtual environment (e.g., collisions);
- observation and evaluation of human motor performance and results;
- adaptation of haptics and task features: the haptic rendering may change, based on the outcome of the former observation, in order to provide "assist-as-needed" forces;
- virtual environment rendering: the control of the display unit to present the task. The complexity of the virtual environment can range from a simple computer graphics interface providing to the patients feedback about performance and results to games with advanced 3D graphics scenarios as those used within the gaming industry;
- data logging: data from all the software components shall be stored in an integrated way, in order to guarantee synchronism between haptics, virtual reality, and external sensors.

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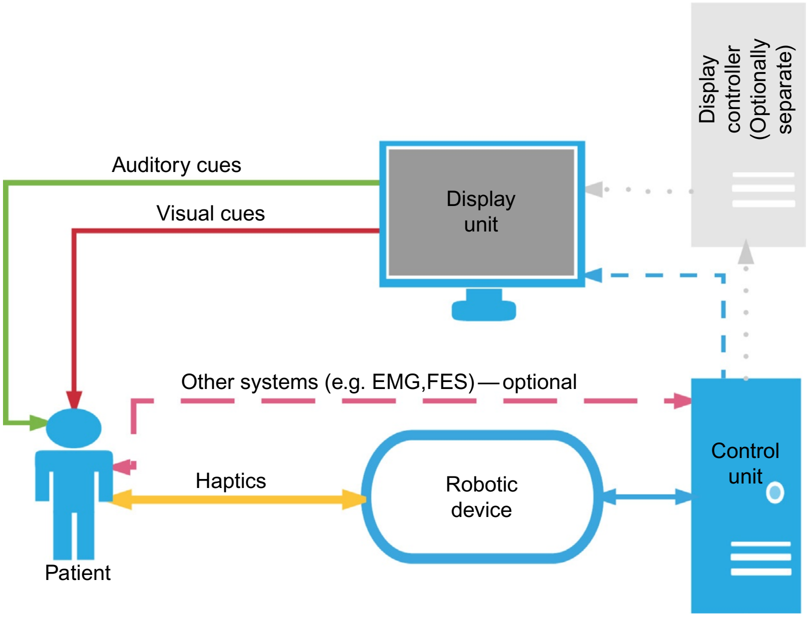

FIG. 1

Typical rehabilitation robotics application: the patient interacts with a haptic device (the robot) while receiving auditory and visual cues. The display controller may be running on the main control unit or separately. Additional systems, such as electromyography (EMG) or functional electric stimulation (FES), may be present.

Clearly, no single environment has all these features. MATLAB and VRML have been used in rehabilitation robotics since its early stages. The 2000s decade saw the start of a number of projects aiming at integrating haptic interaction into virtual environments. Among these, we will consider H3DAPI, Chai3D, OpenHaptics, and Haptik Library, which were adopted in several rehabilitation robotics projects. These software environments share a number of features. All are open-source, free, and support multiple devices (although OpenHaptics officially supports only those from 3D systems, such as the Phantom devices). In addition, all these software consider haptic interfaces as a tool to let the subject probe the workspace and render forces—when collisions with virtual objects occur. For this reason, these platforms are preferable for impedance control devices.

SOFTWARE PLATFORMS

Table 1 summarizes the platforms that we will consider in this chapter and their main features. We will review solutions that have been used for combining robots (or more in general haptic interfaces) and virtual environments. For each of them, we will consider advantages and disadvantages, how their popularity evolved over the years, and we will then discuss their typical applications, focusing on the upper limb.

Table 1 Summary of software platforms used in rehabilitation robotics

Name	First release year	Latest release year	Open source	Supported OS	Supported hardware/ devices	Required—recommended programming languages	Haptics	Collision detection	Graphics	Advantages	Drawbacks
ROS—robot operating system	2005	2016	Y	Unix-based platforms Ubuntu MacOS	None of the most popular haptic devices—but an extensive list of acquisition board and sensors, available here: http://wiki.ros.org/Sensors	Language independent Written in C++, Python and LISP	Y	N	Y	• Largely used in robotics • Extensive hardware support	• Not ideal for human-robot interaction • Graphics are essentially only for displaying simulation output
VRML and Simulink	1995	2001	N	Windows MacOS Linux	https://www.mathworks.com/hardware-support/home.html	Simulink VRML (for graphics, similar to HTML)	Y	N	Y	• Supports hard realtime systems • It has been used for 20+ years in the field	• Graphics functionalities are limited
H3DAPI	2005	2014	Y	Windows MacOS Linux	All Force Dimension and Sensable devices Novint Falcon HapticMaster Template for adding support for custom devices	X3D (similar to HTML) C++ (for creating new objects) Python (for scripting behaviours)	Y	Y	Y	• One virtual environment fuses graphics and haptics • Support for devices can be added easily	• It is no longer developed

Continued

Table 1 Summary of software platforms used in rehabilitation robotics—Cont'd

Name	First release year	Latest release year	Open source	Supported OS	Supported hardware/devices	Required—recommended programming languages	Haptics	Collision detection	Graphics	Advantages	Drawbacks
Chai3d	2003	2017	Y	Windows MacOS Linux	All Force Dimension and Sensable devices, Novint Falcon, LeapMotion, Sixense Razor Hydra, Template for adding support for custom devices	C++	Y	Y	Y	• One virtual environment fuses graphics and haptics • Support for devices can be added easily	• Using only C++, adaptation strategies are harder to implement
HaptikLibrary	2007	2014	Y	Windows Linux	12 haptic devices including Sensable Phantom, Falcon, Force Dimension (complete list: http://sirslab.dii.unisi.it/haptiklibrary/hardware.htm)	C++ Matlab/Simulink Java (for web apps)	Y	N	N	• It has been developed specifically for haptics	• It is no longer developed
Open-Haptics	1994	2017	N	Windows Linux	Touch and Phantom haptic devices (3D System)	C++	Y	N	N	• It is developed by device producers	• Support is limited to 3D System devices
Unity	2005	2017	N	27 including Windows MacOS Linux Android	Microsoft Kinect Leap Motion	JavaScript or C# or Boo	N	Y	Y	• Excellent for game development • Online store with projects available	• There is no native support for haptics

ROBOT OPERATING SYSTEM

The robot operating system (ROS) is a set of software libraries and tools for building robotics applications. This platform-independent, open-source project started in 2007 at the Stanford Artificial Intelligence Laboratory, and it is now a mainstream option in the robotics community. It comprises a visualization toolkit with extensive support for virtual environments (Rviz, ROS visualization).

Despite its name, ROS is not an operating system—but a library of software for robotics. It allows running both robot controller and virtual reality environment on a single laptop or embedded computer. It includes most of the functionalities essential for rehabilitation robotics listed in the previous section, such as data logging and playback, visualization, dynamic simulation, graphic interfaces, kinematics, and motion planning. However, its applications in the health-care industry are limited, and so far, they are almost exclusively confined to the domain of assistive robotics, more specifically to wheelchair navigation [1].

One of the advantages of ROS is the support for the integration of multiple robots, which may be particularly useful in applications where a rehabilitation robot is integrated within an ambient-assisted living solution [2]. Such feature also facilitates solutions with two different robots in a single setup, where one (more affordable) may be used with the unaffected hand and another one with the affected hand [3].

Another advantage of ROS is its comprehensive list of supported hardware, even though there are very few applications in the biomedical field. Among these, the Bento Arm is a system for myoelectric training and research, in which a robotic manipulator is controlled by the user's EMG signal, based on a predictive controller implemented in ROS [4].

Notably, in one of the few applications where it has been used for rehabilitation purposes, ROS was used for a home-based rehabilitation scenario [5]. In this study, the therapist programmed remotely the exercise protocol, which was delivered via a bimanual service robot deployed at patient's home. The visualization toolkit was used to provide the therapist a visual feedback of the robot state.

ROS has also extensive simulation capabilities, thus potentially simplifying the development process [6]. The simulation functionalities, provided by Gazebo (a project formerly included in ROS itself), allow to simulate both robot dynamics and control strategies. The visualization toolkit included in Gazebo can be used to create virtual worlds for functional training of activities of daily living [7]. In this work, the subject's avatar is designed as a human-looking robot, and the graphics and dynamics engine provide feedback to the subject exploring the virtual world through a haptic interface.

MATLAB/SIMULINK AND VRML

MATLAB (Mathworks Inc., Massachusetts, United States) is one of the most used software in the scientific community, and it integrates computation, visualization, and programming in a single environment. Simulink, one of its main packages (toolboxes), offers several hard and soft real-time solutions for robot control. Moreover, a Robotics System Toolbox has been included in MATLAB since 2015. However, such package is dedicated mostly to manipulators, and the advantages of its application in rehabilitation robotics may be limited.

A typical system architecture for applications based on VRML and Simulink is the use of two different units (a host and a target) for achieving hard real-time control of the robot, with clear advantages in terms of safety and robustness. The host computer typically runs MATLAB and Simulink on Windows. All the higher-level software functions (haptics, performance metrics computation, and data logging) are developed as a Simulink model. It includes also connections for communication with the target unit. The target unit runs a software program to ensure the real-time execution of the robot controller. Two types of units are commercially available: QpidE (Quanser Consulting, Canada) and RT-Lab (Opal-RT Technologies, Canada). Both are implemented so that when they are executing the Simulink software, interprocess communication takes place in a seamless way.

The standard method for graphic rendering of MATLAB/Simulink data is the Virtual Reality Markup Language format, VRML (which associated file extension is *.wrl*). The VRML was the first format for virtual reality adopted in 1995. This standard was replaced in 2001 by X3D, which is still the standard for 3D computer graphics.

Also, this function relies on specific Simulink blocks, the virtual reality toolbox (renamed Simulink 3D Animation in 2009). This toolbox is a library of functions to connect Simulink programs with a separate application: the VRML viewer. When such applications are executed, interprocess communication between the two software takes place. Such communication is completely invisible to the programmer. This solution has been adopted for a number of studies, among which some of the earliest systems for rehabilitation robotics, like the ARMIN system [8]. Readers interested in using this system for their architecture may refer to the step-by-step guide provided by Khaled [9].

Virtual environments developed with this system are relatively simple. One typical solution for end-effector robots is to provide biofeedback about the subject's movement and targets to reach, such as done within the earlier prototypes of the Braccio di Ferro system [10]. Applications involving wearable interfaces usually involve grasping tasks. In this case, many studies developed simple models of the hands' segments and joints and eventually of the objects to interact with [11].

Like ROS, one of the core advantages of MATLAB is the large variety of external systems that can be integrated and accessed by the software. Most of the data acquisition boards used by the scientific community provide extensive support for MATLAB, making this solution ideal for the acquisition of sensors in system prototypes. For instance, EMG signals can be acquired to predict patients' intentions, which may ultimately improve the therapy outcome and promote motivation in severely impaired patients [12].

A limitation of MATLAB and Simulink is the weak support for multirobot systems. While there is an extensive number of projects including several mobile robots, there is hardly any multirobot setup based on MATLAB or Simulink for rehabilitation robotics.

H3DAPI

H3DAPI (SenseGraphics, Sweden) is a cross-platform library for graphics and haptics rendering of virtual worlds. Its first release dates back to 2004, and it grew in popularity among researchers. However, this software does not appear to be under development now. Its main advantage is that virtual worlds are collections of objects that have both graphic and haptic attributes. These are specified through an XML-like language, X3D. This is an evolution of VRML that allows to define haptic effects in conjunction with graphics and sounds. In this way, there is one single description for both the graphic and haptic features of the virtual world. A vast collection of objects is already available, and new objects and behaviors can be specified, through either Python scripting or C++ classes.

H3DAPI supports a comprehensive list of haptic devices, and support for new interfaces can be easily achieved—using a wrapper class approach. This eases the sharing of code among researchers, and haptic/graphic virtual reality environments can be run with nearly identical responses regardless of the robot used [13].

The list of supported devices include the Geomagic Touch (formerly Geomagic Phantom Omni), a 6-DOF desktop haptic interface. This implementation has been used to develop virtual reality versions of clinical tests such as the Nine-Hole Peg Test. It has to be considered though that the level of realism may alter the results, which hence may differ from the traditional versions of the test [13a].

An additional advantage of H3DAPI is its support for datagloves with vibrotactile stimulators. These devices perform better when rendering of complex textures, compared with end-effector devices [14], and this makes the use of H3DAPI potentially more appealing for the rehabilitation of fine motor skills.

The typical application of H3DAPI is the exploration of virtual environments. Its application to rehabilitation robotics field is not directly supported but Python scripting can be conveniently applied in order to develop specific applications for training and motor performance evaluation. Gamification can be used, in addition to haptic rendering, to sustain motivation, while assistive forces help to achieve a satisfactory level of performance [15].

Support for multiple devices within the same virtual world allows to further expand the gamification aspect within the domain of machine-mediated human-human interaction. In particular, using H3DAPI, Vanacken et al. [16] developed a collaborative rehabilitation game which can be played by a person with multiple sclerosis and a coplayer using a WiiMote or a force-feedback device.

CHAI3D

Chai3D is a cross-platform framework for computer haptics, visualization and interactive real-time simulation. The project was started, like ROS, by the Stanford Artificial Intelligence Laboratory and is now used by more than one hundred industries and universities. Chai3D supports haptic devices with up to seven degrees of freedom. It is regularly maintained; thus, it supports the most recent devices. Chai3D also supports the Leap Motion (Leap Motion, Inc, United States), a hand-tracking device that can be used to measure the hand movement on the healthy side of a person with stroke to control the robot on the affected side in a bimanual setup [17].

Like H3DAPI, Chai3D simplifies the development of drivers for custom devices. Although this allows reusing the same software with different devices, one should remember that the hardware technical specifications may play a crucial role, as users interact differently with different devices [18]. Chai3D is natively oriented to impedance control devices. Support for admittance-controlled devices can be added by mimicking the impedance control method [19].

The ReHapticKnob is an example of 2-DOF device for hand rehabilitation controlled by LabVIEW software and using visual elements based on Chai3D [20].

Chai3D includes some primitives for collision detection, but they are frequently replaced by the open dynamics engine (ODE). It is an open-source, high-performance library for simulating rigid-body dynamics. The CyberGlove system implements an augmented reality application of object interaction end manipulation. It is based on Chai3D, ODE, and ARToolKit for tracking and recognition functions [21].

HAPTIK LIBRARY

Haptik Library is a component-based open-source library that provides a hardware abstraction layer for access to haptic devices from several manufacturers [22]. Like H3DAPI and Chai3D, Haptik Library can be easily extended and customized and integrated with other applications written in MATLAB and Simulink and Java.

Haptik Library supports a variety of devices, including the Phantom Omni, which has been used for a multitask assessment of sensorimotor control [23].

Several haptic effects have been tested in a motor task with educational aspect using the Haptik Library and the Novint Falcon device. The findings of this application provide preliminary evidence that using educational content can increase subjects' satisfaction. In addition, they suggest that the inclusion of learning elements in rehabilitation tasks can increase the time spent performing exercise and promote learning in a new context [24].

OPENHAPTICS

OpenHaptics software enables developers to add haptics to OpenGL applications. This toolkit is structured similarly to the OpenGL API, one of the most used libraries for graphics rendering. Using the OpenHaptics toolkit, developers can leverage existing OpenGL code for specifying geometry and supplement it with OpenHaptics commands to simulate haptic material properties such as friction and stiffness. Like the previous projects, also OpenHaptics has an extensible architecture.

The OpenHaptics toolkit supports only devices in 3D Systems Phantom series (Geomagic, United States). Because of the popularity of these devices, there are a large number of studies using this software. Since these devices have at least six degrees of freedom, studies using this hardware and software typically include more functional tasks than those developed with other architectures. There are applications of robotic-assisted training for handwriting [25,26] and activities of daily living like door unlocking, water pouring, and meat cutting [27] or tool use and preparing a meal [28].

Similarly, to the other platforms, also OpenHaptics supports a number of third-party libraries. Among these, Ogre3D (for visualization) and PhysX (for dynamic modeling) have been used for the implementation of rehabilitation tasks [29].

UNITY

Unity (San Francisco, United States) is a platform for game design with a built-in integrated development environment (IDE). The technology provides a rendering engine to create interactive 2D and 3D content to publish applications for a variety of platforms, including Windows, Linux, MacOS, iOs, Android, and web applications.

Unity functionalities include rendering of sprites, animations, shading and lighting, input and output operations, user interfaces, physics simulations, audio, network integration, scripting of game logic, and other features that are needed to develop games and interactive applications. Unity is used by a large and growing community; hence, many plugins have been developed to allow the external communication with different applications, and a variety of support options and tutorials can be found online, including on the official online store hosted on the software website.

Unity presents several advantages that led to an increasing adoption in research. It eases the creation of complex environments that may enhance subject's motivation [30], the simplicity of designing complex 3D animation, its flexibility (game development and implementation can be done on various platforms), comprehensive support for multiuser networking, usage of C# scripting code with object-oriented paradigm, and possibility to compile scripts to a dynamically linked library (DLL) using an external compiler [31].

One of these is the presence of plugins to exchange data between Unity and a wide range of input or display devices, including head-mounted displays [32]. Thanks to these features, the platform has been used to design games that interact with a large spectrum of devices [33].

Unity has also been used for real-time display of skeletal models. In some cases, these models are based on inertial measurement units (IMUs), for either upper [34] or lower [35] limb movements rehabilitation in hemiplegic subjects.

A skeletal model is also at the core of the Microsoft Kinect. This optoelectronic gaming system has been extensively used with Unity, either through Microsoft software development kit (SDK), such as the Kinect for Windows SDK, or OpenNI (Open Nature Interaction). Such integration enables the patient to control virtual avatars, trigger events, or allow the user to interact with a virtual environment [32]. Tracking result of the patient's upper-limb movement is recorded in real time through the virtual interaction with the game content, such as point-to-point reaching task. This approach has the potential to allow the practice of tasks similar to conventional rehabilitation both in clinic [33] and at home [36], as the system does not require the attachment of any sensors to the body that would inhibit movement or require setup by the user. The same device has been exploited to test the possibility of using multiuser VR environment to improve engagement in upper extremity therapy [37].

Another end-user system with potential interest for robotics rehabilitation is the Leap Motion device, designed for hand gesture and finger position detection. This was chosen as input device to control a Unity game in which different tasks for hand rehabilitation were implemented, such as 3D grabbing, reaching, pointing, lifting, and throwing [38].The effectiveness of this device for controlling an avatar in a 3D game was found to be lower than the one provided by the Novint Falcon haptic device when the user was asked to control a moving object through a virtual maze and collide with predefined targets [39].The collision detection algorithm in this study was carried out using Unity built-in libraries.

Games developed in Unity have been designed to respond to gestural data and spatial data from the Myo armband, a device containing electromyography (EMG) sensors, a three-axis gyroscope, a three-axis accelerometer, a magnetometer, and a small vibrating motor for haptic feedback. The device has been used to provide visual feedback in the form of a virtual arm replicating the user's movements of the healthy hand that controlled a robotic glove to train the impaired hand [40] and to control a virtual robotic arm to develop applications for hand amputees [41].

A six-degree-of-freedom haptic device (Virtuose by Haption) was used to let subjects grab and move objects in a household 3D scenario [42]. The games have been interfaced with the haptic devices through MiddleVR for Unity, a plugin that acts as a middleware to exchange data between Unity and several VR devices such as 3D trackers and to handle stereoscopy. The online availability of Unity projects to read inputs from the Razer Hydra, a device with two game controllers that can provide hand motion, orientation, and button inputs, benefited the design of an architecture for multiuser human-robot interaction for elderly and cognitive impaired subjects [43].

For more impaired patients, games have been designed in Unity 3D to interact with robotic devices that can provide assistance for the task completion. For instance, the HapticMaster (FCS Control Systems) was equipped with a 4-DOF hand exoskeleton (wrist 3-DoF exoskeleton and modular gripper) to provide wrist movement and pinch assistance during a pick-and-place task in a virtual environment. Trajectories of the wrist and finger were mapped to the virtual representation of the hand movements in 3D space [44]. In another study, the Barrett WAM Arm was interfaced to a game that exploited the Unity collision detection feature to allow the player to pop balloons by touching the pointed end of a thumbtack controlled by the robot end-effector position [45].

Different upper-limb rehabilitation robots have been used to control a game based on the data obtained by sensors in the robotic device sent via TCP/IP [46]. In another study, changes at the wrist joint recorded by an orthosis were sent via TCP/IP protocol by a real-time operating system (RTOS) that acted as a middleware between the robot and the game [47].

Unity 3D has been used also for the design of games specific for bimanual training. In a bimanual system based on the robot HapticMaster, the pose of the bimanual handlebars was used to interact with the game [30]. Gobron et al. proposed a bilateral haptic device consisting of two Lambda Health Systems (LHSs) with two parallel structures for the movement of the feet in the sagittal plane combined with a videogame interface [48].

CONCLUSIONS

In this chapter, we discussed about the history and the features of the software used for developing applications in rehabilitation robotics. While historically MATLAB and Simulink have been the most frequently chosen software, several libraries for haptics have been released in the last 15 years. Among these, CHAI3D is one of the best options for starting new projects, because of its ongoing development and support. While ROS and Unity are the most widely used platform for robotics and game development, respectively, their impact in the field of rehabilitation robotics has been limited so far. With very large users' communities providing extensive support, they both represent candidates toward building a standard platform for rehabilitation robotics.

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CHAPTER

Twenty+ years of robotics for upper-extremity rehabilitation following a stroke

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INTRODUCTION

The ebb and flow of progress requires the convergence of several different factors, technologies, and stakeholders, and there is such a convergence of factors for what is generally described as the human-robot interface. This view on the potential of robotics was eloquently summarized by Bill Gates a couple years ago: "Imagine being present at the birth of a new industry. It is an industry based on groundbreaking new technologies, wherein a handful of well-established corporations sell highly specialized devices for business use and a fast-growing number of start-up companies produce innovative toys, gadgets for hobbyists, and other interesting niche products (like the computer industry) trends are now starting to converge and I can envision a future in which robotics devices will become a nearly ubiquitous part of our day-to-day lives. Technologies such as distributed computing, voice and visual recognition, and wireless broadband connectively will open the door to a new generation of autonomous devices that enable computers to perform tasks in the physical world on our behalf. We may be on the verge of a new era, when the PC will get up off the desktop and allow us to see, hear, touch, and manipulate objects in places where we are not physically present."

This vision might sound ambitious and similar to a tune of “old-fashioned” science fiction, but I claim it is “around the corner.” It includes a new phase of industrial revolution strongly anchored on robotic partners that will cooperate with humans in close contact. It includes widespread automation at smart homes with a multitude of automatic devices embedded in the homes to aid people with everyday activities interconnected at the Internet of things (IoT). It includes self-driving cars and the associated changes in urban development. It includes service robotics that will go

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beyond vacuuming one's carpet to rehabilitation robotics and assisting the rehabilitation process of a person with disabilities.

One cannot overstress the need for this technology. Graying of the world population is increasing the demand on caregivers, rehabilitation services, and payers and is bringing to the forefront the need for technology to assist all stakeholders. By 2050, the contingent of seniors in the United States is expected to double from 13.3% of the population or 40 million to 80 million. With this growth comes an increased incidence of age-related maladies and disease including stroke, and presently, there are already over 50 million stroke survivors worldwide, and this number is going to expand rapidly, particularly in Europe and the Pacific Rim including China. This situation creates an urgent need for new approaches to improve the effectiveness and efficiency of rehabilitation. It also creates an unprecedented opportunity to deploy technologies such as robotics to assist in the recovery process.

It should be of no surprise that large corporations are investing in "rehabilitation robots," which can be used to augment the clinician's toolbox in order to deliver meaningful restorative therapy for an aging population. Rehabilitation robotics can support and enhance the clinicians' productivity and effectiveness as they try to facilitate the individual's recovery, and it is being embraced by large corporations such as Toyota (http://www.toyota-global.com/innovation/partner_robot/family.html) with some market research studies estimating that the market will grow at a brisk pace from US $43 million in 2014 to 1.8 billion by 2020 (Wintergreen Research 2014). The industry's interest has been preceded by a growth of related research in academia as testified by the exponential increase regarding this topic in the last 20 years.

With so much excitement and work in progress, I will focus here on emerging applications of robotics to more traditional upper-extremity rehabilitation with prosthetics, assistive technology/exoskeleton, and lower-extremity rehabilitation covered in other chapters. Here, I will focus on tools to assist the clinician in promoting upper-extremity rehabilitation of an individual so that he/she can interact with the environment unassisted (rehabilitation robotics), and in particular, we will focus on stroke rehabilitation as it is the diagnosis having the largest census presently with over 50 million stroke survivors worldwide.

NEUROSCIENCE PRINCIPLES

Contrary to initial expectations, the major hindrance to the development and deployment of robots for therapy was not engineering but the lack of strong evidence supporting many current rehabilitation practices. Until the 1970s and 1980s, the perception that the brain was hardwired was prevalent. Perhaps the most well-known promoter of this view was the famous Spanish Nobel laureate Santiago Ramón y Cajal. Under Ramón's optics, beyond natural recovery, one should teach compensatory techniques, i.e., how to accomplish activities of daily living and not focus on the paretic limb or impairment. With the understanding of brain plasticity and, consequently, the objective evidence that nurture has a positive effect on nature [1,2], there was the need and the opportunity of harnessing and promoting brain plasticity with robotic tools.

However, conventional practices lacked the support of empirical evidence or any other scientific basis. As a result, there was neither clear design target for the technology nor any reliable "gold standard" against which to gauge its effectiveness. In fact, the biggest hurdle engineers faced in the development of therapeutic robotics was the validation of movement therapy per se. But every challenge is also an opportunity: robots provide an ideal platform for objective, reproducible, continuous measurement, and control of therapy. Furthermore, our research group decided against the merit of following any of the dogmatic approaches that constitute usual care practices. Instead, we took the approach that beyond natural recovery, general neuroscience-based motor learning framework could serve as a good basis for motor recovery, and consequently, we designed rehabilitation robots and its interventions around these concepts.

Kleim and Jones elegantly summarized these neuroscience principles in an easy-to-understand format shown in Table 1 [3]. However, a common mistake that we had observed is for a practitioner or researcher to build an intervention based on one of these motor learning principles without fully considering the interaction among these "10 principles." Indeed, we have demonstrated that, in many instances, embracing isolated principles that on the surface appeared to be sound and grounded proved incorrect in clinical trials.

Table 1 Ten neuroscience principles [3]

Principle	Description
1. Use it or lose it	Failure to drive specific brain functions can lead to functional degradation
2. Use it and improve it	Training that drives a specific brain function can lead to an enhancement of that function
3. Specificity	The nature of the training experience dictates the nature of the plasticity
4. Repetition matters	Induction of plasticity requires sufficient repetition
5. Intensity matters	Induction of plasticity requires sufficient training intensity
6. Time matters	Different forms of plasticity occur at different times during training
7. Salience matters	The training experience must be sufficiently salient to induce plasticity
8. Age matters	Training-induced plasticity occurs more readily in younger brains
9. Transference	Plasticity in response to one training experience can enhance the acquisition of similar behaviors
10. Interference	Plasticity in response to one experience can interfere with the acquisition of other behaviors

REHABILITATION ROBOTIC PRINCIPLES

In this section, I will discuss a few basic principles that are core for successful rehabilitation robotic technology. Of course, the goal is not to cover the engineering fundamentals but instead highlight them referring to well-founded textbooks or papers for depth. Let me mention once again that I am focusing on rehabilitation robotics and will not be discussing assistive robotics.

BACKDRIVABILITY AND PERFORMANCE

In many applications, a system has multiple operation modes that are quite distinct. For example, tug boats have to move fast to reach a ship in need and then move slowly pushing hard (in naval jargon, high bollard pull). Another example, military vessels cruise from one site to another at low speed to reduce fuel consumption but when in need move three to four times faster. Likewise, rehabilitation and assistive robotics generally require two entirely distinctive modes of operation. Typically, assistive technology is intended to provide full support for a person with disabilities; hence, an intrinsically high-impedance device is utilized. Rehabilitation robotics is at the other side of the spectrum and aims at getting out of the way to allow a weak or paretic patient to express as much movement as possible. The robots must be able to gently nudge the patient's limb toward the target, and therefore, the robots must present intrinsically low impedance. In other words, rehabilitation robotics aims at highly backdrivable devices. Closed-loop control might enhance the performance of such devices, but as a rule of thumb, we strive for a target requirement of less than 7% of a weak person's force capability to backdrive the robot. For example, in the MIT-Manus design, we considered that a weak female is capable of exerting 28 N with the arm in the horizontal plane and the robot is able to drive the patient's arm with at least 28 N. On the other hand, we want the patient to be able to express movement, and thus, we aimed at less than 2 N force to backdrive the MIT-Manus end-point friction and inertia [4].

IMPEDANCE CONTROL

An important feature of successful therapeutic robots is their interactivity, which is an essential component of effective robotic therapy. MIT designs achieve this by controlling the robot's mechanical impedance. Shaping the robot's mechanical impedance enables therapy to become directed guidance rather than imposed motion. Furthermore, stability and performance are both addressed directly when impedance control is used for controller design [5,6]. Impedance control regulates the behavior of the robot at the point where it interacts with the environment. The controller modulates the way the robot reacts to mechanical perturbation from a patient or clinician and ensures a gentle, compliant behavior. Importantly, mechanical impedance is a property of the robot alone, regardless of the environment.

Proper selection and ideal implementation of the impedance can guarantee stability with certain environments and desired transparent feel. For example, a programmer could specify a "virtual" spring connecting the patient's hand to a position that moved along a nominal trajectory. When the patient's motion is close to nominal trajectory, the robot exerts little or no force. Conversely, when the patient's hand strays, the robot pushes or pulls it back to the nominal motion; the farther the patient strays, the greater the force the robot exerts. The challenge for rehabilitation robot developers is to create devices that offer a broad range of end-point impedances that includes sufficiently low impedance for a patient to backdrive the robot with ease. This transparency quality differs from traditional factory or assistive robots, which have high impedance; it also differs from haptic devices, which typically offer a broad range of impedances but saturate at comparably low force. Note that impedance control does not specify a unique motion but rather an entire family of motions and shares the burden of producing motion with the patient. Importantly, it allows the patient to make movement errors, while it attempts to minimize the magnitude of those errors and thus is considered key to "adaptive" or "performance-based" rehabilitation. Of notice, as a rule of thumb in our adaptive algorithms, I matched the purported impedances, i.e., I selected the initial robot impedance to be of the same order of magnitude as the interacting patient's limb impedance [7,8].

ADAPTIVE CONTROL

There is no reason to believe that a "one-size-fits-all" optimal treatment exists. Fig. 1 shows examples of unassisted movement attempts to reach the same target of two different stroke patients. This figure illustrates reasonably well that different stroke lesions can lead to very different kinematic behaviors during reach. The first patient can make pretty fast but poorly aimed movements, while the second one aims well but moves very slowly. That requires an adaptive algorithm that can track the patient's needs and abilities. Our research group's performance-based adaptive algorithm explores concepts of motor learning during discrete reaching movements. We include concepts related to knowledge of results (e.g., hitting the targets) and to knowledge of performance (e.g., with every fifth repetition of the game, performance is provided in terms of initiation, aiming, deviation, power, smoothness, etc.) in order to modify the time allotted for the patient to make the move and the amount of assistance afforded. This adaptive controller guides the hand of the patient that aims poorly without holding him/her back and assists the other patient in making faster movements. While tracking allows us to tailor therapy to a particular patient's movement abilities, we need to go beyond that to continuously challenge the patient to avoid slacking.

This approach appears to be valid across different joint segments and diagnoses [7–12] and was demonstrated to work also for children with cerebral palsy making pointing movements with their impaired ankle (different populations and limb segments) [8].

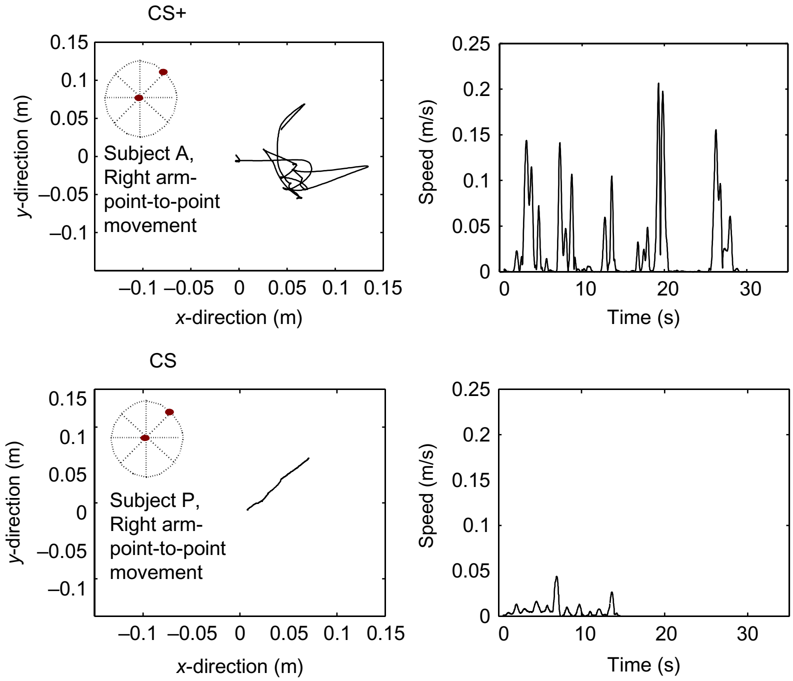

FIG. 1

Reaching movements made by patients with corpus striatum lesion (CS (8.9 cm^3)) and corpus striatum plus cortex lesion (CS + (109.9 cm^3)). The left column shows a bird view of the patients' hand path attempting a point-to-point movement. The right column shows hand speed. Patient with the large lesion (top row) could move at reasonable speed but had poor aim. The opposite holds for the patients with the small lesion (lower row).

MIT-MANUS AND OTHER REHABILITATION ROBOTICS

I will present a snapshot of a few of MIT's rehabilitation robots, discuss the results of meta-analyses for upper-extremity robotics, and finish by discussing two of our research group's exciting examples for acute and chronic stroke. This overview is not intended to offer an exhaustive list of the many other devices and researchers involved in developing rehabilitation robots.

Fig. 2 shows the gym of robots that we developed at MIT for both upper and lower extremities including the MIT-Manus for shoulder and elbow [4], antigravity [13], wrist [14], and hand [15], Anklebot [8,16], and MIT-Skywalker robots [17].

BIG PICTURE

In this chapter, I will focus on upper-extremity rehabilitation following a stroke and present a meta-analysis on the benefits of upper-extremity robotics. For the upper extremity, Kwakkel examined robotic training trials published up to October 2006 with

FIG. 2

MIT gym of robots. Top row on the left shows the MIT-Manus used to promote neurorecovery of the injured brain and control of the shoulder-and-elbow segments and on the right the antigravity device used to promote training of the shoulder against gravity. On the second row on the left, we show the wrist robot that affords training of the three degrees of freedom of the wrist and forearm and to the right the hand module for grasp and release. The third row on the left shows the combination of shoulder-and-elbow robot with the wrist module mounted at the tip of first affording training for both transport of arm and object manipulation. On the right, the alpha-prototype of the MIT-Skywalker for gait training. On the bottom row, we show pediatric populations working with the MIT-Manus and our pediatric Anklebot that provides training in dorsi-/plantarflexion and inversion/eversion.

the first generation of therapeutic robots [18]. A computerized literature search was conducted in MEDLINE, CINAHL, EMBASE, Cochrane Controlled Trial Register, DARE, SciSearch, Doconline, and PEDro, and it returned 173 hits. Only papers that compared robotic training with a control group were included. Excluded were studies that compared different forms of robotic therapy and studies on stroke that compared discharge values with admission values. The results demonstrated small but statistically significant improvements due to robot-assisted therapy, even when compared head-to-head with conventional therapy in stroke. This review demonstrated a small but substantial improvement favoring the robotic therapy group [18] (Fig. 3).

More recently, Kwakkel's team updated the meta-analysis and concluded that shoulder/elbow robotics showed small but significant effects on motor control and muscle strength, while elbow/wrist robotics had small but significant effects on motor control [19]. Our results with both studies for acute/subacute and chronic stroke patients are part of these meta-analyses, and we will discuss a few of the examples:

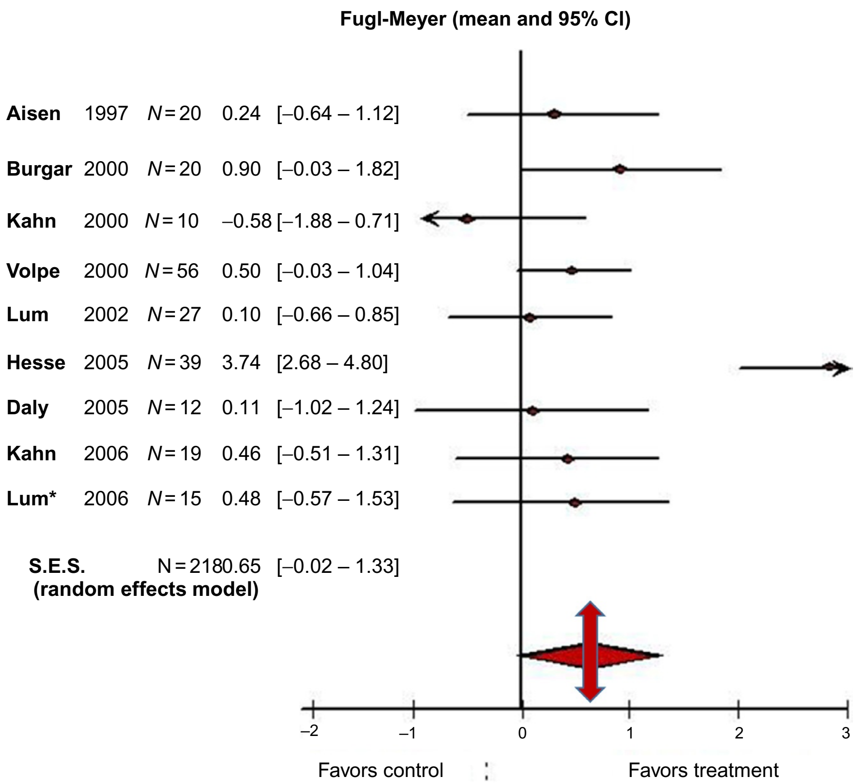

FIG. 3

Meta-analysis of robot-assisted therapy trials on motor recovery following stroke.

1990'S STUDIES: SUB-ACUTE STROKE PHASE

Volpe and colleagues reported the composite results of robotic therapy on 96 consecutive subacute stroke inpatients admitted to Burke Rehabilitation Hospital in White Plains, NY [20]. All participants received conventional neurological rehabilitation during their participation in the study. The goal of the trial was to amass initial evidence to test whether movement therapy had a measurable impact on recovery. Thus, we provided one group of patients with as much movement therapy as possible to address a fundamental question: does goal-oriented movement therapy have a positive effect on neuromotor recovery after stroke?

Patients were randomly assigned to either an experimental (robot-trained) or control (robot-exposure) group. Individuals in the robot-trained group were seen for five 1 h sessions each week and participated in at least 25 sessions of sensorimotor robotic therapy for the paretic arm. Patients were asked to perform goal-directed, planar reaching tasks that emphasized shoulder and elbow movements with their paretic arm. MIT-Manus' low impedance guaranteed that the robot would not suppress attempts to move. When a patient could not move or deviated from the desired path or was unable to reach the target, the robot provided soft guidance and assistance dictated by an impedance controller [4]. This robot action (which we dubbed "sensorimotor" therapy) was similar to the "hand-over-hand" assistance that a therapist often provides during conventional therapy.

Individuals assigned to the robot-exposure (control) group were asked to perform the same planar reaching tasks as the robot-trained group. However, the robot did not actively assist the patient's movement attempts. When the subject was unable to reach toward a target, he or she could assist with the unimpaired arm. The robot supported the weight of the limb while offering negligible resistance to motion. For this control group, the task, the visual display, the audio environment (e.g., noise from the motor amplifiers), and the therapy context (e.g., the novelty of a technology-based treatment) were all the same as for the experimental group. Patients in this group were seen for only 1 h per week during their inpatient hospitalization.

Standard clinical evaluations included the Medical Research Council motor power score for four shoulder and elbow movements (MP, maximum score = 20). Although the robot-exposure (control) and robot-trained (experimental) groups were comparable at admission based on sensory and motor evaluation and on clinical and demographic scales (enrollment into the study between 2 and 4 weeks post stroke) and both groups were inpatients in the same stroke recovery unit and received the same standard care and therapy for comparable lengths of stay, the robot-trained group demonstrated considerably greater motor improvement (higher mean interval change ± SEM) than the control group on multiple clinical scales including the MP scores. In fact, the robot-trained group improved twice as much as the control group in these measures. Though this was a modest beginning, it provided unequivocal evidence that movement therapy of the kind that might be delivered by a robot had a substantially positive impact on recovery.

We recalled these 96 stroke survivors and were able to reexamine one-third of them [20]. Most of these patients had received little therapy after discharge, yet we were able to observe two things: first, the robot-trained group maintained the advantage over the control group, and second, both groups demonstrated greater reductions in impairment. This was contrary to the existing state of knowledge at the time that indicated that the gains in motor abilities were completed after 3 months following stroke onset [21–23]. These results suggest that further improvement is possible in the chronic phase, and bolstered by these findings, we initiated trials with chronic stroke in 2000 [24–27].

2000'S STUDIES: CHRONIC STROKE

Rather than examine our results with chronic patients, we will review a publication in the New England Journal of Medicine in 2010 and related papers [28–31]. The article presented the results of a multisite, independently run, Veterans Affairs trial CSP-558: ROBOTICS involving rehabilitation robotics for the upper extremity of patients with chronic stroke employing the MIT-Manus for shoulder-and-elbow robot plus the corresponding antigravity, wrist, and hand robots. The publication was exciting for many reasons. It was a rare publication on stroke rehabilitation published by this prestigious journal. In fact, we found only one prior paper on rehabilitation following a stroke in the NEJM: "Intramuscular Injection of Botulinum Toxin for the Treatment of Wrist and Finger Spasticity after a Stroke" [32].

ROBOTICS had an unusual design, and it was comparable to a mixture of phase 2 and 3 studies. It evaluated the safety of these rehabilitation robots; they passed with flying colors. There were no serious adverse events in the robot group. A few patients mentioned muscle soreness, which is not surprising considering that they were making 1,024 movements in an hour robot session with the paretic limb (instead of the typical 45 movements in "usual care" for chronic patients) [33]. The study also evaluated efficacy and cost. The first and perhaps most understated finding of CSP-558: ROBOTICS was that usual care (three sessions per week from therapists delivering treatment as they saw fit for the upper extremity) did not reduce impairment and disability or improve quality of life in chronic stroke survivors. The usual care intervention had no measurable impact and was discontinued as futile midway through the study. While it is possible that usual care prevents further decline, we believe that delivering three therapy sessions per week for upper extremity should achieve some level of improvement beyond simple maintenance of the status quo.

The trial lasted roughly for another year and compared robotic training for the shoulder and elbow, wrist, and hand that delivered 1,024 movements three times per week with an intensive comparison training (ICT) protocol that we created to generate a positive control, in which a therapist delivered comparable movement intensity and repetition during the same period [34]. We expected that this positive control would offer an advantage to usual care, likely due to the intense movement training that required the patient to actively use the paralyzed limb for the 50 min session. We also projected that the outcome effect of these two experimental interventions would be comparable, as demonstrated in the pilot study. That result was borne out by ROBOTICS. Specifically, there was no difference between the robotic and intensive-therapy training group in motor outcome measures. However, a note of caution is required since this intervention is not conventional therapy. Given that it is very labor-intensive, it is not practical to implement as standard care in a clinic. We were able to implement this intervention because, in most cases, the VA therapists delivering this form of training were engaged in ICT on average only once per day for the robot and intensive comparison training groups during the whole duration of the trial. Red vertical arrow indicates the change in the primary outcome of the complete robot group in relation to the usual care group (Figs. 4 and 5).

There are additional important comparisons that need highlighting: (a) the comparison between the robot group and usual care involved roughly only the first half of the study, and (b) we were interested in not only the immediate or 12-week impact but also whether the changes were robust and long lasting. On this score, robotic therapy was statistically superior to usual care in Stroke Impact Scale (quality of life) at the completion of the intervention and also in the Fugl-Meyer (impairment) and Wolf Motor Function (function) 6 months following the completion of the intervention [36–39]. The results are far more impressive if we compare the whole robot group with the usual care and not just the analysis that focused on the first half of

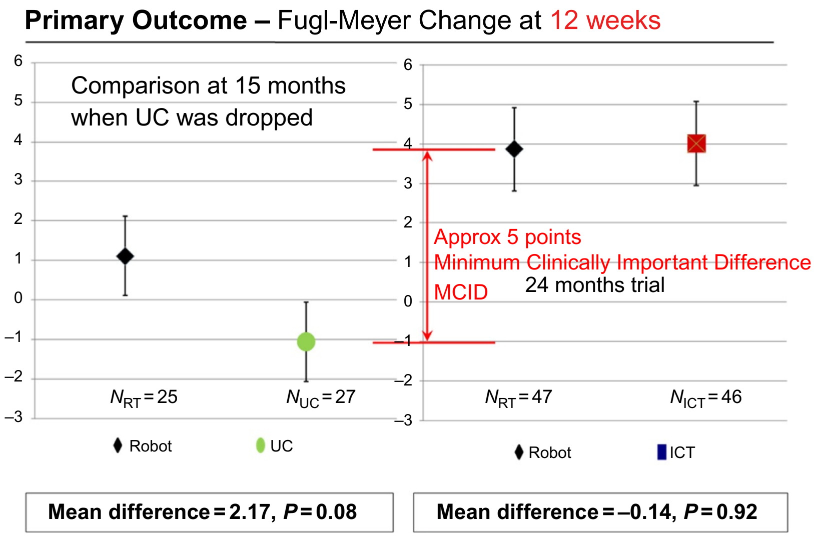

FIG. 4

ROBOTICS (CSP-558) primary results at 12 weeks (therapy completion). Left panel shows the changes in the primary outcome for the robot and usual care groups during the initial half of the trial. Right panel shows the changes in the primary outcome.

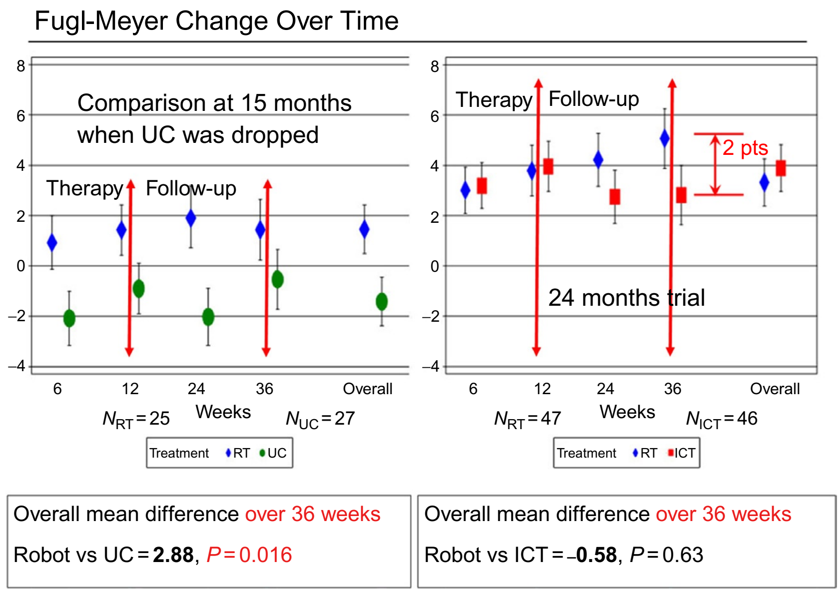

FIG. 5

ROBOTICS (CSP-558) results at 36 weeks (after 6-month follow-up). The figure shows the changes in the primary outcome over the duration of the intervention (evaluations at 6 and 12 weeks) and during the 6-month follow-up period (evaluations at 24 and 36 weeks). Each figure panel also shows the estimated changes at 36 weeks using a fixed model to fit all the data (overall). Left panel shows results for robot and usual care groups during the initial half of the study. Right panel shows results for the robot and intensive comparison training groups during the whole duration of the trial. Note that the robot group continues to improve after the intervention is completed even without further therapy (see evaluations at 24 and 36 weeks). We speculate that on average patients improved above a threshold beyond the minimum required to establish a positive reinforcement cycle [35]. Red vertical arrow indicates the actual change in the primary outcome of the complete robot group in relation to the intensive comparison training group at 36 weeks (instead of the overall fixed model estimate shown on the right).

the study. The results at 12 weeks show that the difference between the first half of the robotic treatment group and usual care was slightly over 2 Fugl-Meyer points. However, the difference between subjects receiving robotic treatment in the second half of the study and subjects receiving usual care during the first half of the study was almost 8 points in the Fugl-Meyer assessment (the total robotic group versus the total usual care showed around 5-point change [40]).

It is quite important to stress that these groups of patients with chronic stroke disability were moderately to severely impaired (admission motor impairment scales averaged 19 out of a total score of 66) and over 30% had multiple strokes. As such, the group represented a spectrum of disability burden that many studies have avoided and, in our case, represented the majority of the cases (65% of the volunteers were enrolled). Thus, even if the positive changes in the robotic therapy group might appear modest, the persistent improvement at the 6-month follow-up evaluation suggests improved robustness and perhaps an incremental advantage that prompted further improvement even without additional intervention. For example, an improvement of roughly 3 points in the Fugl-Meyer scale would enable a very severe patient to start to raise the arm and to bathe independently or to start to stretch the formerly paralyzed arm so that independent dressing could take place. It might enable a more moderate stroke patient to start to tuck in the shirt or to hike the pants independently or to start to reach overhead and actively grasp an object.

More recently, the VA team published part of the secondary analysis adjusted to comorbidities and other factors [31]. Table 2 shows that compared with usual care, the robotic therapy improved 4.2 points in the Fugl-Meyer Assessment (FMA), reduced 7.6 s in completing the Wolf Motor Function Test (WMFT), and improved by 8.3 points in the Stroke Impact Scale (SIS) at completion of training, and these changes were all highly significant. At 6-month follow-up, the robot group advantage was sustained with the robotic therapy, improved 4.6 points in the FMA, reduced 7.8 s in the WMFT, and improved by 3.2 points in the SIS. Even more interesting is the tree analysis breaking down the impact of different cofactors. The younger group of veterans, less than 55 years of age, who had their stroke less than a year at enrollment (i.e., enrollment occurred between 6 and 12 months), were the ones that improved the most. Note that usual care group improved very little independent of age. One note of caution in interpreting this result is that one-third of these veterans had multiple strokes and the VA did not conduct an analysis based on number of strokes. I speculate that age and number of strokes correlate well.

In this era of cost containment, a further important result arose from a cost-benefit analysis. While the active interventions added cost as compared with the usual care (e.g., the added cost of the robotic equipment and the expense of an additional therapist cost the VA approximately $5,000 per patient for 36 months), when we compared with total health-care utilization cost that includes all the clinical care needed to take care of these veterans, there were no significant differences between active interventions and usual care. The robot-trained group consumed $17,831, while the usual care group consumed $19,098 [29]. In other words, the usual care group used the rest of the health-care system for clinical care far more often than the robotic intervention group. This suggests better care for the same or slightly lower total cost. In lieu of this result, the National Health Service in the United Kingdom initiated through its Health Technology Assessment program the largest trial on rehabilitation robotics "RATULS [41]" targeting approximately 800 stroke patients to determine both efficacy and efficiency[1]. One might assume that this trial employing MIT technology will significantly address most of the key questions to allow us to tailor therapy for a particular patient's needs.

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[1] The trial is on target for completion at the end of 2018 with 651 stroke patients completed so far.

Table 2 Secondary analysis of VA ROBOTICS

	12 weeks				**36 weeks**			
	UC	**IT**	**Mean Δ**	***P*-value**	**UC**	**IT**	**Mean Δ**	***P*-value**
Outcome	Mean ± SEM	Mean ± SEM			Mean ± SEM	Mean ± SEM		
FMA	0.03 ± 1.5	4.0 ± 1.3	4	0.005	0.4 ± 1.8	3.8 ± 1.6	3.4	0.051
WMFT	1.4 ± 4.3	−6.4 ± 3.7	−7.8	0.052	−0.2 ± 3.4	−7.7 ± 2.9	−7.5	0.022
SIS	0.003 ± 2.5	7.4 ± 2.2	7.4	0.002	2.3 ± 2.8	4.7 ± 2.4	2.4	0.4
	UC	**RT**	**Mean Δ**	***P*-value**	**UC**	**RT**	**Mean Δ**	***P*-value**
Outcome	Mean ± SEM	Mean ± SEM			Mean ± SEM	Mean ± SEM		
FMA	−0.6 ± 1.6	3.6 ± 1.8	4.2	0.005	0.4 ± 2.1	5.0 ± 2.4	4.6	0.026
WMFT	3.3 ± 4.3	−4.3 ± 4.6	−7.6	0.046	1.2 ± 4.3	−6.6 ± 4.7	−7.8	0.051
SIS	−1.6 ± 3.1	6.8 ± 3.4	8.3	0.005	0.5 ± 3.3	3.8 ± 3.7	3.2	0.3
	UC	**ICT**	**Mean Δ**	***P*-value**	**UC**	**ICT**	**Mean Δ**	***P*-value**
Outcome	Mean ± SEM	Mean ± SEM			Mean ± SEM	Mean ± SEM		
FMA	0.6 ± 1.6	4.9 ± 1.5	4.2	0.007	0.8 ± 1.9	3.4 ± 1.8	2.6	0.2
WMFT	−2.3 ± 5.2	−10.2 ± 4.7	−7.8	0.1	−2.2 ± 3.3	−10 ± 3.1	−7.8	0.016
SIS	2.7 ± 2.7	9.5 ± 2.4	6.7	0.008	4.8 ± 2.7	7.4 ± 2.6	2.5	0.3

UC, usual care; IT, intensive therapy, which includes both the robot and intensive comparison therapy; RT, robot-assisted therapy; ICT, intensive comparison therapy; FMA, Fugl-Meyer Assessment; WMFT, Wolf Motor Function Test; SIS, Stroke Impact Scale; SEM, standard error measurement. Note that the values at baseline were adjusted according to the Comorbidity Disease Index score, the medical center, baclofen administration, and concomitant physical therapy.

CONCLUSION

In summary, I believe that robotic therapy that involves an interactive high-intensity, intention-driven therapy based on motor learning principles and the assist-as-needed principle leads to better outcomes than usual care in acute/subacute and chronic stroke and so do many health-care associations in their clinical guidelines. For example, in 2010, the American Heart Association (AHA) issued "The Comprehensive Overview of Nursing and Interdisciplinary Rehabilitation Care of the Stroke Patient: A Scientific Statement from the American Heart Association" [42]. It recommended that "Robot-assisted therapy offers the amount of motor practice needed to relearn motor skills with less therapist assistance. Most robots for motor rehabilitation not only allow for robot assistance in movement initiation and guidance but also provide accurate feedback; some robots additionally provide movement resistance. Most trials of robot-assisted motor rehabilitation concern the upper extremity (UE), with robotics for the lower extremity (LE) still in its infancy… Robot-assisted UE therapy, however, can improve motor function during the inpatient period after stroke." AHA suggested that robot-assisted therapy for the UE has already achieved class I, level of evidence A for stroke care in the outpatient setting and care in chronic care settings. It suggested that robot-assisted therapy for UE has achieved class IIa, level of evidence A for stroke care in the inpatient setting. Class I is defined as "Benefit >>> Risk. Procedure/Treatment SHOULD be performed/administered"; Class IIa is defined as: "Benefit >> Risk, IT IS REASONABLE to perform procedure/administer treatment"; Level A is defined as "Multiple populations evaluated: Data derived from multiple randomized clinical trials or meta-analysis." The 2010 Veterans Administration/Department of Defense guidelines for stroke care came to the same conclusion endorsing the use of rehabilitation robots for the upper extremity, but not yet for the lower extremity [43]. The 2016 AHA guidelines came to the same conclusion albeit there was no separation between the inpatient (subacute) or outpatient (chronic) setting and hence UE received a Class IIa [44].

Acknowledgment

Dr. H. I. Krebs is a coinventor in several MIT-held patents for the robotic technology. He was the founder of Interactive Motion Technologies and 4Motion Robotics.

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CHAPTER

Three-dimensional, task-oriented robot therapy 14

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EXOSKELETONS

There are various approaches for the design of therapy robots in neurorehabilitation. Two opposite tendencies are evolving with some groups working on simpler mechanical devices, while others develop more sophisticated technology that allows training of more naturalistic movements [1].

Considering the mechanical design, two systems can be distinguished: end effectors and exoskeleton robots. End effectors are attached to the human limb at only one, usually distal, point. This simplifies the structure of the device and the required control algorithms, but it restricts therapy, as the limb posture and interaction torques in each segment are not fully determined. Modular systems that combine several devices or systems that allow changing the device configuration during therapy try to overcome this limitation [2].

Exoskeletons try to replicate the kinematic of the human arm. They consist of several segments that are attached at multiple locations and align to the anatomical segments of the human arm. Similarly, the rotational axes of the device correspond largely to the rotational axes of the human arm, thus assisting more naturalistic movements. The scaffold structure of exoskeleton usually goes along with increased inertia, backlash, and friction [3]. Additionally, the human arm redundancy is critical during movement of the arm in the device [4]. For safe and effective interactions between the human arm and the exoskeleton, it requires complex compensation and control algorithms. Different control approaches exist (for a review, see also [5]). During therapy, setup including alignment to an individual arm may be time-consuming. However, exoskeleton robots bear several advantages: a three-dimensional (3D) workspace (Table 1), they enable to train many activities that are relevant in daily life.

Each arm joint can be controlled and measured independently, single joints can be supported or resisted, and the arm positions can be precisely defined, thus

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Table 1 Range of motion (ROM) of the arm joints required for typical activities of daily living (ADL) in accordance with the literature [6–8] and mechanical limits of the exoskeleton therapy robot ARMin IV

Joint	Movement	ROM [6–8] (degrees)	ARMin IV mechanical limits (degrees)
Shoulder	Elevation	120	125
	Extension	45	40
	Abduction	130	140
	Adduction	115	40
	Inner rotation	100	90
	Outer rotation	60	90
Elbow	Flexion	149	120
	Extension		
	Pronation	65	90
	Supination	77	90
Wrist	Flexion	40	40
	Extension	40	40
Hand	Opening		32
	Closing		

preventing compensatory or synergistic patterns of movement and injuries through abnormal postures [9].

Most clinical studies are performed with patients poststroke, the reasons being that stroke is common and goes along with a high rate of long-term disability, therapy outcome is so far limited, and stroke produces high socioeconomic costs. Furthermore, stroke is not a classical progredient disease but often a one-time event. Thus, recovery in the chronic phase (i.e., 6 months and more after injury) can be largely attributed to the therapy form under investigation rather than the natural and variable process of a disease. That does not mean that these devices are not suitable for treatment of any other neurological disease.

Brain lesions such as stroke result in upper motor neuron syndrome that is characterized by a complex of deficits in motor function including muscle weakness, altered muscle tone, clonuses and spasticity, and decreased motor control with loss of intralimb and interlimb coordinations, pathological synergies, cocontractions, and reduced quality of movement (e.g., loss of smoothness, accuracy, and precision) [10]. Different motor learning strategies target these deficits. Therapy should be intense and highly repetitive, train tasks rather than localized joint movements, integrate multiple sensory modalities, promote active participation, address different degrees of impairment, and adapt to changing performance. While several motor learning strategies can be provided with simple planar devices, task-oriented training with adaptive assistance can only be achieved with robots that train in the 3D space.

HAPTIC GUIDANCE

Haptic guidance refers to physically guiding the subject through a motion by a haptic interface (e.g., a therapy robot) [11]. The role of haptic guidance in motor learning is not clear, and study results in humans are divergent [11,12]. It may be especially helpful when learning motor tasks with complex kinematics. The device can directly demonstrate the task to the patient, and, in contrast to visual guidance, it provides sensorimotor input and does not require transformation by the subject. It is generally accepted that task difficulty should relate to the skill level, and it seems that haptic guidance makes the task easier as particularly patients with severe impairment and elderly profit from guidance [11,13,14].

A drawback of full haptic guidance is that the subject is not actively performing the task but is passive. That is why assistance as needed is implemented in most robots to support voluntary efforts in people with less initial skills [14]. Several of these patient-cooperative control strategies exist that recognize the subject's intention and adapt the level of assistance to the subject's contribution, based either on intersession parameters, on online adaptation, or on anticipatory predicting the trajectory. Furthermore, the robotic support should allow for action exploration, meaning a freedom to exploit different motor solutions. When learning a new motor task, the movement is first highly variable, but with practice, it becomes increasingly precise. This initially higher motor variability can be seen as an initial exploration to exploit the best of different motions and predict faster learning [15]. Taken together, robotic support may be helpful in certain stages of learning. Fitts and Posner defined three phases: a cognitive ("what to execute"), an associative ("how to execute"), and an autonomous phase (automatized execution). Haptic guidance may be helpful in the first two phases to explain the task. In the latest phase, however, any form of additional feedback could prevent the task becoming autonomous [11]. Thus, a controller implemented in robot-assisted therapy for stroke patients should first show the task to the user (full guidance) and then slowly diminish the guidance (assistance as needed) to allow for exploration and later autonomy.

TASK-ORIENTED TRAINING

High number of repetitions has been proven successful for training of the lower extremity [16]. However, simple repetitive motions alone do not induce plasticity to the same extent in the upper extremity. Neurophysiological and neuroanatomical changes in the motor cortex are rather induced by skill acquisition [16,17]. Skill acquisition can be defined as practice-dependent modification of temporal and spatial organizations of physiological muscle synergies. The results are movement sequences that are smooth, accurate, automatized, and persistent over time [18,19]. There is a continuum of increasing difficulty from more basic to complex tasks. Tasks performed in activities of daily living (ADL) are often complex and involve several DOF. They may be too complex to be mastered within a single training session [20]. However, training of complex functional movements seems necessary to increase the transfer of a learned skill to daily life. Difficulty is not objective, and particularly after brain injury, the complexity of a task may be perceived considerably different between subjects depending on how challenging it is relative to the skill level of the subject ("functional task difficulty" [13]). Therefore, tasks should be chosen and continuously adapted in accordance to the abilities of an individual subject. Furthermore, there is a transfer of skill from one task to another, or in other words, learning a skill can be facilitated by prior practice of a similar skill [21]. Thus, task-oriented training in a therapy setting should incorporate movement components and an environment that resembles the targeted task in the relevant functional context (i.e., the home setting) [22].

ARMin

ARMin is an exoskeleton robot with seven DOF that correspond to the functional DOF of the human arm (Fig. 1) [23]. Three DOF are responsible for shoulder movement, namely, abduction/adduction, flexion/extension, and inner/outer rotation; two DOF at the elbow allow for elbow flexion/extension and pro-/ supination and one DOF for wrist flexion/extension; an active hand module supports hand opening and closing. The human-machine interface is integrated through three, six-axis torque sensors, which are attached to the cuffs at the upper arm, the lower arm, and the hand module and measure the interaction forces and torques between the user and the robot. Although mechanical end stops restrict the full range of motion of a

FIG. 1

Subject in ARMin IV.

Courtesy of Stefan Schneller.

healthy subject, the device accommodates a range of motion needed to perform the majority of daily activities (Table 1). ARMin is the research version of ArmeoPower (Hocoma AG, Switzerland), the first commercially available upper-limb exoskeleton robot for rehabilitation.

ARMin MODES OF THERAPY

The ARMin setup with the exoskeleton robot and a monitor aims at providing visual, auditory, and haptic interactions in an engaging manner. Computer graphics present the training scenarios to the user, offer a playful environment, and provide visual feedback on performance. ARMin can be operated in three therapy modes: passive mobilization, active game-supported arm therapy, and active training of ADL [23a].

Passive mobilization serves as a warm-up to increase blood circulation and to improve joint, muscle, and tendon mobility while at the same time reducing muscle stiffness. The therapist moves the patient's limb in ARMin, the device records the trajectory and moves the patient's limb accordingly, and the movement status is visually fed back by animating an avatar on the screen.

In the game mode, mainly single-joint and two-joint movements are trained. In the setting, the joint movement that drives the game can be chosen (e.g., shoulder to move the cursor through a ball game). The intended motor learning process of the game mode is manifold: motor training results in encoding of motor memories. The encoding phase involves cognitive processes that enable to identify a stimulus, select a motor response, and execute the motor command. Games in ARMin such as the ball game train these steps: a ball is rolling down a ramp with varying velocity and end position. The player has to catch the ball with a cursor through single-joint movements (e.g., elbow flexion/extension). In this simple motor training task, the player has to realize the ball direction (stimulus), select whether to flex or stretch the elbow (motor response), and perform the movement, for each ball catch with adjusted angular displacements, velocities, and path length. Thus, this task not only is highly repetitive but also requires cognitive, problem-solving processes to adapt to changing demands (distributed practice). From the visual display ("ball caught"), the player gets immediate feedback whether he successfully associated goal, movement, and outcome. Patients poststroke have difficulty in coordinating elbow flexion with shoulder horizontal adduction, and particularly, patients with severe arm hemiparesis have difficulty changing elbow movement direction from flexion to extension and in coordinating this change with shoulder movement [24]. When the ball game is played with two joints (i.e., shoulder and elbow together move the cursor), intralimb coordination is additionally trained [24].

Training of ADL requires arm movement in the 3D space. ARMin as an exoskeleton enables definition of position and movement of each single joint [25,26]. Only when the patient does not fulfill the task to the end, the robot with its patient-cooperative control strategy guides the arm to the required position ("assistance as

FIG. 2

Graphical display with ticket machine.

needed") [27]. The haptic afferents to the central nervous system during guidance aim to enhance motor learning.

In collaboration with clinical partners and therapists and by asking patients about their preferences and considering safety, nine ADL tasks were implemented into the ARMin setup (Fig. 2) [25]. They together covered the desired key factors of task-oriented training in the 3D space, high repetition, intensity, motivation, and training of joint and task spaces. In a kitchen scenario, frying meatballs, cutting bread, and manipulation of the oven are realized. In the living room scenario, the user can pour wine into glasses, clean the table, or play the piano. In the bathroom scenario, grasping a toothbrush and toothpaste and opening a water tap are trained. The door scenario requires unlocking several doors. Furthermore, buying a train ticket at a ticket machine is trained.

Haptic feedback is provided to simulate interaction with solid objects. For example, the robot offers realistic support of the arm when resting on a table. When colliding with (virtual) objects, these oppose an initial impulsive force (hardness of object) followed by a slower spring-damper force (resting contact) to the virtual contact with the patient [28]. Furthermore, the weight of virtual objects is haptically rendered (e.g., when lifting a pan) [29].

The tasks are visualized on a graphical display. While the required movements are in the 3D space, the visual display on a screen provides only 2D images to the user, and the resulting lack of visual depth may impede task execution. Still, different visual cues on the screen can provide a sense of depth in 2D. Monocular cues such as the size of the objects on the retina, shades and occlusion, texture gradients, and the linear perspectives were integrated into the graphics of ARMin to facilitate task performance [30].

During the training of ADL in ARMin, the patient's arm is visualized by an avatar arm with the joint angles corresponding to those of the exoskeleton. On a graphical user interface, the therapist can set individual parameters for patients such as amount of support or size of workspace.

CLINICAL EXPERIENCE WITH 3D DEVICES

Before devices can be installed in clinical routine, they must be tested for safety and efficacy. Results of clinical studies on task-oriented training after stroke are ambiguous. The ICARE study performed among moderately affected patients in the subacute phase post stroke compared intensive, high-repetition, task-oriented training with unstructured occupational therapy at two different doses and could not find any difference among the therapies [31]. Similarly, a clinical study of repetitive task training could not find any advantage of task-oriented training over conventional therapy forms in chronic patients post stroke [32]. Timmermans et al. developed a special program of technology-supported task-oriented arm training (T-TOAT) and tested it in a study on highly functional, chronic stroke patients [33]. While the experimental group received trajectory guidance through haptic feedback with an end-effector robot that assists shoulder and elbow movements (HapticMaster), the control group had to master the tasks during therapy without support. After 8 weeks of task-oriented training, arm-hand performance improved significantly in both groups. Similar results were found in a small clinical feasibility study on chronic stroke patients, comparing three forms of task-oriented training: patients were either treated over a 6-week period with a therapist or guided by a unilateral or by a bilateral arm robotic setup (UL-EXO7) [34]. Training in all three groups resulted in similar, significantly reduced arm impairments around the shoulder and elbow without significant gains in fine motor hand control, activities of daily living, or independence. The number of participants was too small ($N = 15$) to find differences among groups.

ARMin was the first exoskeleton device to be systematically compared in a clinical study with conventional therapy regarding 3D neurorehabilitation therapy of the arm after stroke [35]. Safety and preliminary efficacy of ARMin therapy were tested in a controlled, parallel-group, multicenter, randomized trial [35]. Four clinical centers in Switzerland were participating in the study. Patients were included if they met the eligibility criteria including a diagnosis of one cerebrovascular accident 6 months or longer before enrollment (chronic stage), with resulting moderate-to-severe arm paresis (Fugl-Meyer Assessment (FMA), 8–38 out of 66 points) [36,37]. As it is known that upper-limb training has the greatest impact for those who show some residual voluntary movement, this lower limit was set at 8 points.

In total, 73 patients were randomly assigned (1:1) to either ARMin therapy (38 participants) or conventional therapy (i.e., occupational or physical therapy, 35 participants) and finished the study. Participants in both groups received 1 h of therapy, three times a week, for a period of 8 weeks (a total of 24 sessions). The ARMin group trained exclusively on the device, and the conventional group received the common neurorehabilitation treatment (occupational therapy or physiotherapy) given in outpatient facilities. Patients assigned to ARMin had significantly greater improvements in arm motor function over the course of the study than did those assigned to conventional therapy (as measured by FMA, $F=4.1$ and $p=0.041$; mean difference 0.78 points, 95% CI 0.03–1.53). Patients assigned to conventional therapy achieved after 8 weeks of therapy the same change in motor function that the ARMin group achieved in half the therapy time (i.e., 2.6 points, after 4 weeks as compared with 8 weeks). Thirteen patients assigned to robotic therapy (34%) and nine assigned to conventional therapy (26%) reached a clinically meaningful difference of 5 or more points during therapy [38]. The most important result of the study was revealed when stratifying by severity (<19 points vs ≥19 points in baseline FMA). Looking at the more severely affected, the ARMin group outdid the conventional group over the course of the study by nearly 1.9 points ($F=17.36$, $p<0.001$, and 95% CI 1.00–2.82). It is for the first time that a therapeutic intervention successfully addresses severely affected patients who generally have an unfavorable prognosis.

Gains in mean strength were significantly higher in patients assigned to conventional therapy than in those assigned to ARMin therapy. The path assistance of the device during training might have been chosen too high, giving too much support, and therefore restricting strength training. No other secondary outcome measure (i.e., the clinical Wolf Motor Function Test (WMFT) and the Motor Activity Log (MAL) questionnaire for activity and the Stroke Impact Scale (SIS) questionnaire regarding participation) showed significant differences in favor of either method of therapy [39–41]. Nonetheless, ARMin therapy and conventional therapy each produced different rehabilitative trends. In contrast to the patients in the conventional group, those assigned to ARMin showed improvements of motor function (i.e., FMA) in clinical tests without associated improvements in the MAL and SIS questionnaires. These questionnaires are filled in by the patients and do reflect not only the transfer of gains into home activities but also the subjective rating of subjects about their performance. While negative correlations between strength and clinical tests (i.e., FMA and WMFT) were observed in the ARMin group, the conventional group showed high correlations. We interpret these results as an indicator that the conventional group trained strength while the ARMin group focused more on skill acquisition.

INTERPERSONAL TASK ORIENTED TRAINING

The sensors in robotic devices provide kinetic and kinematic information that can be exchanged online (i.e., in real time) between devices. This bidirectional approach can be used to integrate the therapist into robotic therapy and enables him to feel the patient's arm during task performance on his own arm (“beam me in”). We realized the “beam me in” setup by the use of two ARMin devices: the affected arm of a patient (e.g., after stroke) is placed in one ARMin, and the therapist arm is placed in the other device. A bidirectional teleoperation control strategy (i.e., the master-slave system) allows two configurations: in the slave configuration, the therapist in the “master ARMin” describes with his arm different trajectories in 3D that are followed by the patient arm in the “slave ARMin.” The interaction torques between the patient arm and the “slave ARMin” are transferred to the therapist in the “master ARMin.” Thus, the therapist can feel the patient reaction (e.g., spasticity) to a described movement. In the master configuration, the roles are switched: the patient arm in the “master ARMin” moves and, thus, guides the therapist arm in the “slave ARMin.” The therapist can behave either passively to assess the patient's movement or actively to follow and thus support the patient or provide resistance. The master configuration enables the therapist to assess the patient movement (e.g., active range of motion) in his own arm. In a single case study, participating therapists showed an overall positive attitude toward the “beam me in” concept and could rate motor performance without being in physical contact with a patient.

OUTLOOK

We are just about to explore the potential of exoskeletons for therapy. For example, the game scenarios in ARMin that were tested in the mentioned clinical study were created in 2008. Since then, more sophisticated visualizations with interactive real-time rendering of computer graphics or head-mounted displays are being integrated into therapy scenarios. The more realistic integration of the user in the simulated environments may change and further increase motivation and presence [42]. Of interest, the technological quality of media (i.e., immersion) has medium importance for the psychological experience of being there (“presence”) for the user. While quality of visuals and sound seem to contribute relatively weakly to the formation of presence, rather tracking level, stereoscopic vision, and a wide field of view seem to be the most important cues [43].

Great amount of research is under way to find ways to promote neurological recovery after stroke. It encompasses new strategies from the fields of neuroscience, medicine, pharmacology, and engineering that all aim to enhance reorganization of the brain through modulation of neural plasticity and through optimized learning protocols. The fundamental premise of most of these stroke therapies is that concomitant training is essential to improve recovery and the beneficial effect of the new strategies can only evolve when administered together with rehabilitation therapy. Animal studies on successful implementation of plasticity-promoting therapies highlight the indispensable combination with active neurorehabilitation therapy [44]. This multimodularity with application of plasticity-promoting therapies in combination with exoskeletons that allow to provide task-oriented training with high intensity hopefully brings a breakthrough in neurorehabilitation [45].

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CHAPTER

Robot-assisted rehabilitation of hand function

15

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INTRODUCTION

The hand is a fascinating and complex neuromechanical system. It occupies a central role in our activities of daily living, being the interface through which we mostly interact with our environment, manipulate objects, and communicate [1]. The ability to place the thumb in opposition to the other fingers and the versatility of our hands, characterized by 21 degrees of freedom (DOF) and redundant actuation through 27 intrinsic and extrinsic muscles, allow us to perform a wide variety of grasps, from precision grip requiring fine finger motion and force coordination to power grip for the generation of high forces [2]. In addition to unique motor abilities, the hand provides rich somatosensory information thanks to a large number of mechanoreceptors located in the fingers and palm. Somatosensory inputs are of primary importance for the exploration of our environment, for the recognition and manipulation of objects (e.g., shape detection, perception of force, and slippage), or for the learning of new motor tasks [3].

After a neurological injury such as stroke, hand sensorimotor function is compromised in a majority of patients. Hand impairments after stroke typically arise from muscle weakness during voluntary movements (especially in the finger extensor muscles) resulting from activation deficits and hyperexcitability of flexor motor units (leading to spasticity—a velocity-dependent increase in muscle tone in response to a movement stimulus) and abnormal muscle activation patterns (i.e., pathological muscle synergies) [4–6]. These are assumed to be a result of damage to the corticospinal tract following focal brain injury. In addition to motor symptoms, deficits in somatosensory function are commonly observed, with decreased tactile sensation, stereognosis, and proprioception [7]. Functionally, these impairments lead to a decreased ability to open and close the hand, a loss of dexterity and control of individual finger movements and forces, and a decreased grip force/load force coordination, required for object manipulation [6,8,9], thereby severely affecting the quality of life and independence of stroke patients.

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Among approaches to support the restoration of hand function in neurological patients, robot-assisted rehabilitation has seen growing interest in the last decades. These developments were motivated by the promises that robotic devices can advantageously support conventional rehabilitation treatments by increasing therapy intensity, which in turn is expected to yield better functional outcome [10]. In addition, robots can precisely control and reproduce movements and assistive forces that can be adapted to the need of a patient and increase physical and cognitive engagement through the use of challenging and motivating exercises [11]. Many robotic devices have been proposed for shoulder and elbow rehabilitation (see Ref. [12] for a review), and there is clinical evidence that robot-assisted rehabilitation supports the recovery of function and muscle strength of the affected arm [13,14] and its use in activities of daily living.

Only more recently, hand rehabilitation devices have been proposed and clinically tested for feasibility and efficacy in stroke patients. Due to the complexity and versatility of the hand and the wide spectrum of possible impairments after a neurological injury, the development of hand rehabilitation devices remains a major challenge. In this chapter, we describe different approaches to robot-assisted rehabilitation of hand sensorimotor function and discuss the current clinical evidence gathered with the robots that were tested in clinical trials. The chapter provides an overview of the current state of the art in robot-assisted rehabilitation of hand function and discusses promising research avenues to optimize the development of robotic systems to support hand sensorimotor rehabilitation and improve our understanding of the mechanisms underlying recovery.

ROBOTIC APPROACHES FOR HAND REHABILITATION

In a review of robotic systems for hand rehabilitation after stroke published in 2010, 30 devices were identified, eight of which had been clinically tested with stroke patients [15]. In 2016, a review focusing on the mechanical design of dynamic hand orthoses for rehabilitation identified 165 devices or design concepts [16]. This remarkable increase underlines the interest of the field of rehabilitation engineering in developing new solutions to support hand therapy and assistance. However, the large majority of these devices have hardly been validated in studies with end users for feasibility and even less for clinical efficacy. Hand rehabilitation robots can be categorized in function of their design principle [15], the number of joints of the upper limb they can control [12], or the mechatronics components they use [16]. In this chapter, we classify robotic devices based on their conceptual design and how they interact with the user. We therefore consider three types of robotic approaches for hand rehabilitation: (i) powered hand exoskeletons, (ii) end-effector-based devices focusing on the hand, and (iii) entire upper-limb solutions where hand training can be combined with arm movements (e.g., reaching movements) (Fig. 1).

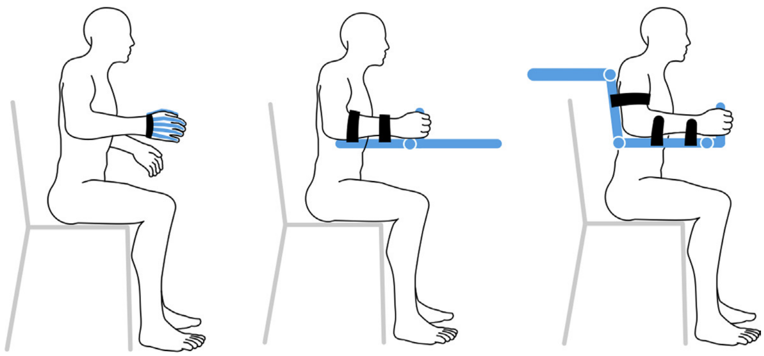

FIG. 1

Schematic representation of the different approaches to robot-assisted rehabilitation of hand function, hand exoskeleton (EXO, left), end-effector hand rehabilitation robot (EE, middle), and entire upper-limb robotic system (EUL, right).

POWERED HAND EXOSKELETON DEVICES

An exoskeleton consists of a mechanical structure that is mounted in parallel with the limb of the user in order to provide assistance. The majority of hand exoskeletons aim at restoring grasping function by helping patients open the hand or provide force augmentation to hold objects. Hand exoskeletons are typically attached to the back of the hand and fingers, leaving the palm of the user free to interact with real objects and process somatosensory information [17]. Conceptually, the structure of an exoskeleton follows the body of the user, so that assistance can be provided at the joint level. As a result, joint motion and forces/torques can be precisely controlled to ensure physiologically correct movements. The desire of precisely controlling each joint is appealing, but in the case of the hand, it can rapidly lead to very complex mechanical systems requiring multiple actuated DOFs (e.g., 18 in Ref. [18]). High system complexity, however, is likely to limit the amount of force that can be transmitted through the mechanical structure of the device, affect the weight (which can be a strong limitation, as exoskeletons are typically designed to be carried by the user during therapy), and lead to extended setup time for ensuring proper fixation and alignment of the exoskeleton with each joint. Altogether, these factors are likely to affect the clinical applicability of such devices. As a result, most hand exoskeletons are underactuated, considering finger flexion/extension as a single DOF by combining the motion of distal phalanges with the metacarpophalangeal (MCP) joint in order to perform the finger movements required for gross grasping. Very often, finger abduction/adduction is not considered or is implemented in a passive way, and the motion of several fingers is coupled. Overall, the majority of exoskeletons for hand rehabilitation or assistance consider between one (i.e., open/close of all fingers together) and six (i.e., individual flexion/extension of each digit and thumb abduction/adduction) active DOFs [19].

A wide variety of designs have been considered for the implementation of hand exoskeletons. Rigid mechanical structures with remote-center-of-motion mechanisms have been proposed, such as in the Hand of Hope (Rehab-Robotics, Hong Kong) [20], the BRAVO exoskeleton [21], the HEXOSYS [22], or the HANDEXOS [23]. In these systems, motors directly actuate each finger (or a group of fingers) and are mounted at the dorsum of the hand. Other approaches consist in mechanically grounding the actuators (e.g., to a supporting table) and externally connecting them to the hand and fingers through rigid links and padded plates, such as for the HWARD [24], the HEXORR [25], or the FINGER [26]. Grounded actuation allows for the use of more powerful motors, thereby transmitting higher forces to the hand, but limits the applications of such exoskeleton to stationary scenarios (i.e., nonfunctional movements).

Another design approach for hand exoskeletons consists of tendon-like systems embedded into a glove. As an example, the X-glove [27] can assist finger extension through cables guided along the dorsal side of the fingers that are actuated by linear motors. In a similar way, the VAEDA [28] provides extension assistance that can be triggered by electromyography (EMG) signals from finger extensors or through voice control for more severely impaired patients. Other types of cable-driven devices are designed to assist both in extension and flexion by pulling or pushing at specific fixation points on the fingers, mimicking the muscle-tendon anatomy of the hand [29–31]. Cable-based systems can transmit high forces while supporting soft grasping motion, allowing the hand to adapt to the shape of the objects being grasped. However, cables need to be routed on both sides of the hand, requiring the use of a complete glove that can potentially disrupt sensory signals from the palm and can be challenging to put on and off for neurological patients. The Gloreha (Idrogenet, Italy) [17] proposes an open palm glove, where the distal phalanges of the fingers are connected to pneumatically actuated flexible beams guided through the glove on the dorsal side of the fingers and can passively flex and extend the fingers.

Other soft hand exoskeleton designs have been proposed based on purely pneumatic actuation systems using inflatable air chambers to move the fingers. The PneuGlove [32] uses five individual air chambers located on the palmar side of the hand to assist in finger extension (hand opening). Other devices use air chambers mounted at the back of the hand to provide assistance in grasping (hand closing), using a reinforced metallic structure in each finger module to ensure physiologically correct finger bending during flexion [33]. Soft exoskeletons using elastic elements actuated by linear motors (i.e., series elastic actuators) have also been proposed. For example, the three-layered sliding spring exoskeleton [34] presents a slim and lightweight mechanism attached to the dorsal side of the fingers. It is composed of fixed and moving spring blades actuated by a single linear motor, creating a remote-center-of-motion system to passively flex and extend the fingers.

To summarize, one of the most interesting features of hand exoskeletons is the possibility to have wearable devices that can be used in the context of activities of daily living, for providing additional therapy outside of the clinic, or become assistive devices to restore grasping capabilities in patients with hand weakness once recovery has plateaued. Devices that could fuse both aspects and allow patients to benefit from high-intensity therapy embedded in their activities of daily living bear high potential to improve the quality of life of neurological patients.

END-EFFECTOR HAND REHABILITATION ROBOTS

Robots based on the end-effector concept train hand and eventually wrist function by only interacting with the distal segments of the fingers, that is, the fingertip or sometimes the middle phalanx. The rest of the arm is not controlled by the robot, although it is commonly supported by passive mechanical structures. As a result, end-effector devices cannot measure or control arm posture during human-robot interactions, which may result in patients using undesired compensatory strategies, especially at the level of the shoulder and trunk. While such strategies can be monitored by supporting therapists or minimized using passive supports or shoulder restraints, they may still hinder the use of such design approach in patients with severe pathological synergies. Advantageously, end-effector hand rehabilitation robots are typically less complex than exoskeletons (both in terms of design and control), with mainly below five DOFs, and allow for advanced instrumentation and interaction control [35]. The majority of end-effector systems are grounded devices attached to a table, relaxing the design constraints faced by hand exoskeletons in terms of weight and size. Also, as interaction only takes place at a few distal points (e.g., through exchangeable handles or finger supports), setup time can be very short, and end-effector robots can easily be adapted to user with different hand sizes or to both left and right hands.

A few end-effector devices for hand rehabilitation aimed at training finger individuation by providing up to five DOFs. The Rutgers Master II [36] consists of four pneumatic pistons connected together at the palm of the user and to the proximal interphalangeal joint (PIP) to assist/resist individual finger flexion/extension (with the exception of the little finger) over a portion of the finger workspace. The HandCARE [37] uses cable loops connected to the tips of each finger and to a single actuator controlling hand opening/closing in a vertical plane. The AMADEO (Tyromotion, Austria) is a five-DOF end-effector robot that provides independent linear motion assistance in flexion/extension to one or all five fingers in a horizontal plane. Fingers are attached to the robot using elastic bands and small magnets, and the wrist is supported by a padded support that prevents the user from moving the arm. Other end-effector approaches focused on functional training and interaction with virtual objects simulated by the robot. For example, the HapticKnob [38], the ReHapticKnob [39], and the EnableHand [40] have two DOFs to train grasping and forearm pronation/supination. In these devices, a linear gripper provides coupled movement of the fingers and thumb to open and close the hand, with the ability to provide high assistive/resistive forces and implement high-quality haptic effects [39].

In summary, end-effector systems are mainly used as stationary devices in rehabilitation clinics. Unlike some exoskeletons, they are not designed to be portable or to provide assistance during activities of daily living, but rather to simulate these activities in a controlled environment where more repetition (i.e., more intensive rehabilitation) can be provided. The grounded structure of end-effector devices generally allows for higher forces (assistive or resistive) to be applied, which could prove necessary to assist patients with more severe impairments, or high muscle tone.

ENTIRE UPPER LIMB SOLUTIONS

According to [12], more than 120 robots (both exoskeletons and end effectors) have been designed for the rehabilitation of arm function, primarily to actively support shoulder and elbow movements. However, the majority of these robotic devices only use a passive joystick-like handle as the interface with the hand of the user. Only a few robots include a module to integrate hand tasks as part of a whole-arm training scenario. In most cases, these hand modules consist of one-DOF mechanical systems assisting hand opening and closing and measuring interaction between the user and the robot (e.g., to control a game). For example, the arm rehabilitation robots ARMin IV [41] or Gentle/G [42] are equipped with actuated handles that can open and close the hand. These handles can be used in virtual reality games simulating activities of daily living (e.g., reach-to-grasp movements). The InMotion2 (Interactive Motion Technologies, United States), the commercial version of the MIT-Manus planar end-effector robot, also proposes a hand module, with a joystick-like handle that can change its outer diameter in order to provide sensorimotor training for grasp and release [43]. Other end-effector robots involving the active training of shoulder and elbow were proposed with the ReachMan [44] and ReachMan2 robots [45], extending the concept of the HapticKnob [38] by adding an additional DOF to perform arm reaching movements.

The idea of a robotic system that can train both the proximal and the distal arm is certainly appealing as it provides the opportunity to train functional tasks involving the entire arm (e.g., reach-to-grasp movements) under robotic assistance. For example, the robot could actively compensate for the weight of the arm in order to facilitate arm and hand movements in severely impaired patients. Nevertheless, training the entire arm significantly increases the complexity of the robot, both in terms of design and control (e.g., large number of DOFs and added inertia and friction) and in terms of usability (i.e., requiring trained personal to ensure proper setup and use).

CLINICAL STUDIES ON ROBOT-ASSISTED REHABILITATION OF HAND FUNCTION

Among the large spectrum of existing robotic devices for hand rehabilitation, only a limited number have been clinically evaluated with stroke patients. In their review of hand and wrist rehabilitation devices in 2010, Balasubramanian et al. reported that only about one quarter of existing devices had been clinically tested with at least one stroke patient [15], a ratio that is likely still valid today. This can be explained not only by the costly and labor-intensive process required for designing and conducting clinical trials but also by the fact that many existing devices, despite clever and innovative designs, are difficult to use with neurologically impaired patients (e.g., too complex, providing too little range of motion/force, requiring too much time to setup, or targeting a too small subset of patients). In the following, we aim at providing an overview of recent clinical studies on robot-assisted rehabilitation focusing on the training of hand function and discuss their study designs and main clinical findings. With the objective of highlighting results that could potentially be generalized, we did not consider scientific publications reporting single case studies, but rather focused on clinical trials (pilot studies and randomized control trials) including at least five patients participating in a robotic intervention and receiving at least five therapy sessions. In the case of incremental work from the same research group, only the most recent study was considered. Table 1 summarizes the results of a systematic search on online publication databases (using combinations of keywords including hand, stroke, rehabilitation, and robot/orthosis and considering the criteria listed above). The search identified 19 clinical studies, out of which 11 are randomized controlled trials comparing a robot-assisted intervention focusing on hand function with conventional therapy (7) or comparing different therapy regimes with a specific robotic device (4). Note that studies evaluating the entire arm of robotic devices were not considered, as the therapy with these devices does not primarily focus on training the hand. Similarly, studies focusing on wrist or forearm rehabilitation were not included (Fig. 2).

DISCUSSION

CLINICAL EVIDENCE SUPPORTS THE APPLICATION OF ROBOTIC SYSTEMS FOR HAND REHABILITATION

The overview of existing clinical studies highlights increasing evidence that robot-assisted rehabilitation can have a positive effect on reducing hand impairment and improving hand motor function in stroke patients. This is well in line with previous reviews that focused on upper-limb robot-assisted rehabilitation, where robotic assistance was shown to improve the ability to perform activities of daily living in people after stroke, functional ability, and muscle strength of the affected arm [13,15]. In all of the reported randomized controlled trials testing robot-assisted rehabilitation of hand function against dose-matched conventional therapy, the group receiving robot-assisted rehabilitation showed similar to larger improvements than the control groups [17,32,47,51,55], without reporting any adverse events linked to the use of robotic technology in rehabilitation. Hand rehabilitation robots were well tolerated and safe both in subacute and chronic stroke patients with various levels of impairment. Overall, the results of these studies support the feasibility of using robotic systems to advantageously complement conventional rehabilitation in clinical settings.

Most studies reported a decrease in arm impairment as a result of robot-assisted hand rehabilitation, which translated to gains on the Fugl-Meyer motor assessment scale for the upper extremity (FMA) [56]. For illustrative purposes, Fig. 2 provides an overview of the changes in FMA reported in the studies that used this scale as

Table 1 Overview of clinical studies investigated robot-assisted rehabilitation of hand function

Device (type)	Study (country)	Study type (protocol)[a]	Sample size (type)	Principal findings
Hand Mentor (EXO)	Kutner et al. [46] (United States)	RCT (30 h robot-assisted wrist and finger extension combined with 30 h repeated task practice vs 60 h repeated task practice, 60 h over 3 weeks)	17 (subacute stroke with severe hand impairment)	Significant improvements were observed in both groups in terms of: (1) hand function (SIS) (2) activities of daily living (SIS) The group receiving robot-assisted therapy had greater increase in rating of mood, and significant improvements in stroke recovery (SIS)
X-glove (EXO)	Fischer et al. [27] (United States)	Pilot study (passive cyclic stretching of thumb and fingers using the robot (30 min), followed by intense active training according to a task-oriented protocol (60 min), 15 sessions, 3 days/week)	13 (subacute stroke with severe hand impairment)	Significant improvements were observed in terms of: (1) reduction of arm impairment (FMA) (2) pinch and grip strength (3) upper limb and hand function (ARAT, CAHAI-9, and WMFT) No change in spasticity was observed (MAS) No increase in finger extensor strength was observed
Gloreha (EXO)	Vanoglio et al. [17] (Italy)	RCT (passive finger mobilization with the robot vs time-matched conventional hand therapy, 30 sessions, 5 days/week)	27 (subacute stroke)	Significantly greater improvements in the robot group were observed in terms of: (1) reduction of arm impairment (MI) (2) grip and pinch strength (3) fine manual dexterity (NHPT)
PneuGlove (EXO)	Connelly et al. [32] (United States)	RCT (grasping and manipulation tasks in VR exercises and with real objects with active assistance using the robot vs no robot, 18 sessions, 3 days/week)	14 (chronic stroke)	Significant improvements were observed in both groups in terms of: (1) reduction of arm impairment (FMA) (2) reduction of hand/wrist impairment (FMA-WH) (3) grip strength (4) upper-limb function (BBT) Although not statistically significant, the robot group showed greater mean improvement on each of these measures
PneuGlove (EXO)	Thielbar et al. [47] (United States)	RCT (individuated finger training using a VR game and finger extension assistance with the robot vs dose-matched task-oriented occupational therapy, 18 sessions, 3 days/week)	14 (chronic stroke)	In the robot group, significant improvements were observed in terms of: (1) reduction of arm impairment (FMA) (2) hand function (JTHFT) (3) finger individuation Improvements in all measures were at least as good for the robot group. The two measures most closely assessing hand motor control (JTHFT and ARAT) showed superiority for the robot group

VAEDA (EXO)	Thielbar et al. [28] (United States)	RCT (voice and EMG-triggered robotic assistance in finger extension vs conventional hand therapy, 18 sessions, 3 days/week)	22 (chronic stroke)	Significant improvements were observed in the robot group in terms of: (1) hand motor control (CMSA) (2) hand function (WMFT) Nonsignificant reduction of arm impairment (FMA) No significant change in conventional therapy group
Hand of Hope (EXO)	Hu et al. [20] (Hong Kong)	Pilot study (EMG-driven robotic assistance during object grasp/release and transportation, 20 sessions, 3–5 days/week)	10 (chronic stroke)	Significant improvements were observed in terms of: (1) reduction of should/elbow impairment (FMA-SE) and hand/wrist impairment (FMA-WH) (2) reduction of spasticity (MAS) (3) upper limb and hand function (ARAT and WMFT)
Hand of Hope (EXO)	Susanto et al. [48] (Hong Kong)	RCT (reach-to-grasp and object manipulation tasks with assistance from the robot vs no assistance from robot, 20 sessions, 3–5 days/week)	19 (chronic stroke)	Significant improvements were observed in both groups in terms of: (1) reduction of arm impairment (FMA) (2) upper limb and hand function (ARAT and WMFT) Improvements in subparts of the WMFT scores related to dexterity were found to be significantly higher in the robot group immediately after the intervention
HWARD (EXO)	Takahashi et al. [24] (United States)	RCT (grasp-release exercises and VR game involving grasping and wrist movements with robotic assistance vs "partial" assistance where the robot only assists in half of the sessions, 15 sessions, 5 days/week)	13 (chronic stroke)	Significant improvements were observed in both groups in terms of: (1) reduction of arm impairment (FMA) (2) reduction of hand/wrist and shoulder/elbow impairment (FMA-WH and FMA-SE) (3) upper limb and hand function (ARAT and BBT) Decrease in spasticity (MAS), improved dexterity (NHPT), and strength were observed but were not significant Results suggest greater gains for subjects receiving higher dose of robot-assisted therapy
HEXORR (EXO)	Godfrey et al. [25] (United States)	Pilot study (passive stretching followed by VR exercises focusing on active finger flexion and extension with assistance from the robot, and isometric training, 18 sessions, 2–3 days/week)	8 (chronic stroke)	Significant improvements were observed in terms of: (1) grip strength (2) reduction of hand/wrist impairment (FMA-WH) Nonstatistically significant improvements in upper-limb function (ARAT and BBT) and a decrease in impairment (FMA) were further observed

Continued

Table 1 Overview of clinical studies investigated robot-assisted rehabilitation of hand function—cont'd

Device (type)	Study (country)	Study type (protocol)[a]	Sample size (type)	Principal findings
FINGER (EXO)	Rowe et al. [26] (United States)	RCT (index and middle finger movements within a VR game with high robotic assistance vs low robotic assistance, 9 sessions, 3 days/week)	30 (chronic stroke)	Significant improvements were observed in both groups in terms of: (1) reduction of arm impairment (FMA) (2) lateral pinch and three jaw pinch strength (3) upper limb and hand function (ARAT and BBT) (4) reduction of depression scores No statistically significant difference in terms of upper-limb function (BBT) increase between groups, but high assistance increased subjects' motivation and secondary motor outcomes
ReHapticKnob (EE)	Metzger et al. [49] (Switzerland)	Pilot study (neurocognitive exercises involving grasping and pronation-supination with assistance/resistance from the robot, 16 sessions, 4 days/week)	6 (subacute stroke)	Improvements were observed in terms of: (1) reduction of arm impairment (FMA) (2) active range of motion and hand sensory function
AMADEO (EE)	Sale et al. [50] (Italy)	Pilot study (finger flexion and extension exercises including passive stretching, active-assisted movements, and VR-based active task-oriented games, 20 sessions, 5 days/week)	7 (subacute stroke)	Significant improvements were observed in terms of: (1) flexor and extensor finger muscle strength (MRC) Nonstatistically significant reduction in arm impairment (FMA and MI) and spasticity was further observed
AMADEO (EE)	Orihuela-Espina et al. [51] (Mexico)	RCT (robot-assisted therapy composed of passive stretching and active-assisted or resisted tasks vs matching occupational therapy program, 40 sessions, 4–5 days/week)	17 (subacute stroke)	Significant improvements were observed in both groups in terms of: (1) reduction of hand/wrist impairment (FMA- WH and prehension section of MI) Improvement in FMA-WH was significantly larger for the group receiving robot-assisted therapy

AMADEO (EE)	Hwang et al. [52] (Korea)	RCT (active robot-assisted finger flexion and extension exercises (4 weeks) vs passive stretching (2 weeks) followed by active assisted (2 weeks), 20 sessions, 5 days/week)	17 (subacute to chronic stroke)	Significant improvements were observed in both groups in terms of: (1) reduction of hand/wrist impairment (FMA-WH) (2) grasping and pinching strength (3) hand function (JTHFT) Higher intensity of active-assisted therapy led to significantly higher reduction of hand/wrist impairment and improvement of hand function Nonsignificant reduction in upper arm impairment (FMA-SE)
AMADEO (EE)	Stein et al. [53] (United States)	Pilot study (active robot-assisted finger flexion and extension exercises, 18 sessions, 3 days/week)	12 (chronic stroke)	Significant improvements were observed in terms of: (1) reduction of arm impairment (FMA) (2) increased ROM (3) hand function (JTHFT) (4) self-reported activities of daily living (MAL) Nonstatistically significant increases in finger strength in flexion and extension were observed
Rutgers Master II (EE)	Merians et al. [36] (United States)	Pilot study (VR games involving grasping and finger individuation, 13 sessions, 4–5 days/week)	8 (chronic stroke)	Significant improvements were observed in terms of: (1) hand function (JTHFT) (2) finger fractionation, thumb and finger range ROM and speed
HapticKnob (EE)	Lambercy et al. [54] (Singapore)	Pilot study (active grasping and pronation-supination VR-based exercises with assistance/ resistance applied by the robot, 18 sessions, 3 days/week)	13 (chronic stroke)	Significant improvements were observed in terms of: (1) reduction of arm impairment (FMA and MI) (2) reduction of hand/wrist and shoulder/elbow impairment (FMA-WH and FMA-SE) (3) reduction in spasticity (MAS) (4) hand function (MS)
HapticKnob (EE)	Ang et al. [55] (Singapore)	RCT (EEG-triggered (passive) vs active grasping and pronation-supination with the robot vs occupational therapy, 18 sessions, 3 days/week)	21 (chronic stroke)	Significant improvements were observed in all three groups in terms of: (1) reduction of arm impairment (FMA) (2) reduction of hand/wrist and shoulder/elbow impairment (FMA-WH and FMA-SE) Both groups involving the robot had significantly higher changes compared with occupational therapy

[a] *If not specify otherwise, a therapy session is 45–60 min.*
ARAT, *action research arm test;* BBT, *box and block test;* CAHAI, *Chedoke arm and hand activity inventory;* CMSA, *Chedoke-McMaster stroke assessment;* EE, *end effector;* EEG, *electroencephalography;* EMG, *electromyography;* EXO, *exoskeleton;* FMA, *Fugl-Meyer assessment for the upper extremity;* FMA-SE, *subpart of the Fugl-Meyer assessment for shoulder and elbow;* FMA-WH, *subpart of the Fugl-Meyer assessment for wrist and hand;* JTHFT, *Jebsen-Taylor hand function test;* MAL, *motor activity log;* MAS, *modified Ashworth scale;* MI, *motricity index;* MRC, *Medical Research Council scale for muscle strength;* MS, *motor assessment scale;* NHPT, *nine-hole peg test;* RCT, *randomized controlled trial;* SIS, *stroke impact scale;* VR, *virtual reality;* WMFT, *Wolf motor function test.*

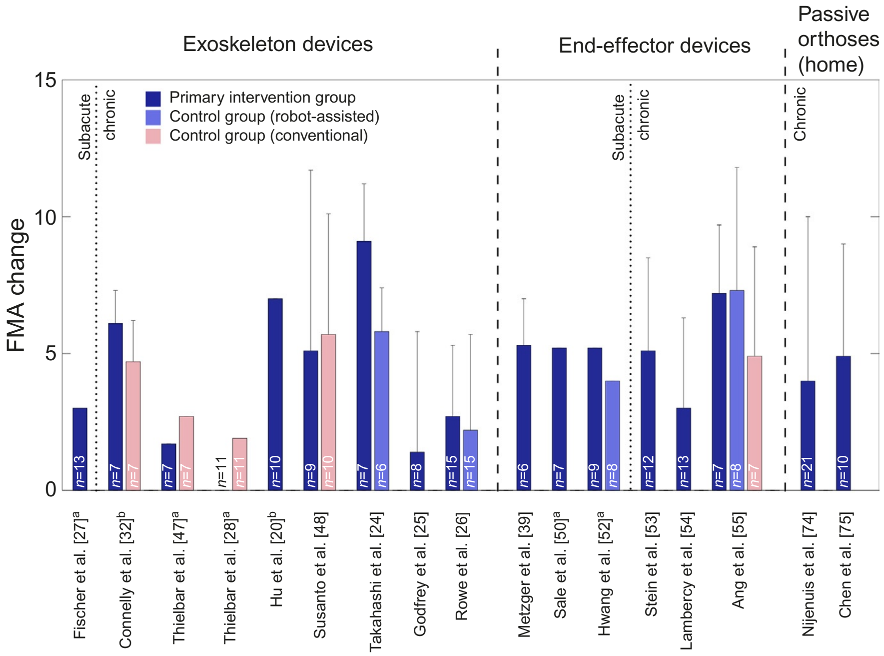

FIG. 2

Overview of the changes in upper-limb impairment (mean ± std out of 66 pts), as measured by the Fugl-Meyer assessment (FMA) for the upper extremity in studies investigating robot-assisted rehabilitation of hand function using the FMA as outcome measure. For randomized controlled studies, both intervention and control groups are reported. For details on the study protocols, please refer to Table 1, [a]std not available; [b]estimate from a figure (numerical data not available).

outcome measure. Nine studies reported average gains above 5 points on the FMA (and up to 9.1 points), which is considered to represent a clinically meaningful change [57]. Nevertheless, these results should be interpreted with care, as most studies still have limited numbers of participants (i.e., typically below 15 per intervention group) and are very heterogeneous. Not only the robotic devices but also study protocols (i.e., type of patients, intensity and duration of intervention, and inclusion and exclusion criteria) are highly variable across studies. It should also be kept in mind that the robotic devices presented in these studies are likely to target a specific subpopulation of stroke patients for which they were optimized and for which the reported clinical trials were designed, resulting in a possible bias.

Training with robotic devices at the level of the hand and fingers seems not only to have positive effects on the distal arm but also to lead to significant improvements at the level of the elbow and shoulder [20,24,48,53–55]. In our work with the HapticKnob end-effector robot, significant improvements were observed on both distal and proximal subparts of the FMA following a 6-week/18-session therapy program in chronic stroke patients, despite a robotic device only interacting with the fingers of the subject. A possible reason for this could stem from the indirect shoulder and elbow contributions required to control and stabilize the arm position while interacting with an end-effector device [54]. This could lead to generalized activity of the impaired arm and corresponding neural pathways [53]. These results support the hypothesis that proximal joints may benefit from exercising distal joints of the arm [10,58] and in general speak in favor of including rehabilitation exercises involving hand movements as early as possible in the rehabilitation program of stroke patients.

TRAINING MODALITIES TO RESTORE HAND FUNCTION AND PROMOTE INCREASED INTENSITY

Passive stretching was used in several studies, as robotic devices are well suited to provide this type of assistance, in particular for finger extension. Passive stretching can contribute to reducing hyperexcitability of finger flexor muscles commonly observed in stroke patients [17,27]. Early after stroke, robotically induced passive movements could be a first step to stimulate the hand and the related somatosensory pathways and help decrease muscle hyperexcitability [59]. Passive motor training could also be associated to active sensory tasks, in which the patient has to identify, for instance, the size of different objects or the positioning of his/her arm/hand [39]. For moderate to severely impaired stroke patients, this training modality could further be included into rehabilitation sessions as a facilitator for subsequent active movement training involving finger flexion [27,59].

In stroke patients with mild to moderate hand impairment, the therapy focus is typically on repetitions of active hand movements (primarily grasping). Robotic assistance can facilitate finger movements, help to increase muscle strength, and train the functional use of the hand by simulating activities of daily living through sensory and/or motor interactions with virtual objects or more complex environments. Thanks to the robotic assistance, even patients with severe impairment can actively engage in exercises and perform a high number of active hand movements. Rowe et al. reported that patients performed up to 900 finger movements per therapy session [26] while Godfrey et al. reported about 200 movement repetitions per session in stroke patients with severe hand impairments [25], which favorably compare with the intensity reported in typical sessions of conventional therapy (i.e., less than 50 repetitions) [60].

THE CLINICAL NEED FOR SIMPLE DEVICES

From an engineering perspective, the robotic devices that were tested in clinical studies are simple systems with a limited number of DOFs, requiring little setup time. While exoskeletons are becoming more and more popular, many of them still face important usability challenges. First, donning an exoskeleton and ensuring that all joints are properly aligned with the mechanical structure of the device can be a time-consuming task requiring trained experts. As the time available for a therapy session is typically limited, this can become a strong barrier for the clinical acceptance of hand exoskeletons. Second, it is necessary to precisely adapt the dimension of an exoskeleton to the dimensions of the hand of each individual patient to ensure physiologically correct movements. Depending on the system, this could be done by adjusting a few parts in the mechanical structure of the exoskeleton or proposing devices of different standard sizes (e.g., gloves), up to the complete parametrization of the exoskeleton components to each individual user [34]. Third, mechanisms supporting thumb movements are often based on the same approach adopted for other fingers (e.g., assisting flexion/extension) without considering thumb opposition or are not even implemented. Thumb modules with more DOFs or that combine flexion/extension and thumb opposition through passive components have been proposed; however, these approaches considerably increase complexity and weight [61,62]. Finally, the weight of a portable hand exoskeleton added to the upper limb of a patient can lead to increased difficulty in using the impaired arm. This is especially relevant for devices targeting applications where the exoskeleton should ideally be worn for a long period of time (e.g., as an assistive device in activities of daily living). As a result, most technology developers focused on optimizing the weight of the mechanical components used in hand exoskeletons (e.g., using polymers or additive manufacturing) or moving the actuators, which typically account for most of the weight, away from the hand using remote actuation systems [28,63].

Ultimately, the selection of the most suitable hand rehabilitation device and training modality strongly depends on each individual patient and their level of impairment. Simple hand exoskeletons that can be used at the bedside to provide passive hand opening could be valuable tools to provide early rehabilitation. Robotic arm devices that include a hand module may be an ideal solution for patients with severe arm impairment, allowing to compensate for the weight of the arm and facilitate the use of the hand and arm in the training of functional tasks. These could progressively be replaced by passive gravity support systems (e.g., SaeboMas, Saebo Inc, United States) used in combination with simple exoskeletons focusing on training hand function or with real objects (e.g., Gloreha, Idrogenet, Italy). Stationary end-effector robots that can generate high assistive/resistive forces and more refined haptic effects can advantageously be used to complement rehabilitation sessions with challenging exercises performed under supervision of trained therapists. Finally, wearable exoskeletons could help to assist hand movements (e.g., grasping) in daily life for patients with less severe impairment or provide solutions to continue hand training after discharge. Covering all these aspects and catering for the needs of every patient with a single-hand rehabilitation robot do not seem realistic. It is therefore suggested to use a combination of simpler robotic platforms that are dedicated to the training of a specific task or for a subgroup of patients for which the design of the robot and the rehabilitation exercises can be optimized.

POTENTIAL TO FURTHER PROMOTE RECOVERY THROUGH ROBOT-ASSISTED THERAPY OF HAND FUNCTION

Apart from increasing the intensity and providing well-controlled and repeatable assistance, robots can provide additional unique features that could improve hand rehabilitation. First, the assistance provided during robot-assisted therapy can be inferred from the intention of the patient (e.g., EMG [20,28,64] or brain activity [55,65]), with the goal of closing sensorimotor loops. Linking the intention to perform a movement (i.e., voluntary activation of the neural pathways responsible for the movement) with the sensory consequences could help strengthening the neural circuits involved in the planning and execution of a task [66]. Second, robots typically quantify motion and forces applied by patients, allowing for the extraction of objective and quantitative metrics that can describe the functional ability or impairment level of a patient [67]. Such metrics could be implemented in dedicated robotic assessments to provide more sensitive alternatives to clinical scales or to evaluate the performance of a patient within a therapy session (or even over a few trials) and automatically adjust specific training parameters (e.g., level of assistance or exercise difficulty) to maintain training motivation and challenge [49,68]. Third, robotic devices can provide well-controlled and repeatable haptic stimuli offering unique opportunities to train somatosensory perception as part of hand rehabilitation exercises and to assess the evolution of somatosensory deficits [69,70]. Sensory and motor functions are tightly linked, and somatosensory deficits in the arm and hand may impede motor recovery [71]. In their work with the FINGER robot, Rowe et al. underlined that subjects with impaired finger proprioception had poorer recovery in terms of hand functional ability [26]. Rehabilitation that includes meaningful somatosensory stimulation at the level of the hand should therefore be further developed [72,73]. In this direction, the RehapticKnob proposed therapy exercises where patients were asked to actively or passively interact with virtual objects rendered by the robot and identify certain object properties (e.g., stiffness, shape, or position) by purely relying on the somatosensory inputs from their arm and hand. A pilot study suggested that this approach is feasible and well tolerated and can help reduce arm impairment as well as improve hand somatosensory function (as measured by robotic assessments) [49].

Finally, arguably, the most exciting opportunity of rehabilitation robots is to provide platforms that can be operated with minimal supervision from therapists or engineers, to support therapy in the home of patients, or to provide additional therapy during the spare time in the clinic. Conceptually, this is a promising way to increase the dose of therapy without the financial burden of longer hospitalization stays. However, it raises other questions related to the safety of unsupervised robot-assisted therapy and the willingness and ability of patients to comply with such home rehabilitation programs involving the use of technology. So far, passive hand orthoses have been tested to support therapy sessions at home for chronic stroke patients. These devices typically use springs of different stiffness to provide an assistive force in finger extension to facilitate object grasping. The SCRIPT orthosis was tested in 24 chronic stroke patients with impaired arm/hand function who trained in their home environment for 6 weeks. Patients trained close to 2 h/week on average with the device, which is considerable given that no specific training schedule was enforced [74]. The HandSOME passive hand orthosis was also tested in a home rehabilitation study focusing on reaching and grasping movements with 10 chronic stroke patients who were asked to train for 90 min/day and 5 days/week for 6 weeks [75]. In both of these studies, hand rehabilitation facilitated by unpowered devices led to a reduction of upper-limb impairment and improved functional ability (Fig. 2).

While demonstrating feasibility of unsupervised hand rehabilitation with passive orthoses, these studies also highlighted limitations in terms of usability (e.g., required time or effort to don the device without assistance and robustness of the hardware/software) that led to high intersubject variability in the amount of use and in some cases to rejection of the technology. These are critical points to take into account for the development of hand rehabilitation robots in general but even more when developing active robotic devices for home rehabilitation. Simple and cost-effective active devices for home rehabilitation would open new avenues for increasing therapy dose and promote hand use, but it is clear that such tools will only be accessible for mildly to moderately impaired patients who have some level of arm function and are able to operate a robotic device.

CONCLUSIONS

This chapter provided an overview of the emerging field of robot-assisted rehabilitation of hand function after stroke, presenting different design approaches for the development of rehabilitation robots to train sensorimotor hand and finger function and reviewing the evidence from clinical trials. Hand and finger functions are crucial for independence in everyday activities, but their recovery is often rather limited following stroke, motivating the need for novel therapeutic and assistive tools. While a number of interesting and exciting engineering developments have been proposed, still, only too few of the existing hand rehabilitation devices have been tested with end users for feasibility and even less evaluated for clinical efficacy. This underlines the need for investing more effort into clinical validation of robotic technology and the underlying therapy concepts they promote, before developing further robotic devices. Finding the appropriate trade-off between the complexity of robotic devices for hand rehabilitation (e.g., design approach, number of actuated DOFs, and interface with the user) and the functionalities they can support (e.g., type of movements/tasks and level of assistance) is key to ensure usability and acceptance by both therapists and patients. The evidence gathered from 19 clinical studies focusing on robot-assisted hand rehabilitation is promising, confirming the potential of robotic devices to complement conventional therapy through intensive and physically engaging training. The majority of studies report positive effects of robotic training on the reduction of hand and arm impairment, with improvements in strength and hand functional abilities that are equivalent or slightly superior to dose-matched conventional therapy. Nevertheless, more evidence is needed to confirm these results with larger patient groups and more homogeneous study protocols. With the ability to adapt rehabilitation parameters based on physiological signals or objective and sensitive metrics reflecting the state and performance of a patient, the unique possibility to combine motor and somatosensory training, and the perspective of simple and wearable tools for home rehabilitation, robotic devices promise further potential for the rehabilitation of hand function in neurological patients.

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CHAPTER

Robot-assisted gait training

16

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INTRODUCTION

Stroke remains a major source of permanent disability worldwide [1]. Almost two-thirds of all stroke survivors (around 300,000 per year in the United States [2]) have lost or limited ability to walk independently [3]. Similarly, patients affected by a traumatic spinal cord injury (SCI) (around 10,000 per year only in the United States) experience a significant reduction in their walking ability [4]. In order to regain part of their former walking ability, patients suffering from a movement disorder should engage in an intensive and expensive neurorehabilitation process. Some conventional physiotherapy treatments are specially promising, particularly those that focus on high-intensity [5] and repetitive task-specific practice [6]. Body-weight-supported treadmill training (BWSTT) is a highly repetitive task-specific training approach where patients walk on a treadmill with their body weight (partially) supported while one or more therapists manually guide their limbs in a normative gait pattern. Many rationales can be given for guiding exercises, none extensively verified in scientific studies. Guided exercises help prevent stiffening of soft tissue and reduce spasticity [7] and provide novel somatosensory stimulation that helps induce brain plasticity [8]. Additionally, creating a normative pattern of sensory input will facilitate the motor system in reestablishing a normative pattern of motor output. Repetition of this normal pattern will reinforce it, improving unassisted motor performance [9].

BWSTT has been shown to improve gait and lower-limb motor function in patients with locomotor disorders, particularly in SCI and stroke patients [10,11]. A recent randomized controlled study with 408 stroke patients (the LEAPS study) demonstrated that BWSTT followed by overground training was superior to usual care in improving walking [12]. However, BWSTT therapy is labor-intensive, often requiring more than two therapists—in an ergonomically unfavorable posture—to support the patient. As a result, the training duration can be limited by the endurance of the therapists, reducing the potential of BWSTT, as longer training sessions and longer total training duration have been shown to have a positive effect on motor recovery [5].

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There is increasing interest in using robotic devices to provide more cost-effective rehabilitation therapy [13,13a]. During robotic gait training, the patients are assisted with partial body-weight support, while a robotic device provides physical guidance to move the patients' legs into a correct gait pattern. The greatest benefit of robotic gait training is the possibility of increasing the training intensity (i.e., the duration and number of training sessions) in a safe environment. One therapist may be able to train two or more patients at once, resulting in a significant reduction in personnel costs. Furthermore, the robot could provide highly repetitive, measurable, and comparable quantitative assessment of the rehabilitation process using the sensors embedded into the system [14]. Finally, robot-assisted gait training can incorporate other technologies (e.g., virtual reality and brain-machine interfaces) in order to increase the patient's engagement and the motivation to participate in the (generally) long rehabilitation programs [15,16].

On the other hand, robotically guiding movements also appear, in some cases, to promote a decrease of patients' physical effort during training. Individuals with incomplete SCI (iSCI) who walked in a gait training robot that was controlled with a stiff assistive controller consumed 60% less energy than during traditional manually assisted therapy [17]. These findings suggest that robotic-guided training could potentially decrease recovery if it encourages slacking, that is, a decrease in motor output, effort, energy consumption, and/or attention during training [18]. Therefore, a commonly stated goal in robot-assisted gait training is to use patient-cooperative control strategies that aim to encourage patients' effort and self-initiated movements [13,19].

Although robot-aided gait training was presented as a promising technique to improve patients' walking ability more than 20 years ago [20], up to date, there are only few clinical studies that have compared robotic gait training with conventional rehabilitation techniques [21–23].

EXAMPLES OF GAIT REHABILITATION ROBOTS

Active gait rehabilitation robots are equipped with electromechanical, pneumatic, and other drives to actively move the patients' limbs. Most motorized rehabilitation robots are powered by electromagnetic motors [24]. The motor torques can be applied directly at the joints [24] or transmitted via Bowden cables in order to reduce the robot inertia [25]. Pneumatic actuators are especially compliant: large forces can be transmitted from the valves to the moving parts to reduce inertia [26]. However, dead times and nonlinear friction forces can make the control of pneumatic actuators very challenging [27].

EXOSKELETAL ROBOTIC SYSTEMS

The mechanical structure of an exoskeletal robot resembles the human limb anatomy, as the robot's joints usually correspond with the human's joints. The exoskeleton is attached to the patient's limbs at several points, usually through cuffs, and guides the body limbs by enforcing determined body postures. This makes the adaptation to different body sizes challenging because the length of each robot segment must be adjusted to the respective limb length of the participant and the anatomical human and robotic joint axes must be well aligned.

The pioneer exoskeletal gait rehabilitation robot, the "Lokomat," was developed in 1995 at the Spinal Cord Injury Center of the Balgrist University Hospital in Zurich, Switzerland [20]. The Lokomat (Hocoma AG, Switzerland) is a bilateral gait orthosis that is used in conjunction with a body-weight support system and a treadmill (Fig. 1, left) [28]. Each orthosis has one linear drive in the hip joint and one in the knee joint to induce flexion and extension movements in the sagittal plane. Passive foot lifters support ankle dorsiflexion during the swing phase. Each orthosis is fixed to the body-weight support system frame that allows passive vertical translations of the orthoses while keeping the orientation of the robotic pelvis segment constant. The Lokomat can passively move the patients' legs by means of conventional position control that follows predefined hip and knee joint trajectories [24]. Patient-robot interaction torques can be determined from the measurements of the force sensors located between the linear drives and the orthoses. These interaction torques can be employed to estimate the voluntary effort produced by the patient to be used in patient-cooperative control strategies (e.g., impedance control). The advanced mechatronic body-weight support system, the "Lokolift," combines passive elastic and active dynamic systems that allow for a constant unloading of patient weight during treadmill walking [29]. Newer versions of the Lokomat also provide lateral translation and transverse rotation of the pelvis, which allows for a more natural gait pattern and the possibility to practice balance. A pediatric Lokomat was designed and developed in 2006.

A similar commercially available device is the ReoAmbulator (Motorika Ltd., marketed in the United States as the AutoAmbulator), developed in cooperation with the HealthSouth network of rehabilitation hospitals at the United States. The ReoAmbulator comprises two actuated leg orthoses and is used in conjunction with a body-weight support system and a treadmill [30]. Each leg orthosis is actuated at the knee and hip joints to provide guidance in the sagittal plane. During training,

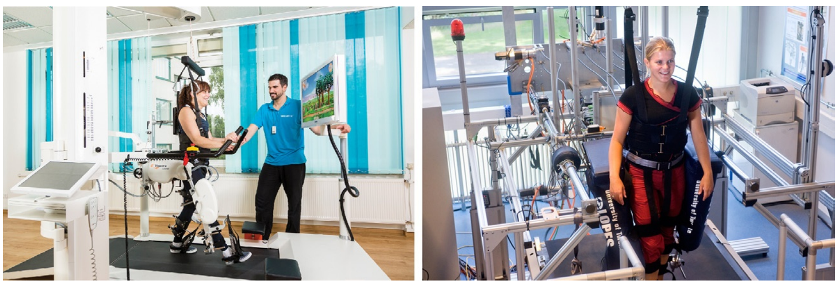

FIG. 1

Left: The commercialized gait orthoses Lokomat (courtesy of Hocoma AG, Switzerland). Right: The research gait exoskeleton LOPES (courtesy of H. van der Kooij, University of Twente).

multiple sensors perform continuous monitoring and adjustment of robotic guidance and speed (up to 3.2 km/h) depending on the patient's specific physical requirements. An interactive display with multiple virtual reality environments aims to increase patients' engagement. The product is suitable for both adults and children.

Pelvic motion is crucial to accomplish naturalistic gait movements. Therefore, several exoskeletal systems have been designed to allow rotation and/or lateral motion of the pelvis. For example, LOPES (lower-extremity powered exoskeleton) is an eight degree of freedom (DOF) treadmill-based robotic exoskeleton developed at the University of Twente that combines an actuated pelvis segment with a leg exoskeleton (Fig. 1, right) [25]. The pelvis can move in 3-D translations and is actuated in anterior-posterior and medial-lateral translational directions. The robotic legs have two actuated rotation axes at the hip (abduction/adduction and flexion/extension) and one at the knee. The robot joints and the medial-lateral pelvis translation are actuated with Bowden-cable-driven series elastic actuators, resulting in a lightweight and compliant robotic system. The joints are impedance controlled to allow patients to influence the robot's movements. The amount of impedance can be varied to allow different levels of robotic guidance based on patients' especial needs [25]. A new version, LOPES II, has been recently presented that actuates the same degrees of freedom but uses an end-effector approach with parallel actuation that eliminates the need for fine human-robot alignment [31].

Another exoskeletal system that allows for pelvic motion is the active leg exoskeleton (ALEX) [32]. The orthosis has several passive and actuated DOF with respect to a walker, which supports the weight of the device. The trunk of the orthosis (secured to the human trunk with a hip brace) is connected to the walker and allows for vertical and lateral translations and rotation about the vertical axis. The robotic legs have two rotation axes at the hip (passive abduction/adduction and actuated flexion/extension) and one actuated joint at the knee. The foot segment is attached to the shank and allows for passive plantar flexion/dorsiflexion ankle rotation. The flexible design of the foot segment also allows limited inversion-eversion motion at the ankle. Human-robot interaction torques can be measured via two force-torque sensors mounted at the orthosis interaction points. The device uses a force-field controller that resists undesirable leg motions and assists toward naturalistic gait motions.

A final example is the pelvic assist manipulator (PAM), a six DOF pneumatically operated robotic device exoskeleton developed at the University of California Irvine that assists human pelvic motion during BWSTT. The pneumatically operated gait orthosis was designed as an attachment to PAM to provide assistance to patient's legs during gait training using pneumatic linear actuators attached to a frame placed around the subject [26].

END-EFFECTOR-BASED ROBOTIC SYSTEMS

End-effector-based robots for gait training are connected to the participants' leg at the robot's end effector. Patients usually stand on footplates whose trajectories simulate the stance and swing phases of normal gait and/or stair ascent/descent. The main advantage of end-effector-based robots is that they are easy to adjust to different patients, since the human and robotic joint axes do not need to be aligned. A disadvantage is that, in general, the knee and hip joint angles are not fully determined by the robot because the patient and the robot interact just through one point. Therefore, individuals suffering from severe disabilities might still require from continuous assistance from at least one therapist.

One of the first commercially available footplate-based systems was the "gait trainer" (GT I), developed at the Free University Berlin, Germany, and currently commercialized by Reha-Stim, Germany [33]. The GT I uses a crank and rocker gear system to guide the feet (strapped into two footplates) simulating stance and swing phases. The robot is used in conjunction with a body-weight support system. The stride lengths and gait phase durations can be adjusted to each patient by exchanging the gear sizes. The GT I can adjust the robotic support according to the patient's ability, which is calculated based on the difference between the desired and measured patient's walking cadence. One of the mean limitations of the gait trainer is that it only has one DOF per leg. To overcome this limitation, the GT I was redesigned into the Haptic Walker to allow for three DOF per footplate (Fig. 2, left). The footplates of the Haptic Walker can be programmed to simulate walking on different surfaces, like walking on rough ground, climbing stairs, and even stumbling or sliding [34]. The Haptic Walker is able to perform walking trajectories in the sagittal plane with speeds of up to 5 km/h. However, its large and bulky mechanical design makes it hardly to be placed in a clinical setup.

The minimal preparation times and low operating costs compared with exoskeletal systems have increased the number of commercially available end-effector-based gait training robots [35,36]. An example is the commercially available G-EO robot, based on the technology developed in the Haptic Walker (Reha Technology AG, Switzerland) (Fig. 2, right). The G-EO consists of two footplates, which move each

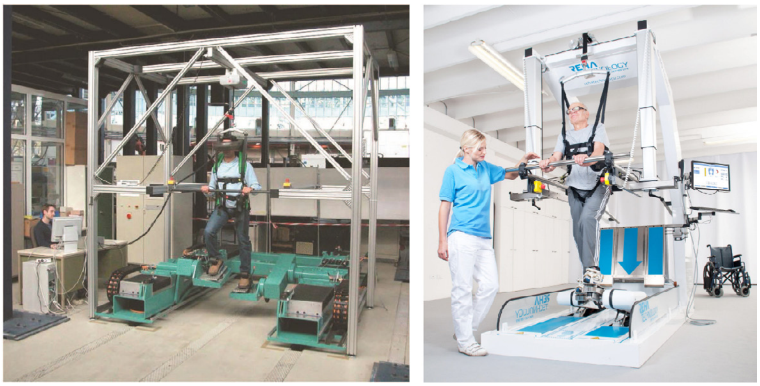

FIG. 2

Left: The Haptic Walker [34]. Right: The G-EO system gait training robot (courtesy of Reha Technology AG).

foot with three DOF and enables the training of simulated overground walking and stair climbing at a maximum speed of 2.3 km/h [35].

SYSTEMS SUPPORTING OVERGROUND GAIT TRAINING

Exoskeletal and end-effector-based robotic systems require that the desired feet trajectory is specified. However, there is no rigorous evidence that “normative” gait trajectories should be enforced in order to maximally stimulate brain plasticity. In fact, some studies have suggested that patients should enroll in more functional gait training exercises, such as free overground walking and balance training [23,37].

Mobile robotic systems may help patients to train more functional ambulatory tasks by relieving them from part of their body weight during training while providing a safe environment by catching them in case of falling or stumbling. One example is the KineAssist (Kinea Design, Evanston, USA), a mobile robotic base that provides partial body-weight support and postural control on the torso; allows many axes of motion of the trunk and pelvis; follows the patient's walking motions overground in forward, rotation, and sidestepping directions; and leaves the patient's legs accessible in order to allow assistance from physical therapists [38]. Another mobile robot example is the recently developed Andago (Hocoma AG, Switzerland) (Fig. 3, left). The patient wears a harness, which is connected via ropes to the frame of the device that supports her/his body weight. The robotic frame has two electrically driven wheels and four casters for moving forward, backward, and turning according to the patient's intention. The dynamic electrically operated lifting system

FIG. 3

Left: The mobile robotic system Andago (courtesy of Hocoma AG, Switzerland). Right: Suspension robotic FLOAT (courtesy of Lutz Medical Engineering GmbH, Switzerland).

can continuously adjust the patient's weight support even from a sitting position and during step and balance training.

Suspension robotic systems are special body-weight support systems based on robot cable technology that allows for overground gait training without suffering from undesired interaction forces, such as inertia. One example is the ZeroG, which provides support by means of a trolley that runs on a rail and contains a pulley mechanism [39]. The FLOAT, developed by Lutz Medical Engineering together with Balgrist University Hospital and ETH Zurich, Switzerland, is a more advanced system that allows for 3-D gait training in a large workspace [40] (Fig. 3, right). Four ropes are spanned by winches and guided over pulleys to a single node on the participant's harness. The system can control the position and forces acting on the patient, supporting training of functional tasks, such as free walking, sitting/standing, and stair climbing.

Powered robotic exoskeletons are multi-DOF wearable electrically actuated exoskeleton devices that strap to the patient's legs [41]. Although these robots have been primarily designed to assist specially weak SCI patients in walking, recent research has presented them as an alternative intervention for overground gait rehabilitation [42]. Powered robotic exoskeletons, though similar in structure to treadmill-based robots, differ in that they require active participation from the user for both swing initiation and foot placement [41]. Therefore, exoskeletons have a great potential to promote brain plasticity and recovery [23,37]. Several powered exoskeletons are already commercially available, such as the Ekso (Ekso Bionics, USA), the ReWalk (ReWalk Robotics, Israel), and the hybrid assistive leg (HAL) (Cyberdyne, Japan).

CONTROL STRATEGIES

The most extended control algorithm in robot-assisted gait training is to physically move the patients' legs in a normative gait pattern during walking, a strategy similar to "active assist" exercises performed by therapists. The first proposed assistive controllers were proportional (plus derivative) (PD) feedback position controllers: as the participant moves away from the desired trajectory, the controller assisting force increases proportionally [28]. However, research on motor learning has emphasized that movement errors and movement variability are fundamental signals that drive motor adaptation [43,44]. One study in spinal-injured mice found that allowing variability around the desired trajectory during robotic gait training improved the stepping ability faster than those trained with a stiff position control [44].

Impedance control allows a variable deviation from predefined trajectories [25]. An adjustable assisting torque is applied depending on the deviation of the current position from the desired trajectory and the patient's effort (e.g., measured using force/torque sensors). Recent controllers (e.g., path control) have also included a deadband or "virtual tunnel"—i.e., a volume around the trajectory in which no assistance is provided—to allow normal human variability [32,44,45].

Novel controllers have been developed based on the common clinical practice of therapists: they provide just enough guidance to allow patients to practice the task while reducing the assistance as participants improve their skills. Several adaptive strategies have been proposed that provide "assistance-as-needed" of the form:

$$P_{i+1} = f P_i + g e_i \tag{1}$$

where P_i is the control parameter that is adapted (e.g., the robot impedance), i refers to the ith movement, and e_i is a performance error (e.g., the patient's ability to track a movement). The constants f and g denote the forgetting and gain factors. If f is chosen such that $0 < f < 1$, then the algorithm reduces the control parameter when the error is small, with the effect of always challenging the patient. An adaptive algorithm of this form was successfully applied to adapt the workspace-dependent impedance of a gait-assisting robot during training in individuals with iSCI [46]. Adapting control parameters is also a key part of the "patient-cooperative" training strategies developed for the Lokomat, in which the robot takes into account the patient's effort [19].

CLINICAL OUTCOMES

Gait rehabilitation robots reduce the labor-intensive demands on therapists, compared with manually assisted BWSTT [36]. They also enable the assessment of a patient's performance and progress [14]. Several studies have examined the effect of robotic gait training with the patients' baseline motor status used as their own control. However, only few clinical trials have compared robotic gait training with conventional rehabilitation techniques.

STROKE THERAPY

Positive effects of robotic gait training interventions have been found in stroke therapy. A clinical trial with 155 nonambulatory subacute stroke patients found that intensive locomotor training from the GT I plus physiotherapy resulted in significantly better gait ability compared with conventional physiotherapy alone [47]. A pilot study with 30 acute stroke patients compared impedance-based robotic assistance from the Lokomat plus conventional therapy with conventional physiotherapy alone and found significant improvements in functional ambulation for both training groups, but no significant difference between groups [48]. One recent study on 107 subacute and chronic stroke patients found that robotic training with the Lokomat combined with conventional therapy produced better improvement in a number of different stroke scales compared with conventional physiotherapy alone [49]. However, two recent studies [50,51] that compared training with Lokomat with conventional therapy in chronic and subacute stroke patients, respectively, found substantially greater improvements in walking speed, walking distance, and single-limb stance time from the conventional training. These studies, however, only included ambulatory patients and rigid controllers (e.g., position control and stiff impedance control).

In general, the best results have been noted when the robot was applied in conjunction with conventional therapy [48,52]. A recent Cochrane report [21] analyzed 23 clinical trials with 999 stroke patients from acute to chronic phase and concluded that people who received robotic-assisted gait training, such as provided by the Lokomat or the GT I, in combination with physiotherapy were more likely to achieve independent walking than people who received conventional gait training alone. Specifically, people in the acute phase seemed to benefit from robotic gait training, but people in the chronic phase did not gain any benefit. Furthermore, stroke survivors who were not able to walk at intervention onset seemed to benefit most from robotic gait training. Therefore, the potential of robotic gait training seemed to be greatest in the earlier stages of stroke, when patients could benefit from the higher degree of support from the robotic device. The role of the type of robotic device (e.g., exoskeleton vs end effector) is still not clear.

THERAPY OF SPINAL CORD INJURY AND FURTHER PATHOLOGIES

Robot-aided gait training has proved to also be feasible in a number of different pathologies such as iSCI [50,53,54], multiple sclerosis [55], and cerebral palsy [56].

Several studies showed improvements in walking ability in acute and chronic iSCI individuals who trained with robotic assistance [50,53,54]. However, there are only few controlled trials that compared the functional outcomes of robotic gait training with conventional rehabilitation techniques [52,57,58]. Recent systematic reviews concluded that, currently, there is no evidence that robot-assisted gait training improves walking function more than other locomotor training strategies in iSCI individuals [22,23,59]. A possible rationale for the observed limited effectiveness might originate from the rigid position controllers employed during training. Patient's effort during physical training is thought to be an important factor in order to provoke motor plasticity [60]. However, a reduction in energy consumption has been observed in individuals with iSCI who walked in a gait training robot that was controlled with a stiff assistive controller, compared with manually assisted therapy [17].

Recent pilot studies evaluated the feasibility of using novel controllers that encourage patients' effort and self-initiated movements [61,62]. For example, in a pilot study with 10 iSCI individuals, training with impedance controller from the exoskeleton LOPES led to improvements in walking ability, muscle strength, and quality of walking [61]. The feasibility of using path control with Lokomat was evaluated in a pilot study with two iSCI (and two stroke) individuals [62]. Patients presented more physiological muscle activity when training with path control compared with training with a noncooperative position control mode.

Only few clinical studies have compared different forms of gait-assisting robotic control strategies [44]. A novel control approach that allowed spinal-injured mice to move their hind limb freely within a moving window inside a virtual tunnel while walking on a treadmill was compared with a classical position control strategy. It was found that the number of steps and periodicity increased significantly more when the mice were trained with the moving window approach. This finding highlights the important concept that the specific form of robot control selected for a rehabilitation application does, indeed, matter.

CONCLUSION AND OUTLOOK

Although robot-aided gait rehabilitation has been presented as a promising rehabilitation technique, up to date, the functional gains obtained after robotic gait training are still limited [23,63]. In general, the best results have been noted when the robot was applied in conjunction with conventional therapy [48,52] and in more severely disabled persons [23]. Nevertheless, robot-assisted gait training is roughly as effective as conventional BWSTT therapy while requiring significantly less physical effort from the therapists [36]. However, the goal of rehabilitation robotics is not to simply automate current rehabilitation practices, but to optimize recovery. Therefore, we conclude by suggesting two directions for future research.

The first direction is to focus on performing randomized controlled clinical trials to rigorously compare robotic control algorithms with each other and with conventional physiotherapy. The specific control strategy selected for robot-assisted gait training seems to play a key role in rehabilitation outcomes [21,54,62,63]. However, the question of the most effective training strategy in robot-assisted gait training is still wide open.

A second direction is to initiate the use of more precision in defining which choice of technical features (robot structure, actuation, control algorithms, etc.) is most appropriate for which rehabilitation tasks, what types of neurological injuries, and at what stage of recovery. Tailoring the technical features to the patient-specific pathophysiology, recovery stage, and specific activity being trained may improve its therapeutic benefit.

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CHAPTER

17 Wearable robotic systems and their applications for neurorehabilitation

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INTRODUCTION

Several recent initiatives aim to assist human motion using mechatronic devices attached near or directly onto the actor's body. Such devices are often referred to as "exoskeletons," or otherwise "wearable robotics" when the structure is sufficiently "soft" or lightweight to be carried without other supporting structures. Contemporary systems are the heir to orthopedic equipment such as braces and orthoses. Wearable systems open new perspectives for rehabilitation in individuals with disabilities (stroke, spinal cord injury, muscle weakness, and other neurological or muscular disorders that can lead to difficulty in walking or making arm movements). Ideally, these systems could be used to facilitate independent training in the clinic or at home. They open the possibility for more continuous therapy and/or fitness training over extended periods, beyond inpatient clinical rehabilitation. This is particularly true concerning the less expensive solutions.

In general, robotic devices used in the field of disability target either rehabilitation or assistance. On one hand, fixed robotic stations are now largely used in the clinics for the rehabilitation of gait (e.g., Lokomat©) or upper-limb function (e.g., Inmotion© and Armeo©), particularly for patients suffering from spinal cord lesions, stroke, or other forms of acquired brain injury. On the other hand, the field of orthotics and prosthetics for patients with a permanent or progressive motor impairment such as amputation or muscular dystrophy is now increasingly relying on robotic innovations for their design and control. The potential use of wearable systems is by design intermediate between rehabilitation and assistance; the difference may only concern the duration of use on a daily basis or as a prolongation of the rehabilitation therapy. Home-based devices or wearable assistive systems enabling the performance of daily life or recreational activities (walking and video games) may prove to be the only way of increasing the dose of movement therapy enough to produce robust functional gains [1]. The long-lasting use of assistive wearable devices may lead to a modification of sensorimotor patterns with an improvement of abilities in the long term ideally leading to reduced dependence on the device itself and the eventual conclusion of the robot-assisted training program. So, the distinction between

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rehabilitation and assistance may not be pertinent concerning clinical populations who can functionally improve with practice (as is typically the case for patients with neurological conditions such as acquired brain injury or spinal cord injury). Ideally, wearable robotics should be autonomous systems allowing independent and ecological movements of the body in the environment. This excludes the mechatronic systems that are fixed to the ground or supported by a rigid frame or that depend on other environmental devices (e.g., virtual reality, large computing units, or fixed power sources). The present text will focus on the devices fitted in parallel with the body to assist a limb function, leaving out the field of prosthetics (devices fitted in series to replace a part of the body). We shall consider genuine robotic systems and other wearable solutions sharing with robotics sophisticated mechatronic systems, active or not, and/or augmented modes of control involving human sensorimotor regulation in the loop (hybrid systems). Although monitoring is an important element of wearable systems, we will not consider the countless wearable objects developed for general fitness and health [2].

Even with these restrictions, the field of wearable systems for rehabilitation is very wide and heterogeneous. It is at the convergence of clinical and bioengineering research developed to compensate for body weakness and applications in military and industrial fields to augment or preserve human performance [3]. The development of wearable systems is flourishing with many innovative technological solutions (such as soft robotics), but the human experiments remain scarce and few prototypes are evaluated and validated in a clinical sense. This text presents some examples and their potential clinical applications, but is in no way exhaustive or systematic.

TECHNOLOGICAL BARRIERS AND SCIENTIFIC CHALLENGES

COMPATIBILITY OF THE MECHANICAL STRUCTURE

The structure of a wearable robot must be interfaced to the human body that is itself a very complex anatomical and kinematic structure (review in [4]). Human movements consist of large and multiple joint rotations performed with fast dynamics and low friction. The axes of joint rotation are not fixed by reference to the adjacent bones, so it is not possible to replicate human kinematics with simple mechanical joints. For example, since the knee is not a hinge joint, the development of a motorized orthosis necessitates sophisticated passive mechanical links conferring sufficient degrees of freedom to allow for physiological motion and avoid excessive constraints on the soft tissues. Kinematostatic constraints are even more important when the orthosis has to fit several joints imposing that the two multilink chains (robot and human) are attached together. An alternative possibility is that of soft wearable systems based on compliant continuous structures [5] or new textile solutions [6].

ACTUATORS

The actuation of wearable devices must be able to generate a high level of forces and to follow, without perturbing, the human movements that are conflicting objectives.

Therefore, soft innovative mechanical transmission and actuation solutions had to be developed: pneumatic, hydraulic, Bowden-cable, or serial elastic actuators, combined or not with conventional electric actuations (review in [7]). In addition, the systems intended to be wearable impose that the power supply (or compressor for pneumatic and hydraulic solutions) should be silent, compact, and light enough to allow untethered use. Wearable systems often combine those diverse technological solutions. In addition, hybrid systems may incorporate functional electric stimulation of certain muscle groups.

SENSORS

The specific requirement of wearable systems is to permanently adapt to human motion. To this end, wearable systems use sensors commonly used in robotics (joint position, force, and pressure sensors) and wearable sensors used to capture human motion (particularly inertial measurement units, IMU) or physiological signals (EMG and EEG). Soft innovative sensors are drawing much attention: optical fibers, resistive bending sensors, MEMS, or innovative soft sensors [8]. Wearable systems also include instrumented clothing and e-textiles [9].

ENERGY EXPENDITURE

Besides technical, biomechanical, and ergonomic evaluation, the most straightforward metric to evaluate the efficiency of wearable systems should be the metabolic cost [9a], but this has rarely been studied in the framework of rehabilitation or assistance [10].

MAIN EXISTING DEVICES

RIGID SYSTEMS FOR ASSISTANCE TO A SINGLE JOINT

Lower limbs

Advances in the design of mechatronics systems have been used to improve the design and passive control of orthoses for people with moderate lower-limb weakness. The mechanical design must be very precise in order to adapt to the instantaneous position of the joint rotation axis that varies during motion and to regulate the position or the stiffness of the joint. For example, an innovative orthotic knee joint was designed, using a hydraulic valve that provides variable knee flexion resistance [12]. In addition, powered orthoses use active actuators to increase the joint torque at a precise timing of the gait cycle with the aim of reducing energy expenditure. The command must be adapted in real time to the human movement by means of embedded sensors used to decode and anticipate user's intended movements. Many laboratory prototypes exist, and several active knee orthoses are already available. They showed interesting functional performances for balance and gait in hemiparetic stroke survivors [13]. Another illustrative example is the actuated ankle joint orthoses addressing the drop-foot gait in hemiparetic patients ([14], Fig. 1A). This device

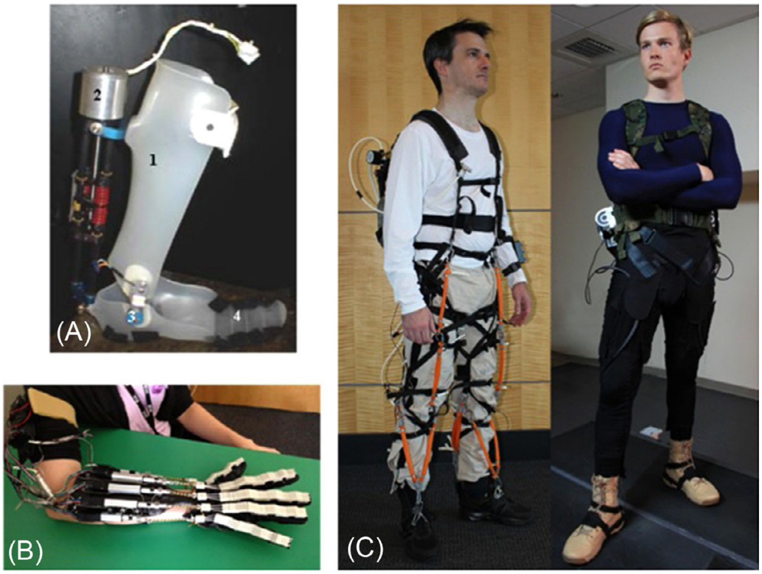

FIG. 1

(A) Ankle-foot orthosis with series elastic actuator [14] [(1) ankle-foot orthosis; (2) serial elastic actuator; (3) ankle-angle sensor; and (4) capacitive force sensors]. (B) The X-Glove, linear actuators provide extension forces according to tension sensor measurements in order to help open the hand [11]. (C) Left, pneumatic powered exosuit with control of the leg in the sagittal plane. Right, Bowden cables driven by geared motors multiarticular exosuit [7].

has its variable joint impedance minimized during the stance phase so as not to impede powered plantar flexion movements and controlled during swing to provide toe clearance. The mechanism of the slight reduction of energy cost and global biomechanical effect is complex (Mooney and Herr, 2016). Another wearable option for drop foot is controlled functional electric stimulation (FES) with external electrodes [15] or implanted systems [16] (e.g., Walkaid©, Bioness©, and Actigait©). Both powered orthoses and FES can improve the kinematic and kinetic parameters of the gait by reference to passive ankle-foot orthosis, but their respective clinical benefits remain to be investigated. The important challenges are to adapt the assistance of the wearable system: first to the phase of the gait cycle thanks to movement signals captured on the human body, second to changing environmental conditions (uneven ground), and third to the desired task (climbing stairs and running).

Upper limbs

A wearable robotic elbow brace controlled by electromyography was developed to provide assistance to elbow flexion and/or extension (Myomo©). Users must initiate muscle contraction or inhibition to trigger the device and modulate the degree of force assistance it provides [17]. A promising clinical study with the wearable device worn while engaging in various tasks at home demonstrated some improvements of the upper extremity impairment and quantity of use [18].

MULTILINK RIGID SYSTEMS FOR THE WHOLE LOWER LIMBS

Passive orthoses

Hip-knee-ankle-foot orthoses are designed to assist subjects with spinal cord injury (SCI) or severe limb weakness to stand and walk. More recent advances proposed passive coupling mechanisms between joints, allowing storage and return of energy at the hips (reciprocal gait orthoses, RGO) and/or constraining hip motion in the sagittal plane (hip guidance orthoses, HGO) to facilitate gait [19]. After a prolonged training, the walking speed of paraplegic patients has been observed to increase; nonetheless, the overall clinical benefit remains to be established [20]. The functional performance of these orthoses remains poor, the main problems being that of stability as users need crutches or a walker for balance support and, secondly, the excessive energy consumption they impose. In addition, users require assistance to don and doff these devices and as such do not currently represent a realistic long-term alternative to a wheelchair.

Powered orthoses and exoskeletons

Several teams added active actuators to the hip-knee-ankle-foot orthotic structures: electric [21], hydraulic [22], or pneumatic [10]. Powered orthoses aim at a better functionality, but the drawback is the extra weight imposed by the battery for energy supply. The actuators can be controlled thanks to various sensors (foot-ground contact, hip angles and angular velocities, and force sensors) and conventional robotic control laws adapting the orthoses mechanical behavior in function of the phase of the gait. Proof-of-concept studies in paraplegic patients showed that powered orthoses could improve walking speed and the kinematic and dynamic parameters of walking [21].

Simpler designs of orthoses involve the pelvis and both hips. This is the case of the Honda "walking assist©" that assists hip flexion for patients who have incomplete paralysis [23]. The clinical evaluation of training in hemiparetic patients showed that this approach was feasible and improved some gait parameters but with a functional gain equivalent to standard rehabilitation. Another team developed an exoskeleton for both hips with pneumatic actuators and showed that the timing of assistance seems to be particularly critical [10].

Recent advances stemming from industrial or military robotics have led to the design of exoskeletons to assist standing posture, locomotion, and load bearing. The weight is reported on the ground through the soles and the control system is held in a backpack. Two types of exoskeletons are already available commercially: structures that actively flex across both the hip and knee, mobilizing the user's legs, but not ensuring balance, thus imposing crutches (e.g., Ekso© Bionics, Indego©, and Rewalk©) and more complex structures with active ankle and hip abduction/adduction joints that aim to facilitate balance (Rex© or the structure developed by the company Wandercraft©). In the clinical context, these exoskeletons are used in patients with severe lower-limb paralysis, in particular paraplegic patients. They allow locomotor training in a physiological and rewarding way. The steps are programmed as sequences of rotations in the hips and knees as a function of the individual patient. Typically, on a flat ground the patient triggers each step of bipedal walking by a small trunk movement (in the Rewalk©) or through a joystick (in the Rex©). The system can also be controlled by switches (placed in a watch, e.g., in the Rewalk©) for other programmed actions such as sit to stand. The clinical benefit is probably linked to the physical exercise and general trophic effect on the clinical condition [24].

Hybrid systems

Hybrid systems tend to associate more closely the mechatronic device with human physiology. Some authors combined powered actuation to functional electric stimulation in order to increase the step length during walking with the orthosis [22]. Another hybrid solution is to use EMG signals to control the actuators in order to enhance external torques to assist the corresponding joints [25]. This solution is used by the exoskeletons from Cyberdyne (HAL© that exists with several structures: uni- or bilateral lower limbs with powered knees and hips and even the upper limbs), but there are few academic publications on its technology. A pilot study showed encouraging results for rehabilitation in patients with spinal injuries [26]. In hemiparetic stroke patients, the gait pattern on the less affected side was used to generate a reference trajectory for the next step of the most affected side so that overall gait symmetry was improved [27].

MULTILINK RIGID SYSTEMS FOR THE UPPER-LIMB AND THE HAND

Full body exoskeletons

Full-body exoskeleton platforms can address the mobility of the four limbs and the trunk. In this configuration, the exoskeleton can also assist the holding and manipulation of heavy objects. The effect of the exoskeleton is to manage load-bearing tasks through weight distribution via the multilink structure rather than increasing upper-limb joints power alone. To date, these platforms have been developed for defense (HULC©, from Lockheed Martin and BLEEX© from Darpa) and industrial purposes (Hercule© from RB3D, the exoskeletons from Daewoo Korea, or Panasonic Japan, HAL© from Cyberdyne). The industrial tasks are shared between the robot (which bears the most part of the load) and the human (who skillfully executes the precision task). For the most part, however, design and performance details of these commercialized exoskeletons have not been made public. It is therefore difficult to project the utility of those devices in rehabilitation, despite their apparent potential in health care or assistance of the elderly.

Upper limbs

There are also specific multilink exoskeletons developed for the rehabilitation and assistance of the upper limbs. Some passive supports (orthoses) have sophisticated mechanical design to reduce the effect of gravity on the arm for partially paralyzed individuals. They are not really wearable since they must be attached to furniture or wheelchairs and are only used as assistive devices or adjuncts during rehabilitation or occupational therapy. Powered exoskeletons were designed to complement and enhance classical rehabilitation of the upper limb. There are several existing platforms or laboratory prototypes targeting the training of shoulder and elbow for hemiparetic patients after stroke [4]. However, they are not really wearable since they are supported by fixed structures (Armeo Power© from Hocoma, Alex© from Kinetec, and ABLE© from CEA-LIST).

Hands

Simple and lightweight passive devices were developed to assist hand function at home. They target the reinforcement of the tenodesis effect for tetraplegic patients [28] or the assistance of hand opening for stroke patients [29,30]. Proof-of-concept studies showed their biomechanical efficiency, but their clinical use is not yet documented.

Many active robotic systems are targeting the rehabilitation of the hand. A recent review [31] lists 165 dynamic hand orthoses with very different designs, actuation, and control modes, among them 56 target home rehabilitation tools and 46 assistances for daily living. However, many of these devices need a support for the device itself (often in continuity with a proximal exoskeleton) or for the energy supply or compressor and thus cannot be considered as wearable. In other cases, the hand rehabilitation device is integrated as a haptic interface into a virtual reality system. At this stage, most of these devices are laboratory prototypes, and testing with healthy humans and patients are yet to be conducted [32]. A promising wearable system is an instrumented glove developed for the rehabilitation of hands and fingers in stroke patients ([11], Fig. 1B). This system can stretch the finger flexors and assist hand extension during manipulation of daily life objects under the supervision of a therapist.

Functional electric stimulation integrated in a wearable system can provide assistance for grasping in tetraplegic patients or rehabilitation therapy in stroke patients [33]. These systems are available (Bionic glove© and Hand Bioness©), but their benefit for rehabilitation or as assistive devices needs to be further investigated.

SOFT ROBOTICS AND SUITS

Soft robotics or exosuits were developed to avoid the drawbacks of rigid exoskeletons, namely, the incompatibility of the mechanical structure and the inertia due to the mass added to the segments [7].

A full-body soft exoskeleton (Exosuit©, [7], Fig. 1C) was developed to assist walking and augment endurance of healthy subjects by reducing the metabolic expenditure. It uses structured textiles and flexible actuators (pneumatic actuators or electromechanically driven cables) to apply tensile forces via straps and cables anchored to the human body and compliant enough not to restrict movements. The tensile forces generate moments around the human biological joint. According to the design, the actuators may be mono- or pluriarticular, spanning adjacent joints.

The Exosuit© applies moments at the hip and ankle (but not knee) so that the power absorbed at the early stance is returned in the late stance. Experiments with healthy subjects showed that it did not perturb the kinematics of gait [7]. A more recent prototype showed that the saving in energy consumption could compensate the effect of the added cost of carrying the suit [6]. This observation is encouraging for future applications in gait rehabilitation.

Future perspectives on the design of soft robots rely on innovative conception, precisely structured fabrics and patterning of the stitched suit itself. In addition, innovative soft sensors are needed to measure strain, pressure, curvature, and shear (ongoing developments use microchannels with liquid metal embedded in a silicone material). One objective would be to develop a "second skin" that could be able not only to monitor kinematic activities and other body properties but also to physically interact with the body to assist or correct actions. The premises of such a device are appearing in laboratories thanks to ongoing advances in nanotechnologies [34]. Wearable sleeves with integrated electric stimulation (Biosleeve© and Axiobionics) are already commercially available for muscle therapy, spasm relief, and pain alleviation in patients with muscle paralysis. Yet, while the effect of neuromuscular electric stimulation is known to be efficient in rehabilitation [35], clinical studies of such commercial systems are lacking.

In the field of soft robotics, the development of wearable devices for hand rehabilitation is a hot topic with many ongoing projects. Some prototypes are currently undergoing tests with encouraging immediate functional results [36–38].

WEARABLE INTERACTIVE SYSTEMS

Wearable systems for rehabilitation also include interactive devices associating sensors for monitoring the activity and effectors to provide some feedback to the end user. Interactive feedback for rehabilitation used in virtual reality are most often visual [39], but alternative sensory feedback (auditory, vibratory, tactile, etc.) could usefully replace vision for wearable systems. A great number of wearable posture/motion monitoring systems for rehabilitation have been reported through the literature in recent years, though very few have been used in clinical studies [40]. The wearable interactive systems for rehabilitation will probably progress thanks to advances in smart textiles, wearable electronics, and the improvement and increased affordability of IMUs. Such advances have allowed, for example, the development of the Philips stroke rehabilitation exerciser and the Valedo© by Hocoma both being wearable home-based rehabilitation systems built around a specifically designed interactive software program (often referred to as "serious games") and a set of IMUs to place over the body for the rehabilitation of upper-limb and/or low-back pain treatment.

CONCLUSION

Wearable robotic systems are currently developing and offer several promising perspectives in neurorehabilitation. In particular, they could be used to support rehabilitation during more natural and rewarding activities (self-directed locomotion and resistance training) or even at home, offering an extension to the conventional rehabilitation durations with potential improved recovery for the patients. Moreover, the fact that they are worn allows these devices to "act" over the wearer's body, in a more intense and extended way (it is thought that soft suits may be eventually be worn all day long) than what could be offered by a standard therapy session.

There are many laboratory prototypes exploring various technological solutions adapted to different clinical perspectives. However, despite encouraging results during proof-of-concept studies, most of these innovative concepts are yet to be proven as clinically effective techniques. Significant advances are likely in the midterm, most notably in soft robotics and wearable sensors systems. In all cases, the success of wearable systems for rehabilitation rests on a comprehensive interface between the artificial system and the human in order to ensure efficient task sharing.

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CHAPTER

18 Robot-assisted rehabilitation in multiple sclerosis: Overview of approaches, clinical outcomes, and perspectives

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative immune-mediated disease of the central nervous system and is the leading cause of nontraumatic disability in young- and middle-aged adults [1,2]. The pathogenesis of MS is characterized by inflammation, demyelination, axonal degeneration, and axonal loss in the CNS. The most prevalent MS phenotypes are relapsing-remitting and primary or secondary progressive MS. The clinical course of MS is unpredictable and varies within and between people with MS (pwMS). In fact, a new conceptual framework has been introduced in recent years referring to defining patients to have "active" or "nonactive" MS disease activity independent of the relapsing-remitting then progressive MS type [3].

The signs and symptoms that define the clinical picture of MS are heterogeneous and variable since the location and extent of the lesions in the CNS differ across pwMS [1]. MS typically presents with neurological deficits such as impaired vision (e.g., optic neuritis and eye movement disorders), cognitive deficits (e.g., memory loss, delayed information processing, deficits in attention, and executive functions), impaired sensation (e.g., abnormal sensations, pain, and impaired or loss of positional sense and vibration sense), motor impairments (e.g., muscle weakness and spasticity), cerebellar symptoms (e.g., tremor, ataxia, and balance problems), fatigue, speech and swallowing problems (dysarthria and dysphagia), bladder and bowel disorders, and sexual dysfunction [1,4]. Recently, Kister et al. documented the prevalence and perceived severity of different symptoms across 11 domains commonly affected in MS: mobility, hand function, vision, fatigue, cognition, bowel/bladder, sensory, spasticity, pain, depression, and tremor/coordination [5]. The majority of

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pwMS perceived impairment in all domains, even in the early stage of the disease. The most frequently reported symptoms in the first year of the disease were impaired sensory function (85%) and fatigue (81%) followed by impaired hand function (60%) and mobility (50%). The impairment severity increased with disease duration across all domains, but the patterns of disability accumulation differ. A combination of these symptoms causes disability that often hampers the ability to perform ADL and social activities, resulting in a decreased quality of life.

Disability in MS can be clinically evaluated and described by a number of scales. Although it has recognized shortcomings, the expanded disability status scale (EDSS) [6] is still widely used to evaluate and describe disability in MS [1]. The score ranges from 0 to 10, with a higher score indicating a higher disability level. Besides the EDSS, other outcome measures on different levels of the International Classification of Functioning (ICF) can be used to describe or evaluate pwMS. The ICF is a well-established framework to describe and measure health and disability at individual and population level and is frequently used in clinical settings for functional status assessment, goal setting, treatment planning, and monitoring. Outcome measures or rehabilitation strategies can be classified according to different ICF levels: "body functions and structures," "activity," and "participation." Body functions and structure level focuses on the physiological functions and anatomical parts of the body. Activity level contains abilities or disabilities a pwMS has in performing activities of daily living (ADL). Within this level, the terms capacity and performance are used. Capacity describes the maximal ability to execute a task or an action in a given domain at a given moment in a standardized environment. Performance describes the person's habitual performance of a task or action in his/her current environment. Participation level describes the restrictions an individual may have in involvement in life situations.

So far, no single pharmacological treatment is available to cure MS. Current treatment strategies focus on slowing down the disease course in order to maintain the functional status of the pwMS by providing pharmacological treatment in combination with (multidisciplinary) rehabilitation and care management. Rehabilitation can be effective in improving or stabilizing some of the above-mentioned symptoms [7–9]. Rehabilitation is generally defined as an active process of education and therapy, focusing on the appropriate management of disability and minimizing the impact of the disability on ADL. The goal of rehabilitation is to achieve the best physical, mental, and social potential of pwMS so that they can remain, or become, integrated into their social environment [10]. To achieve these goals, a multidisciplinary perspective is needed including symptomatic treatment and patient activation [11]. For motor function, different literature reviews have indicated the positive effects of rehabilitation strategies such as exercise training for the lower limbs [7,9] and upper limb rehabilitation [12]. Overall, training programs need to consist of sufficient exercise volume over multiple weeks in order to achieve effects. Rehabilitation technology may allow to provide tools for autonomous high-repetition training of movements at body function level so that skilled therapists can afford to focus on personalized treatment goals.

PART I. UPPER LIMB TRAINING

A recent literature review [12] investigating upper limb rehabilitation in pwMS found that robot-based upper limb training was the most frequently investigated rehabilitation strategy in the MS rehabilitation literature. In general, these RCT and uncontrolled studies showed that robot-based upper limb training in MS can improve motor coordination, manual dexterity, and upper limb capacity. An overview of the different studies, the devices used, and their effects are given in Table 1. The first robot-assisted rehabilitation device used in MS upper limb rehabilitation was the Braccio di Ferro that is a planar robotic manipulandum with two degrees of freedom [13]. The device is capable of delivering different kinds of forces on the end effector, which are then perceived by the subject's hand grasping the handle. The robot can be programmed to deliver either resistive, assistive, or perturbing force fields, which, in turn, can help or disturb the subject during the execution of movements of the upper limb. This pilot study aimed to investigate the feasibility and the preliminary effects after eight sessions of robot-assisted training (200 reaching movements/session, 1 session/day, and 5 days/week) in small sample size (seven pwMS and nine healthy controls). The preliminary results of this pilot suggest that robot therapy was feasible and could be beneficial for pwMS, as four of seven pwMS showed a clinically relevant improvement on the nine-hole peg test that assesses manual dexterity.

Three years later, a pilot study investigating the effects of the Armeo Spring in pwMS was published [14]. The Armeo Spring is an exoskeleton apparatus with integrated spring mechanism allowing variable upper limb gravity support that facilitates proximal and distal upper limb training in an engaging virtual learning environment. The results of this pilot study suggest that an 8-week Armeo Spring training program (3 days/week and 30 min/session) supplementary on the customary maintaining care in high-level disability pwMS can lead to an improved proximal and distal upper limb capacity even after 2-month follow-up.

The group of Carpinella et al. further explored the possibilities for upper limb rehabilitation with the Braccio di Ferro. In 2012, they published the results of a pilot RCT investigating if involving both objects' reaching and manipulation in the robot-assisted training leads to better outcomes than training involving only the transport of the upper limb [15]. Twenty-two pwMS received eight sessions of either a protocol involving reaching tasks (RT) requiring upper limb transport only or a protocol requiring both objects' reaching and manipulation (RMT). During RT training, pwMS were asked to move the handle of a planar robotic manipulandum toward circular targets displayed on a screen. The RMT protocol required pwMS to reach and manipulate real objects, by moving the robotic arm equipped with a handle that left the hand free for distal tasks. In both trainings, the robot generated resistive and perturbing forces. Both robot-assisted training protocols significantly reduced tremor and improved upper limb kinematics and upper limb capacity. Compared with RT, RMT protocol induced a significantly larger improvement in movements involving grasp but not precision grip.

Table 1 Overview of studies investigating robot-assisted upper limb training

Publication	N	Training	EDSS	Name of the device	Type of device	Significant treatment effects
Carpinella et al. [13]	7 pwMS 9 HC	8×1 h over 2 weeks	5.7	Braccio di Ferro	End-effector 2DOF with haptic forces	Manual dexterity
Gijbels et al. [14]	9 pwMS	24×30′ over 8weeks	7.9	Armeo Spring	Exoskeleton with antigravity support	Manual dexterity, proximal and distal upper limb capacity
Carpinella et al. [15] RCT	22 pwMS (11/11)	8×1 h over 2 weeks	6.4–6.9	Braccio di Ferro	End-effector 2DOF with haptic forces	Tremor, manual dexterity, proximal and distal upper limb capacity
Feys et al. [16] RCT	17 pwMS (8/9)	24×30′ over 8 weeks	7.3–8	HapticMaster/I-TRAVLE	End-effector 3DOF with haptic environment	More efficient movement execution measured with the system, no clinical effects
Sampson et al. [17]	5 pwMS	18×1 h over 10 weeks	NR	Armeo Spring/ SAIL System	FES with Exoskeleton 3DOF with antigravity support	Accuracy of tracking performance, amount of FES needed to perform the movements, range of motion, and motor control in the proximal upper limb
Maris et al. [18]	13 pwMS 14 stoke	18×1 h over 8 weeks	6.5	HapticMaster/I-TRAVLE	End-effector 3DOF with haptic environment	Active shoulder range of motion, handgrip strength, perceived upper limb strength, proximal and distal upper limb capacity, speed and movement duration measured with the system

RCT, randomized controlled trial; pwMS, persons with multiple sclerosis; HC, healthy controls; EDSS, expanded disability status scale; DOF, degrees of freedom; FES, functional electric stimulation.

Based on the findings of these pilot studies, a European multidisciplinary consortium developed I-TRAVLE, which stands for “individualized technology-supported and robot-assisted virtual learning environment” and consists of used interfaces for evaluation of arm movements and performance of 3D exercises in a custom-built virtual learning environment. I-TRAVLE was used in combination with the HapticMaster robot (MOOG, the Netherlands) that functioned both not only as an output device, providing haptic feedback during the training by guiding or hindering movements with exerted forces, but also as an input device, allowing navigation within a virtual learning environment. In their first pilot RCT, they investigated the effects of additional robot-supported upper limb training in pwMS compared with conventional treatment only [16]. Their main conclusion was that the additional robot-supported upper limb training for 8 weeks (three weekly sessions of 30 min) leads to more efficient movement execution measured with the system. These findings were however not reflected by significant changes on the clinical outcome measures. In-depth case analyses indicated that the pwMS with more marked upper limb dysfunction seem to benefit more from the additional training compared with those with only mild upper limb dysfunction. In the following study, 13 pwMS and 14 chronic stroke patient performed between 36 and 40 sessions with the I-TRAVLE system [18]. After training, the pwMS significantly improved on the active shoulder ROM, handgrip strength, perceived strength, and upper limb capacity measured with the wolf motor function test, while the stroke patients only improved on the perceived strength. Both pwMS and stroke patients significantly improved on the robot-assisted outcome measures of speed and movement duration. At 3-month follow-up, pwMS deteriorated on the clinical measures, while the stroke patients maintained their upper limb capacity.

In 2015, Sampson et al. investigated the feasibility of combining functional electric stimulation (FES) with passive robotic support during VR to improve upper limb function [17]. Their system comprises an instrumented passive robotic support, providing kinematic data to a real-time processor that interfaces with a custom FES hardware, a VR task display, and a graphical user interface. An iterative learning control was used to adjust the assistance provided to correct performance error in the next attempt of a specific task. This iterative learning control encourages and supports the participants' voluntary effort by supplying just enough FES on the triceps and anterior deltoid muscle to perform the movement. Five pwMS underwent a training program with this system for 18 1-h session over 10 weeks. Significant improvements were found for the accuracy of tracking performance and amount of FES needed to perform the movements. On the clinical measures, only an improvement of the proximal upper limb impairment was found, while no improvements were found on the capacity measures and perceived performance measures.

In conclusion, the pilot studies in pwMS indicate the potential of robot-assisted upper limb training in MS. However, RCTs with larger sample sizes are needed to confirm this. The majority of the pilot studies showed significant improvements on robot-generated measures, but these changes were not reflected by significant improvements on the traditional clinical measures. A possible explanation of this finding maybe that the majority of the robot-assisted rehabilitation programs are unilateral and focus on training the proximal part of the upper limb while 75% of the pwMS have bilaterally impaired manual dexterity and more than 65% have bilaterally diminished tactile sensitivity in their fingertips [19]. In the future, developers of robot-assisted upper limb rehabilitation tools should incorporate important MS rehabilitation principles such as task-oriented training of both the proximal and distal part of both upper limbs separately and together taken into account important MS symptoms that may hamper the rehabilitation such as motor fatigability, visual, and cognitive impairments.

PART II. GAIT TRAINING

Gait dysfunction is the main complaint of 85% of pwMS [20]. On average, 18 years after the onset of the disease, persons with MS (pwMS) have an EDSS score of six, implying a dependency on aids to walk for 100 m [21]. Therefore, gait training is an important element in the therapy of pwMS. Here, we discuss technical body-weight-supported (BWS) tools that can assist higher intensities of gait training than can be achieved compared with unsupported overground walking for particular patient groups.

Body-weight-supported treadmill training (BWSTT) can be used to assist gait rehabilitation, particularly important for patients who are not able to carry their full body weight. The use of a BWS system makes it possible to practice reciprocal stepping at faster speeds with greater safety and less fear of falling compared with overground or treadmill training without BWS [22]. Additionally, it also reduces the risk for the development of compensatory strategies that could occur when using walking aids during overground walking [23]. Further, robot-assisted gait training (RAGT) can be used for gait therapy in pwMS [24]. The implementation of robot assistance (RA) during gait therapy in pwMS can be in different ways and with different tools (i.e., end-effector devices or exoskeleton devices can be used).

CLINICAL EFFECTS OF BWSTT AND RAGT

BWSTT can be considered as an effective tool for gait training in pwMS [24]. Several studies demonstrate that BWSTT in pwMS has a beneficial effect on walking speed, maximum walking distance, EDSS score, spasticity, muscle strength, balance, and quality of life [25–27]. For instance, in the study of Giesser et al., a case series of four patients, one patient who could not walk before completed the 10 MWT after training, and two patients who could not walk before completed the 6-min walk test afterward [25]. However promising the results, at the moment, in literature, there is in no ambiguous evidence that training with BWS is more effective compared with other rehabilitation methods, neither for MS [24] nor for other neurological disorders such as hemiplegia and complete or incomplete spinal cord injury [28,29].

An overview of the different studies of RAGT, the devices used, and their effects is given in Table 2. In a systematic literature study concerning the effectivity of

Table 2 Overview of studies investigating robot-assisted gait training (RAGT)

Publication	N	Training (RAGT)	EDSS (RAGT)	Robotic device	Type	Significant treatment effects
Lo et al. [26] NNR—pilot RCT BWSTT and RAGT	13 (crossover design)	2×40′/week for 3 weeks, 6 sessions	4.9	LOKOMAT	Exoskeleton	Walking speed (timed 25 ft walk), walking capacity (6-min walk distance), percentage of double support time, severity of MS (EDSS)
Pompa et al. [30] MSJ	13 (crossover design)	idem Lo et al. [26]	idem Lo et al. [26]	idem Lo et al. [26]	idem Lo et al. [26]	Quality of life
Beer et al. [31] MS—RCT RAGT versus CWT	35 (19 RAGT)	5×30′ walking time/week for 3 weeks, 15 sessions	6.5	Lokomat	Exoskeleton	Walking speed, distance and knee extensor strength
Vaney et al. [32] NNR—RCT RAGT versus CWT	49 (26 RAGT)	3×30′/week for 3 weeks, 9 sessions	5.9	Lokomat	Exoskeleton	
Schwartz et al. [33] MSJ RCT RAGT versus CWT	32 (15 RAGT)	2–3×30′ walking time/week for 4 weeks, 12 sessions	6.3	Lokomat	Exoskeleton	Functional mobility, functional independence measure, overall disability
Ruiz et al. [34] JNPT	7 (immediate/delayed treatment group)	2×20′/w for 2 months, 16 sessions	5	Lokomat	Exoskeleton	Walking distance, functional balance

Continued

Table 2 Overview of studies investigating robot-assisted gait training (RAGT)—cont'd

Publication	N	Training (RAGT)	EDSS (RAGT)	Robotic device	Type	Significant treatment effects
Gandolfi et al. [35] Front Hum Neurosci—RCT RAGT versus balance training	22 (12 RAGT)	2×50′/week for 6 weeks, 12 sessions	4	Gait trainer GTI	End-effector device	Static and dynamic balance, balance confidence
Straudi et al. [37] NR—pilot RCT RAGT versus CT	16 (8 RAGT)	2×30′ walking time/week for 6 weeks, 12 sessions	5.8	Lokomat	Exoskeleton	Walking speed, distance, gait pattern, and kinematics
Straudi et al. [37] MS—RCT RAGT versus CT	52 (27 RAGT)	2×30′ walking time/week for 6 weeks, 12 sessions	6.4	Lokomat	Exoskeleton	Walking distance, balance, quality of life
Pompa et al. [30] MSJ—pilot RCT comparing RAGT with CWT	43 (21 RAGT)	3×40′/week for 4 weeks, 12 sessions	6.2	Gait trainer GTII	End-effector device	Walking speed, ability, overall disability, fatigue, overall mobility and activities of daily living, lower limb spasticity

RCT, randomized controlled trial; RAGT, robot-assisted gait training; EDSS, expanded disability status scale; CWT, conventional walking training; CT, conventional training.

different gait training modalities for pwMS published in 2012 [24], four studies were found that investigated the effect of exoskeleton-based RAGT in pwMS [26,31–33]. Positive effects on overground walking speed, walking endurance, double support time, and EDSS score were found, although in the RCTs comparing RAGT with conventional therapy no significant differences between groups were found [31] or were in favor for the conventional walking therapy group [32]. Since then, a few more trials investigated the effect of RAGT in pwMS. Wier et al. focused on the effect of RAGT versus conventional BWS gait training on quality of life for pwMS (same protocol as Lo et al., 2008). Thirteen pwMS and gait impairment were included. They found no statistically significant differences between RA BWSTT and unassisted BWSTT for improving quality-of-life (QoL) outcome measures and concluded that both types of BWSTT may improve QoL for people with gait dysfunction secondary to MS [36]. In the pilot RCT of Ruiz et al. with seven patients with MS, it is reported that there was an increase in walking endurance and functional reach [34]. They used a combination of RAGT and BWSTT within each session. In the RCT of Gandolfi et al., 22 patients with MS were included (EDSS score between 3 and 5.5). One group underwent end-effector system training (gait trainer GTI) and the other group specific balance exercises. The within-group comparisons showed significant improvements in both groups on the Berg balance scale. However, between groups, no significant differences were found [35]. Straudi et al. [37] and Pompa et al. [30] focused on severe MS patients (EDSS score between 4.5 and 6.5 or 6 and 7, respectively). In the RCT of Straudi et al. published in 2015, 52 pwMS were included, and increased walking endurance, balance, and perceived physical functioning QoL were found after RAGT with the Lokomat system. They compared Lokomat training with conventional training [37]. In the pilot RCT of Pompa et al. with 43 nonautonomous ambulant in-patients with MS, it was found that the number of subjects who achieved a clinical significant improvement was significantly higher in RAGT group than in the control (conventional walking therapy) group for gait capacity (measured with the 2 min walk test) and the functional ambulation category (FAC). Improvements in global ability, global mobility, EDSS, and fatigue were also reported for the RAGT group. Some studies suggest that superior clinical effects of RAGT compared with conventional treatment are greatest in more severely affected pwMS, while equal effects of intervention strategies are found for moderately disabled patients who still have substantial overground walking abilities [38].

BIOMECHANICAL EFFECTS OF BWSTT AND RAGT IN THE TRUNK AND LOWER EXTREMITY

Although overall evidence supports clinical effects after BWSTT and RAGT in disabled pwMS, one needs to be cautious on its mechanical impact on the quality of gait that is achieved. Changes in kinematics and muscle activity are found in the lower and upper limbs and the trunk during walking with BWS in healthy persons [39–48]. Only a few studies focus on pwMS. Swinnen et al. analyzed in healthy participants and in pwMS the differences in trunk kinematics during walking with six different levels of suspension (0%, 10%, 20%, 30%, 50% and 70% BWS) [45]. They found in general that the movements of the trunk and the pelvis were significantly decreased compared with walking without BWS. Especially during the highest levels of BWS, the pelvis movements were influenced when using a BWS system. When increasing the level of BWS, smaller movement amplitudes appeared with exception of the anterior-posterior movement of the pelvis. These changes could be a compensation of the fixed trunk and pelvis during walking with BWS and imply less need for active dynamic stabilization in mediolateral direction and can result in a passive swing from one side to the other [45]. Furthermore, a decreased level of activation of the erector spinae and the multifidus muscles during walking with high percentages of BWS was reported in pwMS [46]. At the level of the multifidus, there was a significant decrease during almost all levels of BWS, while in the M. erector spinae, the most significant differences were found during 50% and 70% BWS. On the other hand, increased levels of activation of the M. obliquus externus were reported during walking with BWS. This increase in activity of the abdominal muscles suggests a certain need for forward stabilization of the trunk during gait with BWS [46].

Also changes in the kinematics and muscle activity of the lower extremities during RAGT have been reported [49–53], although no studies in pwMS were found. Nevertheless, Hidler et al. described that overall, the kinematics during walking in the Lokomat is more or less similar to those on a treadmill; there was significantly more hip and ankle extension and greater hip and ankle range of motion measured during walking in the Lokomat [54]. Swinnen et al. investigated changes in the thorax and pelvis kinematics when walking with different levels of robot assistance (RA) and different levels of BWS [55–57]. In general, a decrease in trunk and pelvis movement amplitudes was found, with exception of the anterior-posterior tilting of the pelvis that was increased during walking with RA and BWS. The combined effects of guidance force, body-weight support, and gait speed on muscle activity during walking in the Lokomat were studied by van Kammen et al. They found that in healthy participants, guidance generally reduces muscular activity, but that the nature of these effects depends on settings for speed and BWS [51].

In the recent published systematic review of Lefeber et al., it is found that short-duration exoskeleton walking is less energy consuming and cardiorespiratory stressful than walking without robot assistance. They concluded that these results might implicate that the exercise intensity is safe for neurological patients at risk of cardiovascular diseases [58]. No specific studies concerning these parameters during RAGT were found on pwMS.

CONCLUSION OF RAGT

In conclusion, promising results were found for RAGT and BWS training in pwMS, although there is no consistent evidence yet of the superiority of one training method over the other or compared to conventional gait training. Still, relatively small trials with a large variability in patients' motor characteristics were published. Due to this limited number and rather small studies, it is also not possible to draw firm conclusions concerning the differences in effectiveness concerning end-effector devices and exoskeleton devices or in relation to the type or severity of the pwMS. Physiotherapists should be aware of the changes in biomechanics during walking with different types of devices used for gait rehabilitation. For example, as described above, wearing a harness with a high level of body-weight support or an exoskeleton fixated around the hips changes the movement amplitudes of, for instance, the trunk during walking. This change in balance during training could have an influence on overground gait outcome, and the therapy programs should be adapted to this. A strong cooperation between the engineers who are constructing and developing new technologies and the physiotherapists who apply these technologies during gait rehabilitation is of great importance, since functional gait outcome is a priority.

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CHAPTER

Robots for cognitive rehabilitation and symptom management 19

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INTRODUCTION

The consideration of the role and advantage of robot embodiment versus a virtual presence with regard to retention of restoration of cognitive skills is a point of contemplation. Unlike nonembodied technologies, embodied robotics allow personality to be expressed not only through voice, facial expressions, body position, and appearance but also through physical interaction involving movement as a means of attracting and directing user attention and behavior and the utilization of the user's personal space [1].

Many users express the perception that an embodied robot is more engaging than a virtual agent on a computer screen, suggesting that their performance on a specific task is better when stimulated by a physical robot rather than by a computerized on-screen presence [2]. A few studies suggest that involvement with a social robot decreased after several successive weeks of exposure, but no studies to date have addressed rehabilitative or task-driven interactions with specific goals required in successful cognitive rehabilitation therapy [3].

Many forms of neurocognitive injury and decline leave an individual affected with some loss of movement in addition to cognitive impairment and necessitate aggressive intervention to regain and retain function. For example, aggressive use and training of the affected limbs following a stroke can significantly reduce lasting disability. The rate and amount of recovery greatly after a neurocognitive injury or maintenance of function in neurocognitive decline often hinges on the amount of focused, continued training. However, since such rehabilitation normally requires supervision of trained professionals, the lack of resources and personnel often limits the amount of time available for supervised rehabilitation and maintenance of function. As a result, the quality of life of patients with neurocognitive conditions is dramatically reduced, and medical costs and lost productivity continue to be incurred [4].

Due to the increasing numbers of older adults and the need for more resources for neurocognitive therapy, research concerning the use of robot-assisted therapy has enjoyed heightened interest. A number of effective systems have been developed, using

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physical assistance in order to achieve rehabilitative goals. However, not all effective rehabilitation therapy requires the use of physical contact between the therapist and the patient. Noncontact therapy, such as that supported by robotic interaction, can often be utilized to stimulate improved outcomes with patients. Such methodology fits well into current therapy, since the goal of robotics is not to replace existing therapies and therapists but to augment current treatment options and to allow for greater flexibility in treatment plans [5].

Fong et al. first described a taxonomy for socially interactive robots (SIR) that engage patients primarily through social interaction [6]. The term SIR distinguishes the teleoperated (i.e., remote control robots) from social interaction in human-robot interaction (HRI). Socially assistive robotics (SAR) is defined as the intersection of assistive robotics (AR) and SIR. SAR shares with AR the goal of providing assistance to human users, but SAR constrains that assistance to be through nonphysical social interaction. Rather than focus on the interaction itself, as is done in SIR, SAR focuses on achieving specific convalescence, rehabilitation, training, or education goals [7]. Wada, Shibata, and Kawaguchi, for example, utilized a type of SAR, a mental commit robot (PARO seal), to help promote function and calming behaviors in individuals with dementia [8].

The utilization of SIRs in therapy focuses primarily on peer-to-peer human-robot interaction. Specifically, SIRs are designed to exhibit "human social" abilities. In order to provide therapeutic benefit, according to Fong et al., the SIR must be able to express or perceive emotions, communicate in some form of dialogue, possess the ability to establish and maintain social relationships, use or understand natural cues such as gaze or gestures, exhibit a unique personality and character, and learn or develop social prowess. The successful use of a SIR or SAR in the therapeutic setting depends upon the assumption that the human patient is willing or prefers to interact with the robot in the way that he or she interacts with other humans [6–8].

In the therapeutic sense, SIRs and SARs function as companions, peers, or assistants, which means that they must be adaptable and flexible in their abilities to stimulate interaction with a wide array of humans. Both types can have different shapes and functions, ranging from robots whose sole purpose and only task is to engage people in social interactions to robots that are designed to conform to social norms within human environments. Some robots proactively encourage social interaction, while others show their social competence through biofeedback; thus, they rely on humans to assign mental states or emotional reactions to the robot. Either modality can be effectively combined with more traditional approaches of the trained therapist to motivate and engage patients to participate.

Some therapies utilizing SIRs and SARs are aimed at slowing cognitive and behavioral decline and focus on maintaining or improving existing cognitive abilities [7]. The therapist directs active involvement in specific tasks (memory, orientation, motivation, and physical training) or to work on all the residual abilities together [6]. Some neurodegenerative diseases result in a progressive deterioration of function in which targeted therapies may become ineffective. Nonspecific therapies on the other hand based on sensorial stimulations, consolidated procedures, and social or emotional engagement can be applied throughout a longer period of time obtaining to impact a wide range of functionalities [5–8]. The most popular of these therapies throughout the years have been music therapy, sand therapy, occupational therapy, and pet therapy. The key focus of these interventions for behavioral and social problems underscores influencing the patients' internal states providing them with a means of creating meaning and purpose through the activity. Activities of this sort create connection between abstract thought and patients' concrete experiences.

Sand therapy, music therapy, and engaging in a structured activity or interacting with a pet are mechanisms for building a positive therapeutic relationship. Patients are engaged in a meaningful activity, actively using cognitive abilities. Therapists formulate interventions to address patients' specific deficiencies. Field observations, interviews with therapists, and literature surveys conducted by Marti et al. [9] found that these therapies adhere to a common model of activity described in three stages:

Familiarization: The patient explores the therapeutic setting and engages in simple tasks; patterns of activities interspersed with sensory stimulation sustain the interaction, motivating the patient to complete the tasks to receive positive feedback.

Engagement: Enjoyment of the activity and positive feedback induce the subject to emotionally engage with the object of the activity. Manifestation of emotions causes the patients to project their internal states into the activity.

Communication/exchange: When this exchange of emotions occurs, the therapist can intervene. The emotional connection between the patient and the object of the activity allows the therapist to connect with the patient, to negotiate meanings, and to directly externalize internal states.

These three phases have different weights in different therapies, and their balance is manipulated by the therapist. The way in which this general model of nonspecific cognitive therapy is implemented in each single intervention critically depends on the therapeutic objectives and protocols defined by the therapist after an in-depth evaluation of the patient's deficiencies.

Each specific therapy makes use of techniques such as regression, role play, reminiscing, and storytelling to assist patients in externalizing their feelings. Pet therapy, as an example, is primarily focused on the first stage; the physical contact with the pet creates an intimate experience that stimulates senses and favors posture maintenance. Pet therapy is particularly appropriated with patients affected by serious neurobiological problems that prevent the elaboration of complex stimuli. It can also be used with less severe cognitive decay; in this case, therapist can go through all the three stages. Music therapy, sand therapy, and occupational therapy are more balanced on the three therapeutic activity stages. Nevertheless, even in these cases, it is part of the therapist's work to decide on which of the three stages to focus the intervention [9].

The consideration of these three phases of therapy opens the way for the utilization of SIRs and SARs in cognitive rehabilitative therapy. A case study with a group of cognitively impaired elderly is utilized to illustrate the effectiveness of the

PARO robotic pet seal, a SAR, in the clinical setting to improve overall function, decrease symptoms, and improve overall quality of life in a cognitively impaired elderly.

A CASE STUDY: USE OF A SAR IN THERAPEUTIC INTERVENTIONS WITH COGNITIVELY IMPAIRED ELDERLY

In recent literature on the use of SARs in the care of elderly individuals with cognitive deficits, the most widely studied is PARO (the abbreviation for "personal robot" in the Japanese language). PARO is a therapeutic SAR with an appearance of a baby harp seal and is equipped with different kinds of sensors, including tactile, light, audition, temperature, and posture. The device can respond to different stimuli from patients such as voice, stroking, striking, or holding. It was designed by Shibata et al. and has resulted in positive patient outcomes since 2003 in many countries including Japan, Denmark, Canada, Italy, and the United States [10]. In 2009, PARO was certified as a type of neurological therapeutic device by the Food and Drug Administration (FDA) in the United States. In 2010, a caregiver's manual for robot therapy was published to achieve effective therapeutic benefit from the device [11]. In 2015, Petersen et al. conducted a randomized controlled study to evaluate the utilization of the PARO with cognitively impaired elderly with a variety of neurocognitive disorders [12].

Pet therapy availability and the therapeutic performance of live animals in the clinical setting may be inconsistent. Consequently, robotic pet therapy with a SAR (like PARO) is seen as a viable substitute for animal therapy and a venue for introducing positive therapeutic interventions. The FDA-approved device is designed to look like a baby harp seal, which is a nonfamiliar animal to most people. Unlike similar devices that resemble familiar animals such as dogs and cats, the PARO is unfamiliar to most people. As a result, individuals can readily engage with PARO without preconceptions or expectations of its actions or behaviors. PARO promotes the therapeutic results of psychological, physiological, and social effort from those who interact with it, lowering stress, improving depression, and reducing anxiety in many cases, allowing the therapist to create rehabilitative regimens that can be effective while the patient is in a relaxed, receptive state.

CLINICAL PROTOCOL FOR SARs: USING PARO IN THE CLINICAL SETTING

A protocol for presenting the seal to patients was developed to maximize and evaluate the effectiveness and therapeutic benefit of the intervention with the PARO. A set of well-validated outcome measures was evaluated before and after training [13–16]. Education was provided for the facility nurses and staff regarding the administration of the robotic pet seal (PARO) as a therapeutic intervention. Subjects routinely participated in group programming activities throughout the day. Subject groups were randomly assigned by the toss of a coin to receive either the PARO robotic pet or standardized programming.

A sample of 60 was estimated based on an effect size (0.35) with a power of 0.80 and a 10% rate of attrition. The participants were equally divided into study and control groups, and each group included five subgroups. Experimental group participants were exposed to treatment with the PARO robotic pet once a day for 3 days a week. Each session lasted 20 min, and sessions continued for 3 months. Therapy nurses conducted the sessions with the PARO robotic pets in the activity room of the assisted living memory care units. The 20 min sessions involved seating six residents at a round table, placing the PARO robotic pet in the center of the table, and encouraging the residents to interact with the robotic pet by demonstrating interaction. The comparison control group received what is considered the facilities' standard of care that includes physical activity, music, and mental stimulation in 20 min segments.

Pulse oximetry, pulse rate, galvanic skin response (GSR), and medication utilization [17] were collected before and after each 20 min exposure to the robotic pet. The Cornell Scale for Depression in Dementia (CSDD) and the Rating for Anxiety in Dementia (RAID) were utilized for staff observations of selected behaviors prior to and after the study. [18,19] Residents were assessed as to the severity of their functional and cognitive abilities with the Global Deterioration Scale (GDS) before and after the study [20]. Observation and measurement of pulse oximetry, pulse rate, and GSR, along with the assessment of severity of functional impairment with the GDS, occurred in the same manner with a control group of residents, who did not receive intervention with the PARO robotic pet seal.

The RAID scale is a reliable and valid scale for measuring anxiety in dementia patients. In a previous study, interrater reliability and test/retest reliability were moderate, with an overall agreement of over 80% for individual items. Scores of 11 and above on the scale indicated significant clinical anxiety. The scale correlated significantly with other anxiety scales and with independent ratings. Criterion validity and construct validity were established when the instrument was piloted on 51 inpatients and 32 day-hospital patients who had a diagnostic and statistical manual (DSM) diagnosis of dementia [18].

The sensitivity and specificity of the CSDD have been reported to be 93% and 97%, respectively. The CSDD was chosen for this study because its validity as a screening tool for depression dementia patients exceeds the Geriatric Depression Scale in progressing dementia. A score >10 indicates a probable major depressive episode. A score >18 indicates a definite major depressive episode [19].

Interrater reliability for the GDS was found to be high, ranging from 0.87 to 0.97 in various studies. Concurrent validity of the GDS was established by comparing scores of this scale with scores from the mini-mental state exam (MMSE) and showed high correlation between the two tools. Clinical/biological validity was also demonstrated to be satisfactory by comparing GDS results with results from psychometric tests (r=0.30–0.60), CT scan measures (r=0.50 for sulcal enlargement and 0.60 for ventricular dilation), and cerebral blood flow (r=0.70–0.80) [20].

Pulse rate and pulse oximetry have long been validated as indicators of stress and anxiety. As stress or anxiety decreases, the pulse rate decreases. Both of these are autonomic responses that fluctuate regardless of cognitive ability. Pulse oximetry readings improve as stress decreases. Galvanic skin response, or skin conductivity, can also be used as an indication of one's state of arousal. GSR has been observed to continuously change over time and is correlated to the activity of the eccrine sweat glands. Located in the dermis, the eccrine sweat glands regulate body temperature by manufacturing and excreting sweat onto the skin's surface. GSR can be measured through the collection of skin conductance and used as the quantitative indicator of anxiety and stress. The development of bias potentials and polarization were minimized through the use of silver chloride cup electrodes. Velcro fasteners were used to secure the electrodes to the volar surfaces [21–23].

A total of 61 patients, with 23% males and 77% females, with an average age of 83.4 years, were randomized into the control and treatment groups. Compared with the control group, pulse oximetry and GSR were increased, while RAID, CSDD, pulse rate, pain medication, and behavior medication were significantly decreased in the treatment group. After adjusting for demographics and time variable, the group status showed a significant effect on GSV, pulse oximetry, and pulse rate. The changes in GSR, pulse oximetry, and pulse rate over time are plotted for both groups in Fig. 1. The difference between the two groups was seen consistently throughout the study for pulse oximetry and pulse rate, while changes in GSR showed no difference between the two groups for several weeks.

Using the data from the 3-month study, researchers found that intervention with the PARO robotic pet seal provided a viable alternative for controlling symptoms of anxiety and depression in elderly patients with cognitive impairment, often in lieu of pharmacological modalities, promoting an optimum cognitive therapy environment. Oxygen saturation, pulse rate, GSR, RAID, and CSDD and medication use were all positively impacted in patients participating in the interventional group, indicating improvement in symptom control, thus suggesting the potential for the SAR (PARO) to act as a "gateway" for traditional therapeutic interventions, as previously reported by Marti et al. [9].

Implications for practice for therapists working with this population include [1] older adults with cognitive impairment typically take higher numbers of prescription medications. Additionally, some of these medications can negatively impact the benefit of cognitive therapy, and [2] intervention with the PARO robotic pet three times weekly for 20 min significantly reduced the need for some of these medications. As the literature suggests, the use of benzodiazepines in the elderly population result in falls, sedation, decreased cognition, and physical dependence [24]. Additionally, antipsychotics may be used off-label to treat negative behaviors in individuals with neurocognitive disorders; these medications can cause or worsen heart arrhythmias in the older adult and worsen other chronic conditions such as renal impairment, gastrointestinal distress, and mobility and liver impairment, further impairing function [25]. The use of pain medications in the treatment group was significantly decreased as well, which may lead to further utilization of the PARO. Other applications for the

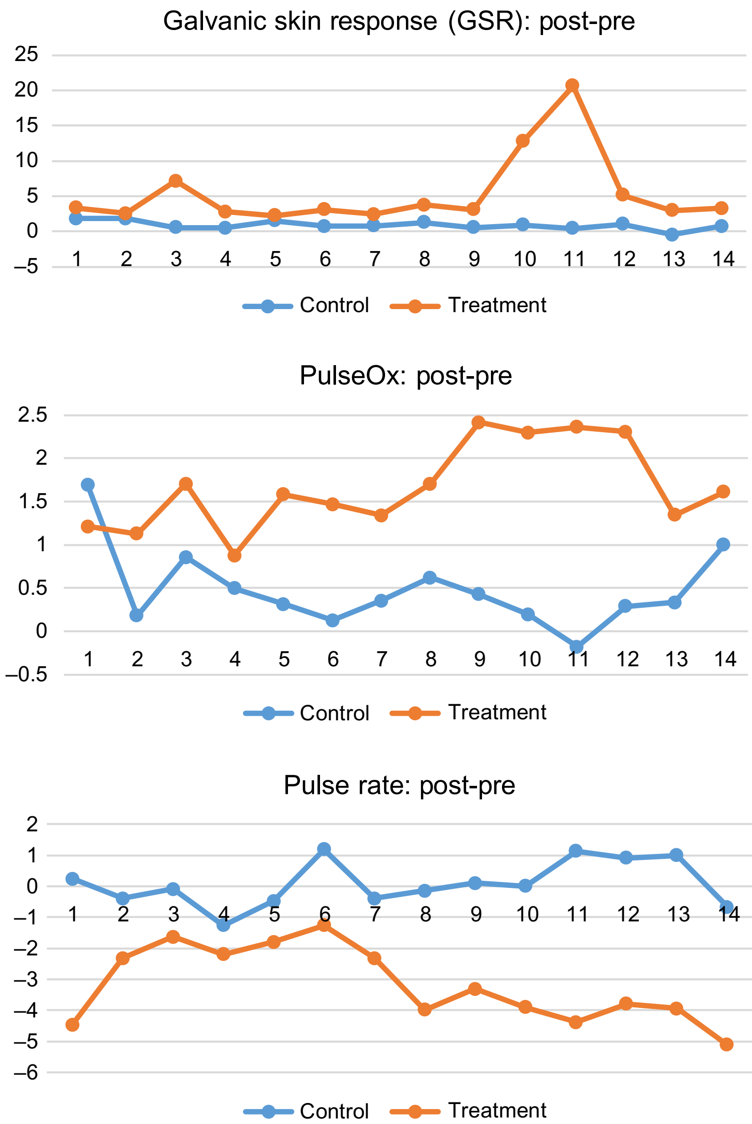

FIG. 1

Profiling of changes in biometric measures over time [23a].

PARO (and perhaps similar devices), in addition to reducing stress, may include improved oxygenation, improved cardiac status, and improved cognitive performance.

Significant improvements in observed pain and decreased pain medication use were noted in the interventional group. Recent literature advises an observed overlap between pain, psychiatric disorders, and declining cognitive function because some neurotransmitters, such as serotonin and norepinephrine (typically lower in individuals with significant cognitive impairment), are involved, albeit in different brain regions, in pain and sensory processing, as well as in modulating mood and cognitive engagement [25].

CONCLUSION

Examination of the impact of cognitive therapy with robotic pets and similar SIRs and SARs in acute and long-term care settings with various patient populations across the life span may continue to reveal the positive impact robots can have in cognitive therapy. As resources available for cognitive therapy become more limited, the use of robots to enhance the clinical efficacy, reduce costs, and improve the efficiency of traditional cognitive therapeutic interventions will continue to be of great importance.

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CHAPTER

Hybrid FES-robot devices for training of activities of daily living

20

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INTRODUCTION

Research and clinical results suggest that intensive exercise of functions significantly contributes to the rehabilitation of persons with sensorimotor impairment caused by lesions of the central nervous system (CNS). Voluntary or externally augmented motor activity of paralyzed limbs leads to the reorganization of the sensory-motor systems. Movement can be augmented by two methods, which can be used either in parallel or independently: (1) powered robotic devices (exoskeletons—EXO) controlling the joint angles by acting on the body segments and (2) functional electric stimulation (FES), which controls joint angles by activating paralyzed muscles.

An EXO substitutes the lost function by controlling the joint angles, thus assisting limb movements. It can be a single module attached to two neighboring segments (e.g., an ankle-foot orthosis—AFO) or a more complex mechanism that controls several joints (knee-ankle-foot orthosis—KAFO and reciprocating gait orthosis—RGO). Early EXO versions had simple joints, with brakes to lock a joint angle in a fixed position. Humanoid robotics research led to actuated EXOs [1]. Significant problems in the daily use of EXOs for training are (i) the weight of the exoskeleton, (ii) the need to fit the exoskeletal axes to the biological joints' axes, (iii) the large interface forces between the exoskeletal and bodily segments, (iv) the considerable power and joint torque requirements ($P \approx 150\,\mathrm{W}$ and $M = 100\,\mathrm{Nm}$ per joint for standing and gait), and (v) the control, which needs to be integrated into the preserved sensory-motor systems of the user. A particular problem is related to the process of donning and doffing when an EXO is used for standing and gait restoration.

Functional electric stimulation (FES) was found useful for the control of paralyzed extremities [2]. The alternative term neuromuscular electric stimulation (NMES), often used in literature, emphasizes the target of the stimulation, yet the term FES includes the word “functional” being essential for the recovery of function (Fig. 1).

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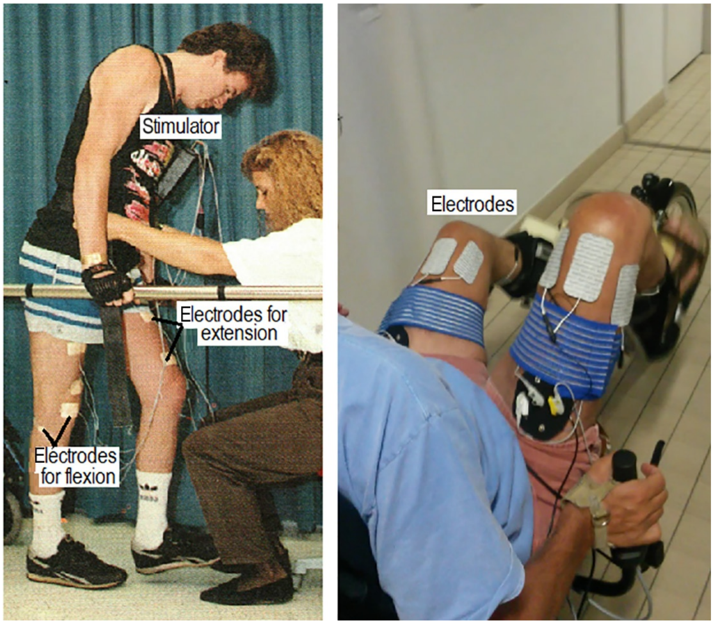

FIG. 1

FES with surface electrodes used for the control of gait and pedaling (tricycle).

An FES system interfaces the sensory-motor systems via surface or implantable electrodes. Surface electrodes of the appropriate size need to be positioned in the vicinity of the innervations of the target muscles. Electric stimulation generates an electric field in the surrounding tissue that is a function of the size and position of the electrodes and of the intensity of stimulation. Most sensory and motor nerves that are within the space where the electric field is generated by stimulation will be activated. This nonspecific activation is a problem for direct motor or reflexive selective activation of synergistic muscles. The use of implantable electrodes improves selectivity since the electrodes can be positioned close to the target nerves, but does not eliminate the problem entirely, since a nerve is composed of ascending and descending pathways that are anatomically organized in fascicles that innervate various muscles (synergist and nonsynergists) and communicate with the higher levels of the CNS.

To generate a fused muscle contraction, a minimum frequency of 20 pps is required. The external activation recruits neural fibers in the reversed order compared with the natural order of the recruitment, which is determined by the size principle [3]. These issues limit the practical use of FES, because high pulse rate causes muscle fatigue. A way to postpone the onset of fatigue is to use asynchronous activation of different motor units of a single muscle at a lower pulse rate (e.g., 8–10 pps) by using multicontact electrodes. The intensity of stimulation (pulse amplitude) is much lower for implantable FES (1–10 mA), if compared with surface FES (20–140 mA). The typical pulse duration of charge compensated pulses is between 10 and 500 μs.

The product of pulse amplitude and pulse duration ($Q = I \cdot T$) must be above the chronaxie (strength-duration or I-T curve) for the stimulated structure. Recent research suggests that the amount of charge can be reduced if the stimulating pulse has very steep rise edge (in the ns range), yet this needs to be validated.

Implantable systems have advantages compared with surface FES systems for long-term daily usage (e.g., control of grasping in tetraplegic patients and control of walking and standing in complete paraplegic patients). Current implantable systems are still not perfect since the power source is outside the body; hence, the energy must be transmitted wirelessly between the power unit and the implanted output stage. Surface FES is a preferred solution for the training (therapy) of persons with a CNS lesion. Nevertheless, surface FES is not applicable to the many muscles that are located deep in the body (e.g., iliopsoas muscle).

HYBRID ASSISTIVE SYSTEMS

The idea of using a combination of FES and EXO was first proposed in the 1970s [4] based on the observation that each of the components had functional limitations. An hybrid assistive systems (HAS) could be built starting from the FES as the core and adding minimal hardware (modular EXO) to assist only the functions that are not achievable by FES [5,6].

The first system that combined four-channel stimulation with an unilateral self-fitting modular orthosis with a powered knee joint was tested in a complete SCI subject whose voluntary activation of muscles for extending and flexing one leg was compromised due to muscle denervation. The system used rule-based control based on the finite-state model of gait [6].

A different approach to HAS is to use EXOs as the core and add FES for the functions that are not feasible using the EXOs [7]. More specifically, joint stability and prevention from unwanted movements were delegated to the EXO, while the FES was envisioned as the actuation system of selected functions. Solomonow and associates used a reciprocating gait orthosis (RGO) and a hip guidance orthosis (HGO) enhanced by a four-channel FES [8]. Clinical results reported that ambulating with the Louisiana State University RGO (LSU RGO) were associated with high energy cost. Also, most subjects were unable to stand up without assistance. To reduce the load over upper extremities and to reduce the energy requirements during the walking surface, electric stimulation of the rectus femoris and hamstrings muscles was added. The stimulation electrodes were incorporated in a plastic polymer cuff. Phillips [9], in addition to the stimulation of hamstring muscles, stimulated the ipsilateral gluteal muscle to improve hip extension during the stance leg. The system using three-electrode configuration with two channels for the knee extension for each leg activated the entire bulk of the quadricep muscle. Two stimulators were used to activate paralyzed hamstrings and gluteal muscle.

A version of the hybrid system is shown in Fig. 2 [5]. The hybrid device combines two implantable stimulators (one per leg) and the exoskeleton that controls the hip and knee joints.

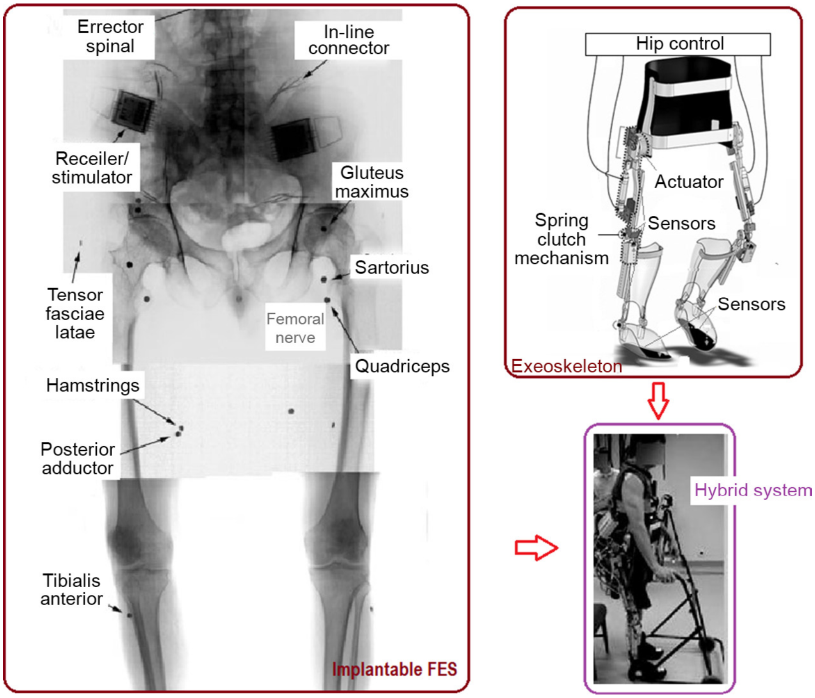

FIG. 2

The implantable FES for activation of paralyzed muscles and the exoskeleton controlling the hip and knee joints. The sensor-driven control based on a finite-state model of gait was used for control.

Modified from Solomonow M, Aguilar E, Reisin E, Baratta RV, Best R, Coetzee T. Reciprocating gait orthosis powered with electrical muscle stimulation (RGO II). Part I: performance evaluation of 70 paraplegic patients. Orthopedics 1997;20(4):315–324, IEEE©.

A critical component for hybrid assistive systems is the controller of the EXO joints.

Goldfarb and Durfee designed and evaluated a magnetic particle brake for FES-aided walking [10]. Parallel operation of the EXO and body parts was the basis for the design of a joint-coupled orthosis (JCO) [11].

Upper extremity assistive systems are much more complex in comparison with those for the lower extremities. No existing exoskeleton perfectly fits all the degrees of freedom of the human arm. The exoskeletons designed to support manipulation control either the end point (single contact cuff near the wrist) or the relative orientations of arm segments (rings or cuffs in touch with the arm and forearm). There are as yet no exoskeletons that are capable of controlling fingers and thumb movements during grasp/release operation. Mechanisms that can partly replicate the movements of the fingers and the thumb have been designed, but they are not practical. The main technical difficulty comes from the fact that the hand must contact objects during operation; hence, the exoskeleton can only be mounted on the volar side of the hand.

Digits of the hand (fingers and thumb) can be controlled using FES. The resulting motions are not the same as in healthy humans, yet they allow prehension of the hand, grasp, hold, and release of objects. The idea of using surface stimulation has been exploited, and there are commercial products allowing synchronized finger extension/flexion and thumb extension/opposition allowing the prehension, grasp, and release of various objects used in daily life [12]. The development of a FES system for upper extremities was motivated by the lack of ability of tetraplegic population to grasp and release resulting in a total dependence from caregivers. The main application of FES for upper extremities today is as training devices, which aim at facilitating the recovery of function.

The commercially available device NESS H200 is an FES system integrated into a splint to hold the wrist in a neutral position. The stimulation module uses a preprogrammed sequence for opening and closing of the hand, holding the object and finally releasing it (Fig. 3, left panel). The NESS H200 can be classified as a hybrid system since it combines FES with an EXO. The alternative to splint-based control of the wrist posture is a more sophisticated FES system, which activates the wrist muscles (Fig. 3, right panel). The cocontraction of agonists and antagonists increases the stiffness and holds the wrist in the desired orientation. The muscles controlling fingers and thumb extension and flexion are activated in parallel, thus enabling grasp/hold and release functions.

The combination of wrist, fingers, and thumb control is feasible through asynchronously distributed stimulation over an array of electrodes and implementation of the triphasic stimulation pattern [13,14]. The development and design of a system that benefits from array electrodes are carried by the company Tecnalia, San Sebastian, Spain [15].

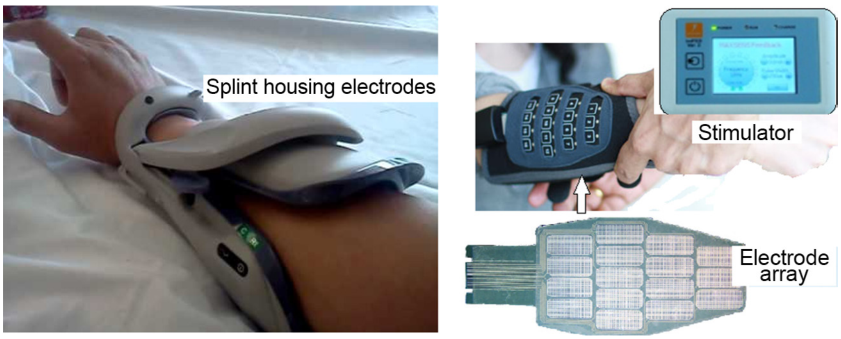

FIG. 3

NESS H200 (left panel) for the control of hand opening and closing and FES-A from Tecnalia, Spain (right panel), allowing the control of the wrist and fingers with the free wrist.

The control of shoulder rotations has never been accomplished in a useful manner using FES, but the control of the elbow joint was shown to be feasible. Stimulation of the shoulder joint has been incorporated into the therapy for the strengthening of muscles to reduce the shoulder subluxation caused pain. Implantable systems for restoration of arm and hand movement [15] are not described in this chapter as these systems are meant for the life-long substitution of function, and are not practical for the training alone. The clinical findings related to the prolonged use of implantable systems showed carryover effects leading to a substantial increase of the reaching and grasping abilities.

HYBRID ASSISTIVE SYSTEMS FOR THE FUTURE

Two types of hybrid systems are of interest for neurorehabilitation: (i) systems for clinical use in the early phases of rehabilitation and (ii) systems for home use for prolonged rehabilitation in chronic conditions. The selection of which exoskeleton is the best candidate for the home activities must take a number of constraints into consideration. The basis for the selection of the appropriate design of exoskeleton are (i) the system must be wearable, comfortable for daily use, and cosmetically acceptable by the user; (ii) modularity must be a desirable feature since various types of disability require different types of assistance; (iii) control must consider that many functions are under biological (volitional or reflex) control that is different from control in healthy persons; and (iv) compensatory movements imposed by the impairment must be anticipated. The systems for clinical use are much less constrained since they are meant to be used for a shorter time.

We discuss first the clinical systems for assisting gait. A robotic platform that partially supports body weight and controls the motion of the leg segments has been developed and translated into a commercial product (i.e., Lokomat, Hocoma, Switzerland). This robotic system demonstrated that intensive training of the gait is beneficial for the recovery of function [16]. The Lokomat system can be hybridized by adding the FES for the control of leg movements aiming to strengthen the neural activation, thereby increasing CNS excitability and facilitating cortical plasticity [17].

FES eliminates the need for external actuators; thus, EXOs should operate as a balance assistant and partial body-weight supporting platform during the stance phase of the gait (Fig. 4). This approach has been tested, for instance, in combining the Walkaround system [18] with multichannel FES. The postural assistant Walkaround (lumbar belt, connected with springs to the powered walker) fits the body contours and orients the trunk in the space. Four-channel FES per leg provides sufficient balance control during gait over the ground and allows the CNS to develop new motor control strategies.

The home usage of hybrid systems needs to provide simple donning and doffing and comfort that fits into the tolerance boundaries of the patient and the environment. The definite preference goes to modular multijoint systems, allowing synergistic control of the neighboring joints (i.e., JCO). The activation of the exoskeleton should

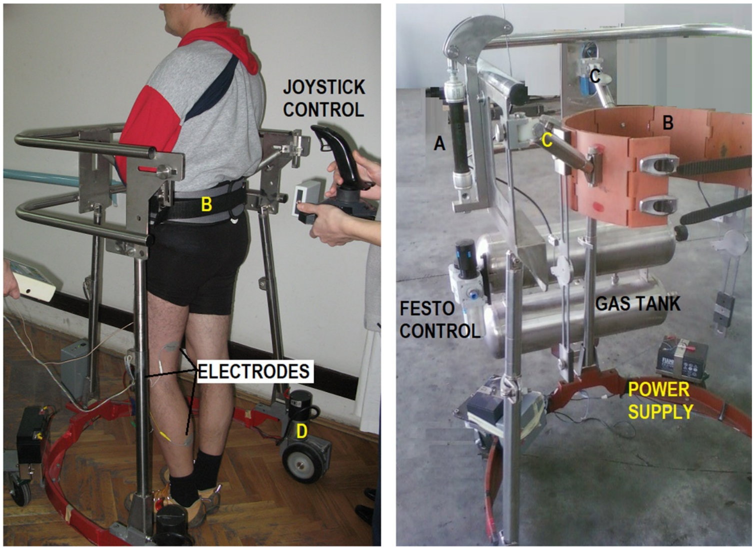

FIG. 4

A hemiplegic patient assisted by four-channel FES supported by the Walkaround. The powered walking support is providing posture orientation and preventing fall with the control of pelvic motions utilizing a pneumatic actuator. A—one of three pneumatic actuators for the control of pelvic region action; B—postural lumbar belt; C—adjustable spring; and D—actuators for the motion of the Walkaround controlled remotely via joystick.

incorporate as much self-powering as possible. The soft interfaces replace rings and cuffs, thus providing cosmetically more appealing systems, while guaranteeing distributed interface forces between the EXO and the body.

Soft robotics is introducing new types of actuators that fit much better into the EXOs when compared with electric or hydraulic actuators. Soft actuators operating like muscle-tendon systems provide joint stability and control of the stiffness resulting with smooth, powerful joint rotations [19]. Futuristic ideas on how to increase the support zone have been suggested, and most likely, they will be integrated into hybrid systems.

Hybrid systems for upper extremities are in their pioneering phase. There are no clinical systems with the fully integrated FES and exoskeletons; however, the platform for combining operations has been established. The hybrid system would use the FES for the control of the hand functions and the exoskeleton for the control of the position and orientation of the hand. The best candidates are systems (Fig. 5) that provide powered assistance [19]. The FES system to be combined with these devices should use the concepts that have been integrated into systems like NESS H200 and STIWELL med4 [20].

The reason behind the hybridizations is that the stimulation modality used in the paradigm termed functional electric therapy [21] leads to the recovery of function in

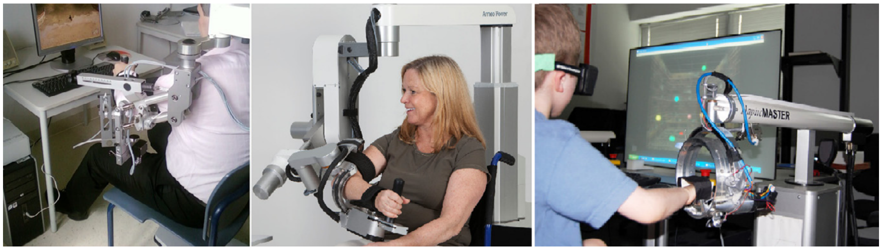

FIG. 5

Exoskeletons for the control of the position and orientation of the hand: Armeo Spring (left panel), Armeo Power (middle panel), and Haptic Master (right panel).

patients who had control of manipulation, yet it has a subtle impact on the recovery of functions in individuals who could lack control of arm movements. The training of arm movements with robotic systems was tested with systems like InMotion ARM [22]. Training with these devices showed temporary improvements in the manipulation, but the regained ability to control the movement was diminished shortly after the therapy. The most likely reason is that the function regained was not useful for daily life. In fact, the treatment needs to bring the motor functions above the level required for regular usage; otherwise, nonuse will counteract the gains.

Another excellent example of improvements by using soft actuators is an OrthoJacket exoskeleton that was tested in combination with the FES using array electrodes.

One final issue in this chapter relates to control. The major challenge for conventional control methods is the accurate estimation of the parameters characterizing the sensory-motor system of the user. Therefore, the hybrid control (Fig. 5) with the top level using rule-based control and the lower level using the model-based control has a better chance to be applied [23] This hybrid system mimics the natural motor control.

Future systems will benefit from the direct brain-derived signals for interfacing voluntary and external control and sensory feedback for the integration of the hybrid system and the body.

An option that needs to be considered is the tonic stimulation of the central nervous system above the lesion added to the phasic stimulation below the lesion [24].

TAKE-HOME MESSAGE

Providing forms of assistance that allow patients with paralysis to regain function is a valuable element for the rehabilitation. Intensive exercise of functions is a key to regaining control of paralyzed extremities. The recovered condition needs to be maintained through a regular usage of the regained function to prevent the consequences of nonuse. Assistance can be maximized by using hybrid systems that combine EXO and FES.

Future hybrids (Fig. 6) should implement light exoskeletons that (1) provide assistance to motor function that cannot be established by FES (e.g., flaccid paralysis), (2) control stiffness of joints that is unfeasible by FES due to the muscle fatigue

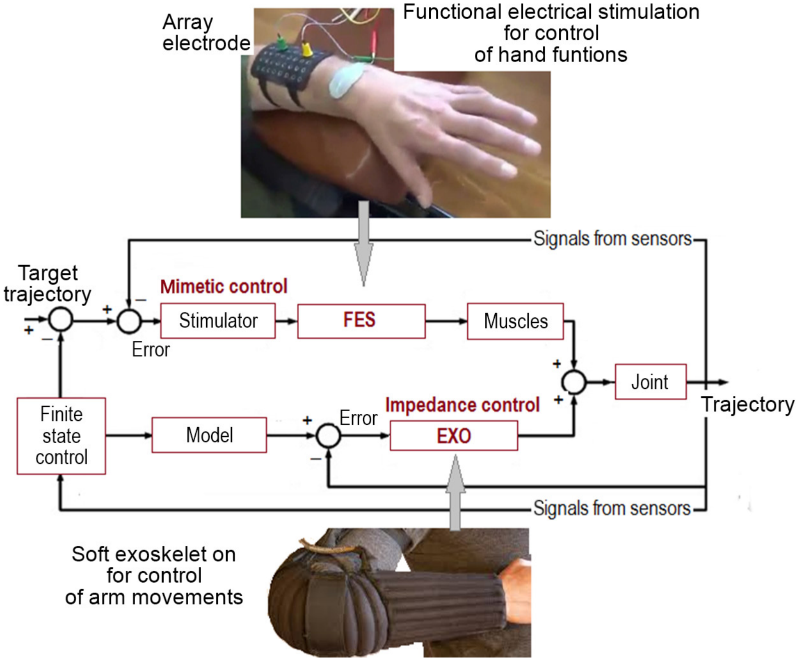

FIG. 6

The schema of a desirable hybrid for the training of activities of daily living and the hierarchical control for the FES-EXO.

associated with prolonged electric stimulation, and (3) reduce the number of degrees of freedom to facilitate control. Future hybrids should use multichannel FES with asynchronously distributed activation of muscles *via* arrays built into the garment. Hierarchical hybrid control needs to mimic biological control and respond to the commands from the user to accommodate environmental requirements.

The communication link for selecting the activity and triggering the start and end should be designed to allow operation at the subconscious level. The particular link that is adding value to the neurorehabilitation is the use of the brain-derived signals (brain-computer interface, myoelectric control, etc.).

Finally, the new hybrid systems need to include sensors that are used not only for the control of the actuation of the hybrid but also for the assessment of the regained function. The assessment needs to be communicated with the rehabilitation expert (telerehabilitation).

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CHAPTER

Robotic techniques for the assessment of proprioceptive deficits and for proprioceptive training

21

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WHAT IS PROPRIOCEPTION AND WHY IS IT IMPORTANT?

Proprioceptive signals originate from mechanoreceptors within the muscles, tendons, and skin. Through a complex process of multisensory integration, they give rise to at least two important perceptual channels, namely, the sense of limb movement (or kinesthesia) and the sense of joint position; these sensations are crucial for bodily awareness, as well as voluntary motor control, regulation of muscle tone, and postural stability. The term proprioception comes from the Latin words "proprium" and "percipio" indicating the "perception of own self."

Neuromotor impairments caused by neurological injuries or diseases (such as stroke, spinal cord injury, Parkinson's disease, and multiple sclerosis) are frequently associated with acquired deficits or loss of proprioceptive abilities. Proprioceptive deficits are common also after orthopedic injury and are often the cause of repetitive injury in sport players. These deficits compromise the ability to perform everyday activities since proprioception contributes to the control of posture, motion, and forces. Specifically, it has been demonstrated that the loss of kinesthetic sensation contributes to impaired control of reaching and stabilization behaviors that are vital to an independent life style [1–4]. Although people suffering loss of proprioceptive feedback can move by relying on vision, long processing delays inherent to the visual system (100–200 ms, [5]) yield movements that are typically slow, are poorly coordinated, and require a good deal of attention [6,7]. As a consequence, visually guided corrections may come too late and result in jerky, unstable movements [8]. Often, stroke survivors give up using their contralesional limb because of their sensorimotor deficits [9] even though this reduces the quality of life [2,10]. Proprioceptive deficits or losses might also interfere with motor learning processes [11–13], as well as with

[a]Equal contribution.

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the motor outcome of rehabilitative treatment and the recovery after neurological injury [14–16]. Therefore, it is important to evaluate proprioceptive accuracy in a quantitative manner and to determine how proprioceptive deficits impact the ability to perform daily living activities.

Since proprioception results from complex cortical and subcortical processes that integrate sensory inputs from across the different peripheral receptors, measurable indicators of proprioceptive integrity are likely to be affected in the early stages of many neurological diseases, thus providing an opportunity for early diagnosis. Currently, standard neurological examination techniques lack sufficient precision and accuracy to reliably detect early-stage deficits of proprioception. By contrast, robot devices and their resolute measurement technologies are naturally suited for that purpose and for the twin objective of integrating assessment functions with assessment-based rehabilitation interventions.

ASSESSMENT OF PROPRIOCEPTIVE DEFICITS

CLINICAL SCALES

It is common wisdom among health-care professionals treating neurological diseases that somatosensory assessment is an essential part of the clinical evaluation process and that it provides valuable information for prognosis of functional ability and rational identification of treatment protocols. However, no gold standard for assessing the integrity of proprioceptive sensation has been established so far. A recent review of currently used clinical scales of somatosensory assessment [17] evaluated 16 sensory scales from the point of view of psychometric properties and clinical utility. Of these, 11 were rejected because they were not available for a researcher or clinician to use. The five remaining scales include the following:

1. Nottingham Sensory Assessment (NSA, [18])
2. Rivermead Assessment of Somatosensory Perception (RASP, [19])
3. Sensory section of the Fugl-Meyer Assessment (FMA-S, [20])
4. Moving and Sustained Touch-Pressure Tests ([21])
5. Touch Perception Threshold test ([22])

Of these five, a variant of NSA [23] and the sensory section of the Fugl-Meyer Assessment exhibited the best balance of clinical utility and psychometric properties [17].

The original NSA assessed the following sensory modalities: tactile sensations (light touch, pinprick, pressure, tactile localization, and bilateral simultaneous touch), temperature, proprioception, and stereognosis. The complete assessment takes about 1 h to administer, and interrater reliability is poor. Subsequent revisions (in particular the Erasmus MC modification) removed some items (e.g., temperature), and scoring was standardized, thus achieving improved interrater reliability, with a significant reduction of the time to complete (now 10–15 min).

The sensory section of the Fugl-Meyer Assessment contains 12 three-point items, 4 for light touch and 8 for joint position sense to yield a maximum score of 24 points.

For light touch, the patient is asked whether they can feel touch on the arms, palms of the hands, legs, and soles of the feet on both sides. Joint position sense of the interphalangeal joint of the thumb, wrist, elbow, shoulder, big toe, ankle, knee, and hip is also tested. Interrater reliability is weak to excellent for individual items, with the proprioception tests being more highly reliable than the light touch tests. The time required to complete the FMA-S is about 15 min.

As for the lower limb, the most used clinical assessments are two rather simple tests: movement detection at the big toe and the Romberg sign [24]. Romberg's test is an exam of neurological function for balance. The exam is performed in quiet standing and is based on the premise that a person requires sufficient integrity in at least two of the three following sensory feedback systems to maintain balance: visual, proprioceptive, and vestibular. The test compares the amplitude of sway movements (i.e., small involuntary oscillations of the standing body) in normal conditions and in the absence of vision. The higher the proprioceptive and/or vestibular deficits, the higher the difference between the amplitudes in the two conditions.

ROBOTIC ASSESSMENT METHODS

Currently available clinical scales or assessment methods cannot be used in any kind of closed-loop treatment paradigm, where treatment parameters (e.g., force intensity and kinematic thresholds) should be monitored and adjusted online or with a trial-by-trial frequency. Several robotized tests have been developed in the recent years to address this need, and among them, two specific classes have been gaining interest: joint position matching (JPM) tests (e.g., [25,26]) and psychophysical threshold method (PTM) tests (e.g., [27–29]).

JPM tests measure the subject's accuracy in replicating the position or velocity of a joint angle or a limb in the absence of vision. The outcome of a JPM test is an evaluation of the matching error. By contrast, PTM tests quantify the subject's sensitivity in detecting the intensity of proprioceptive stimuli or in discriminating two stimuli of equal nature but of different amplitude (e.g., position/motion, tactile, or vibrational). With respect to position sense, for example, subjects might be required to indicate which of the two sequentially presented passive movements has the larger amplitude. Of course, clinical personnel could perform both types of tests directly by means of commonly used tools such as handheld goniometers. However, evidence for the reliability and/or accuracy of manual methods is scarce. Thus, a number of research groups have recently developed methods and testing protocols based on robotics [28,30–33], optoelectronics, and magnetic devices to assess proprioception (see [34] for a review). Here, we will focus on methods based on robotic techniques, which are probably the most commonly used ones and which represent a natural link between objective assessment and treatment/rehabilitation. The possibility to implement the JPM and PTM tests on robotic platforms facilitates collection of large normative data sets through reliable procedures that yield objective and high-resolution data. Previous reports have highlighted the efficacy of robotic devices in providing meaningful information on proprioceptive sensitivity for both healthy and neurological subjects. Most studies have focused on the proximal joints of the upper limb, although a few have focused on joints of the lower extremity including the hip, knee, and ankle.

Tests for assessing proprioception have been implemented using a variety of different robotic devices, although the most commonly used devices for both the lower and upper limbs have had an exoskeletal structure (e.g., the Lokomat (Hocoma AG, Volketswil, Switzerland) for the lower limb and the KINARM (BKIN Technologies Ltd, Ontario, Canada) or the Wristbot [35][1] for the upper limb). For example, [25] used a Lokomat to implement a JPM test for assessing hip and knee joint proprioception in healthy subjects and incomplete SCI subjects. By contrast, a PTM protocol was used by [27] to assess separately hip and knee proprioception. Another device largely used for lower limb testing is the isokinetic dynamometer (e.g., Biodex, [36]). A modified version of this device was used by [37,38] for assessing passive flexion/extension and varus/valgus movements of the knee in healthy subjects and osteoarthritic patients. It is worth also to mention the system for detecting the toe motion developed by [39]. More details related to the lower limb assessment of proprioception may be found in [40].

For the upper limb, [28] developed a robotic device that was used to test proprioception at the wrist using threshold detection paradigms and ipsilateral joint position matching tasks in the absence of vision [41,42]. Testing was performed in adult subjects [42] and in children [41] to delineate developmental changes in limb position sense across childhood and adolescence. Similarly, Dukelow's team has developed robotic tools and testing algorithms that quantify motor dysfunction after stroke in adult and pediatric populations [32,43]. In our opinion, their work is the most important contribution to the robotic assessment of proprioception integrity. Over the past years, they have built a database of clinical, robotic (using the KINARM device), and neuroimaging assessments from more than 230 adult stroke survivors and more than 60 hemiparetic survivors of pediatric stroke. At the time of this writing, the adult database included additional reach tests for 160 subjects at 6, 12, and 26 weeks post stroke. Neuroimages collected for each individual include structural magnetic resonance images (MRI), which provide information about the site and size of stroke-related brain damage (lesions) allowing identification of the relation between those factors and the proprioceptive deficits. This comprehensive data set has the potential to identify neural circuits within pediatric and adult brains critical for the rehabilitation of—and/or compensation for—deficits of proprioceptive sensation after stroke. Fig. 1 illustrates some robotic devices used for proprioceptive assessment.

Joint position matching methods (JPM)

In joint position matching methods, subjects are required to match the position of a joint or a limb with either the same joint or limb (cf. [25,41,42,44]) or with the

[1] Wristbot is derived from an original design by Masia et al. [35]. It went through several reengineered versions with the goal to achieve the CE marking and will be commercialized in the near future with the support of the technology transfer office of IIT.

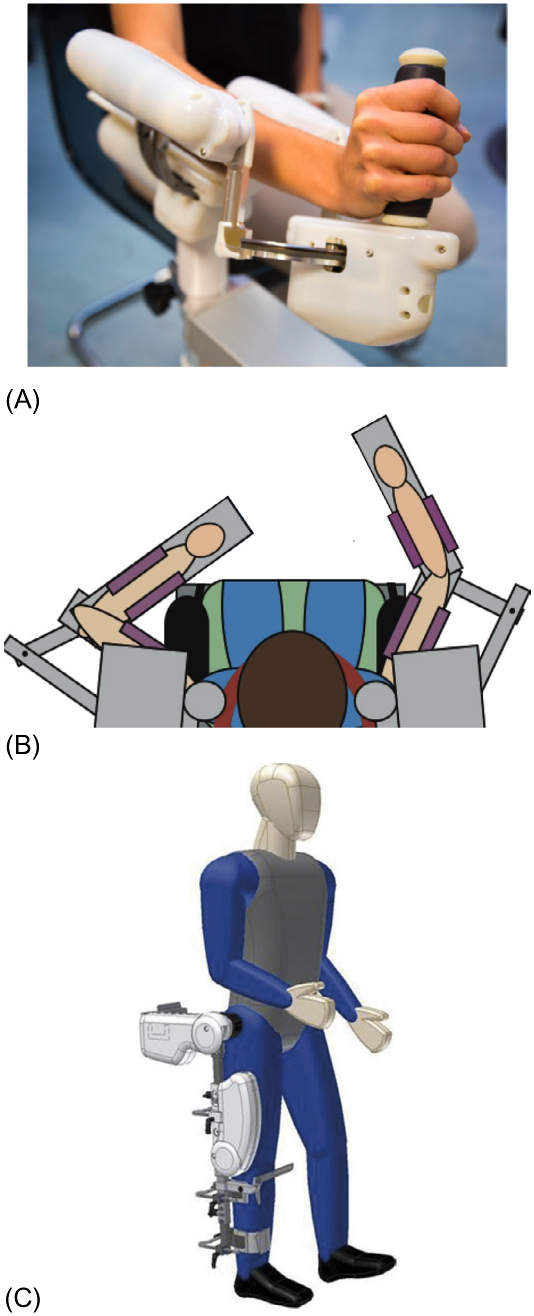

FIG. 1

Robotic devices used for proprioceptive assessment. (A) Wristbot [47], (B) KINARM (BKIN Technologies Ltd, Ontario, Canada), and (C) Lokomat (Hocoma AG, Volketswil, Switzerland).

Modified from (B) Cammarata ML, Dhaher YY. Proprioceptive acuity in the frontal and sagittal planes of the knee: a preliminary study. Eur J Appl Physiol 2011;111:1313–1320 and (C) Hocoma website, http://www.medicalexpo.es/prod/hocoma/product-68750-773915.html.

contralateral limb (cf. [26,31,32,43,45]). Most commonly, the target position is indicated by passively moving the limb to a desired position in the absence of vision. Less often, the target is only presented visually. It is worth mentioning that although the subject's task is to match the final position, the subject might use both position and velocity information in order to match simultaneously the final target position and the velocity profile used to reach that point.

Unilateral vs bilateral matching protocols

There are two main matching protocols used to test position sense. In the *ipsilateral* or *unilateral* matching protocol, a joint (or a body part such as the hand or foot) is passively moved to a certain target angle (or position) and then brought back to a neutral initial position. The subject's task is to remember the target position and then to actively move that same joint (or limb) to reproduce the desired endpoint position or limb configuration as accurately as possible. This method has a clear memory component and thus assesses cognitive function in addition to proprioceptive sensation.

In the *contralateral or bilateral* matching protocol, a joint or a body part is passively moved, and the final position, once achieved, is matched with the contralateral joint or body part. In *contralateral concurrent* cases, the target position of the target limb is maintained, while the other performs the matching movement; this approach does not require explicit memory of the targeted proprioceptive sensation. However, this version of the matching task requires integration of proprioceptive information across two sides of the body, thus requiring communication between the two brain hemispheres via the corpus callosum. The concurrent matching protocol is the version most similar to assessments currently used in clinical practice, where clinicians move one limb of the subject to a specific position and ask him/her to replicate that position with the contralateral limb. In a less common version of the protocol, the subjects are asked to reach the target position with their matching limb after the contralateral limb is back in the neutral position: This version of the protocol is called *contralateral remembered* approach, and it is dependent on both the integrity of the working memory and the communication between the two brain hemispheres. Another approach that requires both working memory and integrity of proprioception uses an “active movement extent discrimination apparatus” (AMEDA) (see [46] for a review).

Performance assessment: Accuracy vs precision

Matching tests typically quantify the acuity of limb position sense using two complementary performance measures: accuracy and precision. Accuracy indicates how close a sensed limb position corresponds to its true physical position, and it is measured as the mean value of the matching error. For an ideal response, matching error would be equal to zero. Precision corresponds to the variability of performance, which indicates the degree of agreement between repeated tests; the lower the variability, the higher the precision, which is typically expressed as the standard deviation of the repeated measurements. Details about some of the parameters used to evaluate the position sense can be found in Chapter 11.

Adapting testing protocols to limitations due to neuromotor deficits

Matching methods typically require subjects to perform active movements that can be difficult or impossible after neurological injury [30]. Moreover, the variable limitations in the extent of voluntary control between patients can bias the results of some matching tests. To overcome these drawbacks, some studies have adapted the testing protocol to the subject's active range of motion. Other studies instead required subjects to use a body part that retained sufficient mobility to manipulate a joystick (or other control interface) to cause a robot to passively move the matching limb to the indicated, desired location. [25]

Psychophysical threshold methods (PTM)

Psychophysics is a branch of experimental psychology concerned with the study of perception or the relation between physical stimulation and perceptual events [47]. The objective of many psychophysical experiments is to infer information about the neural mechanisms contributing to sensory perception through the observation and analysis of repeated stimulus-response pairings. There are two main categories of psychophysical threshold assessment techniques: One estimates the *detection threshold*, which is the smallest perceptible stimulus, whereas the other estimates the *discrimination threshold*, which is the smallest perceivable difference (or just-noticeable difference, JND) between two perceptible stimuli. The detection threshold is considered a measure of sensory sensitivity while the discrimination threshold a measure of sensory acuity. Specifically, in the case of proprioception, PTMs are used to assess movement perception in terms of either amplitude or direction.

Threshold-based paradigms require devices that passively move a person's limb in a highly controlled manner [48]. During threshold detection in passive motion tests, participants are typically seated or lying down. The body part to test is isolated by constraining the adjacent body segments. Other peripheral information, such as tactile, visual, and aural information, is usually occluded by using air cushions, blindfolds, and headphones. With all these variables controlled, the joint or body segment under investigation is passively moved in a predetermined direction. To estimate the smallest perceivable stimulus, participants are instructed to indicate—for example, by verbal report—the direction of movement as soon as they perceive it. Although there are several different protocols described in the literature, testing in most cases proceeds until three to five correct judgments of the same stimulus are achieved. One of the most important tests for establishing whether proprioceptive deficit exists in the lower limb is the PTM test performed on the big toe [24].

Several other psychophysical testing approaches can be used to assess the integrity of proprioceptive sensation. For example, one robotic test used two alternatives, forced-choice paradigm and the psychophysical *method of constant stimuli* to assess proprioception in tasks directly relevant to laboratory tests of motor function and learning [49]. Specifically, Simo and colleagues used a horizontal planar manipulandum to repeatedly apply controlled displacements and controlled forces of various magnitudes to the hand in order to evaluate the ability of subjects to detect such displacements. A psychometric function parameterized the decision process underlying the detection of hand displacements. The shape of this function was characterized using two parameters: a signal detection threshold and the variability of responses about this threshold. The automatic procedure differentiated between participants with and without proprioceptive deficits and quantified functional proprioceptive sensation on a magnitude scale that is meaningful for ongoing studies of degraded motor function in comparable horizontal movements. A significant limitation of the approach described by [29], however, is that the method of constant stimuli is a lengthy testing procedure that can take up to 45 min to complete, which makes it impractical for common clinical use. Recently, Mrotek and colleagues have described an abbreviated robotic assessment of arm proprioception that uses the psychophysical *method of adjustments* to estimate the movement detection threshold and the variability of responses about that threshold [50]. In this case, participants repeatedly adjust the magnitude of the stimulus until it is just perceptible, with an equal number of trials approaching that threshold from below (i.e., starting from smaller stimulus magnitudes) and above (from larger magnitudes). This alternative test takes less than 15 min to administer and appears sensitive not only to proprioceptive deficits that arise consequent to stroke but also to subtle changes in proprioception that occur with aging [50].

ROBOTIC PROTOCOLS OF PROPRIOCEPTIVE TRAINING

There is a rich rehabilitation literature that establishes the efficacy of various forms of proprioceptive training for improving proprioception and aiding motor recovery. However, there is little agreement about what aspects of proprioceptive training may have most clinical utility. In an attempt to clarify this situation, [51] provided a recent review paper that systematically searched the literature on the basis of keywords indicative of proprioception and proprioceptive training. Their three main inclusion criteria required (1) pre- and posttreatment proprioceptive assessment, (2) training aimed at improving proprioceptive function, and (3) possibility to discriminate proprioceptive effects from effects related to other sensory modalities. Based on their summary, the authors proposed the following definition: “Proprioceptive training is an intervention that targets the improvement of proprioceptive function. It focuses on the use of somatosensory signals such as proprioceptive or tactile afferents in the absence of information from other modalities such as vision. Its ultimate goal is to improve or restore sensorimotor function.” The review addressed several different pathologies (stroke, cerebral palsy, Parkinson's disease, focal dystonia, traumatic injury, and multiple sclerosis), different intervention types (e.g., active movement training, passive movement training, somatosensory stimulation, or discrimination training), and different outcome measures. The authors found that (i) proprioceptive training can improve proprioception and can lead to recovery of somatosensory and sensorimotor functions, (ii) improvements are greater if the intervention lasts longer, and (iii) a large population may gain benefit from proprioceptive training regardless of the neurological or musculoskeletal origin of the somatosensory deficits.

Despite these findings and despite the fact that a majority of people with neurological diseases are affected by both motor and proprioceptive dysfunctions, sensory re-training as defined by Konczak and colleagues [51] is often disregarded in current rehabilitation practice. There are currently only a small number of reports of robotics being used to implement or enhance proprioception training, whereas there are many reports of robotics being used to either promote recovery of some aspect of motor function or assess proprioceptive deficits. Fig. 2 illustrates the robotic approach to proprioceptive training.

Other examples where robotics have been used to implement proprioception training include the study by [52], who used an ankle rehabilitation robot to provide passive stretching and active movement training to subjects with multiple sclerosis, finding that the approach induced improvement of the proprioceptive acuity at the ankle joint. A number of studies that have trained proprioceptive control of standing balance on unstable surfaces can also be implemented using mobile robotized platforms (e.g., [53]). In addition, several studies have focused on proprioceptive training that exploits haptic feedback provided by robotic devices coupled to the upper limb. Casadio and colleagues [54–56] proposed a proprioception-based motor training technique to augment kinesthetic awareness via haptic feedback mediated by a robotic manipulandum. Specifically, they alternated blocks of reaching trials performed with and without visual cues. In blocks without vision, subjects were blindfolded, and the target was represented with a haptic cue, that is, subjects had to feel and respond to a guiding force that attracted their hand toward the target. The magnitude of this force field was constant during the reach and was titrated continuously down to the minimal level that allowed the subject to perform the task. The protocol was tested on a small cohort of chronic stroke survivors. With practice, all subjects exhibited an increased amount of voluntary control. Moreover, training with closed eyes appeared to be beneficial for subjects with abnormal proprioception, suggesting that training by alternating vision and no-vision blocks might improve the ability to use proprioception both in conditions with and without visual feedback. Squeri et al. [57] subsequently adapted that protocol such that the position of the unimpaired hand became the target for the robot-assisted, paretic arm. When the target was reached, the concurrence between the proprioceptive signals between the two limbs provided a reinforcement mechanism that may promote the recovery of sensorimotor functions.

As a further extension of the same line of research, the continuous assistive force field of minimal intensity described in [53–55] was modulated in time by means of a sequence of small and short impulses: two impulses per second, with a duration of 200 ms [58]. The protocol was similar, namely, chronic stroke survivors were asked to perform targeted reaching movements in the absence of vision under the guidance of the minimally assistive-pulsed forces described above. The rationale of such modulated assistive paradigm is double: (1) It enhances the proprioceptive training aspect of the robotic treatment because the pulsed nature of the guidance provides subjects with transient kinesthetic clues about their position relative to the target, inducing them to focus on proprioceptive sensation in order to produce a movement

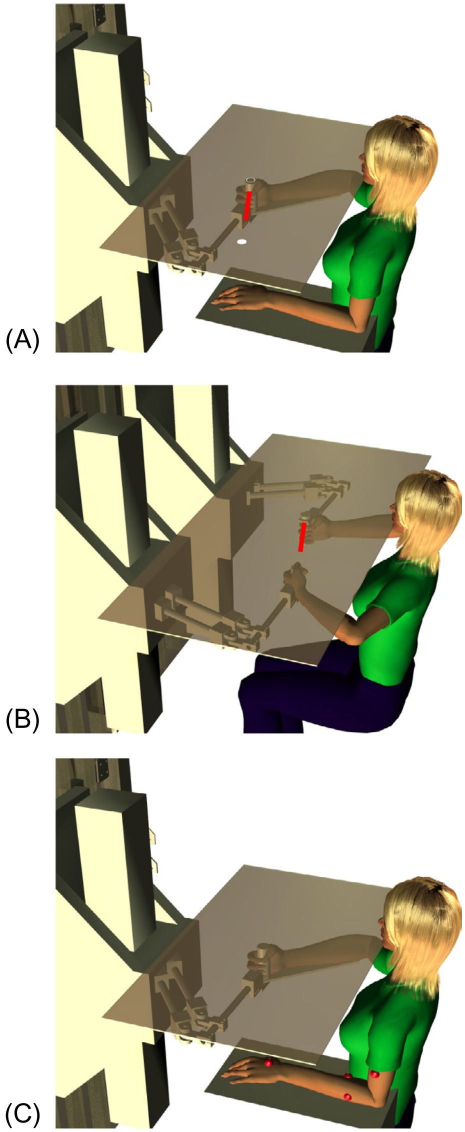

Fig. 2 Robotic approach to proprioceptive training. (A). Haptic feedback—subjects are blindfolded, and the target is represented using a haptic cue. The subject has to feel a guiding minimally assistive or pulsed force that is attracting their hand toward the target. (B) Haptic feedback with proprioceptive target—the protocol of (A) was adapted such that the position of the unimpaired hand became the target for the robot-assisted paretic arm. (C) Robotic training in combination with supplemental proprioceptive feedback. The dots on the arm of the subject correspond to vibrational, tactile, or electrotactile stimulators.

in the correct direction, and (2) it allows the online estimation of an active contribution (AC) index (i.e., a quantitative evaluation of the degree of active participation of the patient in the acquisition of the target vs the degree of passive “slacking” in response to the assistive force field [58]). In that study, the intensity of the haptic feedback was adaptively modulated along each movement direction according to the AC index, and the level of guidance was automatically adjusted to match variations that can arise from learning or mental fatigue. In this way, the protocol assured a uniform level of task difficulty across reaching directions throughout the training session. That study represented the first attempt to integrate active perceptual and motor training with an online quantitative evaluation of performance within the same exercise. Moreover, the pulsed paradigm, using half the assistive force magnitude, allows patients to achieve the same level of performance as the continuous minimal assistance paradigm.

ENRICHING ROBOTIC ASSISTANCE WITH SUPPLEMENTAL PROPRIOCEPTIVE FEEDBACK

Another approach for training or improving impaired proprioception in the real-time control of movement is to supplement proprioceptive feedback with additional sensory signals. In particular, two main types of additional stimuli have been exploited most frequently in practice, vibrational or tactile stimuli. As for vibration stimuli, the literature describes two main conceptual approaches. The first, *stochastic resonance*, is based on the observations that muscle spindles (the primary limb proprioceptors) are particularly sensitive to vibratory stimuli and that a proprioceptive signal that is normally too weak to be detected by the nervous system can be boosted to detectible levels by adding vibratory stimuli containing a wide spectrum of frequencies [59]. In stochastic resonance applications, no meaningful information is encoded in the vibratory stimulus. This approach has been shown to have utility for increasing equilibrium during standing [59] and has also been applied in the upper and lower extremities. The second approach is referred to as either *sensory substitution* or *sensory augmentation*. It is a noninvasive technique for overcoming deficits in one sensory modality by injecting information related to the lost or impaired sensations into an alternate sensory channel using synthesized, supplemental, sensory signals. By combining vibration with motor training, it is possible not only to substitute for degraded sensory signaling but also to enhance proprioceptive sensations beyond existing constraints imposed by injury or inherent physiological limitations of the sensory system.

Regardless of the feedback encoding approach—whether vibrational or tactile—these stimuli require a cognitive effort that appears to increase as the supplemental feedback encodes increasing degrees of freedom. This becomes important when providing supplemental feedback with the goal of improving proprioception in individuals with neurological diseases, where the cognitive effort required to understand the information could be a critical limiting factor for the effective use of tactile and vibrational displays.

CONCLUSION

Movement and proprioception are aspects of sensorimotor control that are hard to study separately, at least in neurologically intact humans. Moreover, proprioceptive deficits and motor impairments interact in a complex manner making it difficult to establish shared standards of evaluation and treatment. Consequently, clinical practice commonly characterizes the integrity of proprioception using qualitative and unreliable assessments, and treatment protocols are almost never optimized for the specific sensorimotor deficits of a given patient. Robot technologies—together with smart data processing tools and well-formulated experimental protocols—have a chance to provide unbiased, accurate, and objective methods to assess proprioception, which can provide the knowledge needed to develop individualized treatment protocols that are matched to the patient's specific deficits and needs. Ultimately, the establishment of diagnostic standards and accepted functional assessment protocols will aid therapeutic intervention, although there remains much to do before this goal will be reached.

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CHAPTER

22

Psychophysiological responses during robot-assisted rehabilitation

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INTRODUCTION

Rehabilitation systems increasingly implement combinations of rehabilitative haptics along with associated visual and audio modalities. In addition to the desired motor activity, these modalities elicit a variety of volitional and other hidden or subconscious human responses. The biocooperative control approach consists of acquiring and integrating various responses. Based on that, decisions are made to thus modify the set of multimodal parameters in order to guide the user into the most pleasant and in rehabilitation terms the "optimal" state.

Yerkes-Dodson's law is over 100 years old and states that an intermediate level of arousal is required for optimal human performance [1]. The law suggests that performance increases with physiological or mental arousal, but only up to a point. When levels of arousal become too high, performance decreases. This is reflected in novel rehabilitation technology approaches that should ideally place the human in the loop. The human's motor functions and cognitive functions are observed using various biomechanical and physiological sensors (Fig. 1) [2].

Within the controller, the fast feedback loop at a frequency of 1 kHz or more ensures a biomechanical closed loop; in this case, the haptic device acts as a media channel to the human. Motor functions reflected in biomechanical signals (position, velocity, acceleration, and force) define biomechanical states. As an example, a robot assists a human in a compliant way, with only as much force as is needed, so the patient can contribute to the movement with their own voluntary effort.

Physiological signals that define physiological states change slowly, within a few seconds after stimuli. Consequently, the feedback loop is characterized by intrinsically much slower dynamics. It involves recording and controlling the patient's physiological reactions, and it then brings about the psychophysiological integration such that the patient receives appropriate stimuli and challenges in a moderate yet engaging and motivating way. The slow feedback loop (i.e., biocooperative loop)

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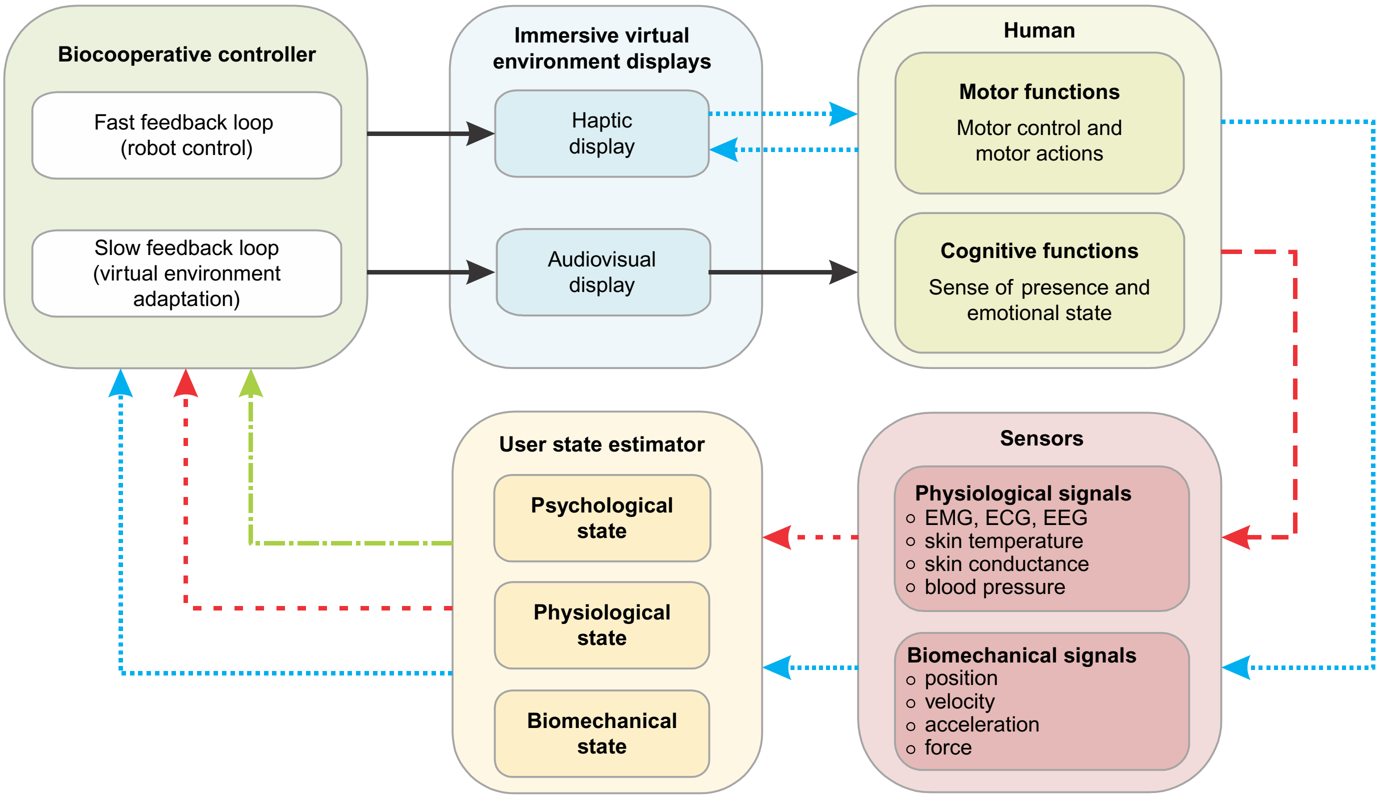

FIG. 1

The human is in the loop with respect to biomechanical (dotted), physiological (dashed lines), and psychological aspects (dot-dash line).

From Riener R, Munih M. Guest editorial special section on rehabilitation via bio-cooperative control. IEEE Trans Neural Syst Rehabil Eng 2010;18(4):337–338 with permission.

influences all three modalities (haptic, visual, and audio) presented to the person in a matter of seconds. In this way, the technical rehabilitation system takes the user's properties, intentions, and environmental factors into account.

EXPRESSION OF HUMAN EMOTION

Specific and repeatedly occurring patterns of human behavior include emotion and its expression [3]. Two opposing communities exist, one defining a discrete and the other using a dimensional classification of emotions. In the first, the universal discrete states are acceptance, anger, anticipation, disgust, joy, fear, sadness, and surprise or, in another classification, happiness, surprise, anger, sadness, disgust, and fear. In the second, emotions appear and are classified in a two-dimensional space with axes of arousal and valence [4]. Valence, sometimes also called pleasure, defines positive versus negative affective states (e.g., tranquility, relaxation, or excitement at one end versus humiliation, disinterest, and anger at the other). The definition of arousal is in terms of mental alertness and physical activity (e.g., sleep, inactivity, boredom, and relaxation at the lower end versus wakefulness, tension, exercise, and concentration at the higher end).

Psychophysiology employs various methods, including subjective, behavioral, and physiological measures to quantitatively access the emotions [5]. The subjective approach employs questionnaires. The behavioral component focuses on (1) the analysis of facial expressions, (2) the analysis of amplitude and pitch of voice, and (3) the coding of body posture and gesture. The psychophysiological measurements of emotion rely on human physiological responses [6,7]. General background principles linking physiological responses (skin temperature, conductivity, heart rate, breathing frequency, etc.) with arousal and valence are presented in the following two paragraphs.

Human physiological responses are primarily a reflection of an autonomous neural system (ANS), which maintains somatic homeostasis, has little or no voluntary influence, and regulates vital body functions such as heart rate, respiratory rate, digestion, salivation, perspiration, pupil diameter, micturition, and sexual arousal [5]. As an ANS input, the sensory part ranges from the blood vessels, thorax, abdomen, and pelvis to the brain. The efferent pathway of ANS (output pathway) includes glands, cardiac muscles, and smooth muscles. The latter are found in the blood vessels, gastrointestinal tract, respiratory tract, urinary bladder, reproductive tracts, and iris and ciliary body of the eye and in the arrector pilorum in the skin. An important observation for someone trying to acquire a physiological response from the body skin is thus to acquire the signal from relevant points at the body's most distal parts in order to capture more of the ANS effects and thereby increase the sensitivity.

The ANS has two branches: the sympathetic nervous system and the parasympathetic nervous system. The sympathetic part recruits the body in the cases of exertion, stress, or emergency; in some way, this is related to arousal [5]. The emotion of anxiety is expressed by physiological changes as an increase in heart rate, shortness of breath, dizziness, nausea-related symptoms, trembling, tensed muscles, and dry mouth. In the opposite, the parasympathetic part is dominant under rest and in states of relative quiescence. For example, the heart pumps more blood out to supply the skeletal muscles for higher performance and vice versa periods of lower activation. The sympathetic pathway also activates sweat glands in the skin to secrete sweat and cool the body down.

PHYSIOLOGICAL SIGNAL ACQUISITION

Four physiological raw signals enable several psychophysiologically relevant features to be extracted. (1) The electrocardiogram (ECG) is usually regarded as one of the lead derivatives of Eindhoven's triangle. (2) The measurement of peripheral skin temperature is obtained through a miniature thermistor with a small temperature constant [8]. Placement may be on the distal phalanx of the fifth finger [9]. (3) The skin conductance measurement is usually obtained by applying voltage between two electrodes and measuring the current flowing between them. They are usually placed on the medial phalanxes of the second and third fingers. (4) Respiratory rate may be obtained using a thermistor beneath the nose, with this sensor able to measure respiration through both the nose and the mouth.

PHYSIOLOGICAL FEATURES

Physiological features are represented by indicators calculated from raw physiological signals. The calculations are usually performed over a fixed-length interval, ranging from a few seconds to a few minutes (2–5).

ELECTROCARDIOGRAM PHYSIOLOGICAL FEATURES

The electrocardiogram (ECG) is the most complex signal to process. After denoising, a 50 Hz notch filter is applied to cut the power-line interference. To reduce the baseline drift and noise caused by electrode movement, a high-pass filter can be applied with $f_{cutoff} = 0.5$ Hz. The combination of the derivative and simple amplitude threshold enables the detection of the R-peaks of the ECG QRS complex, that is, the central and most evident part of the ECG waveform that corresponds to the depolarization of the right and left ventricles of the human heart. The time elapsing between two normal (nonpathological) R-peaks is called the NN-interval. The instantaneous heart rate value is defined as the reciprocal value of the NN-interval. The mean heart rate parameter is an additional ECG feature.

Several time and frequency-domain features can be calculated from the NN-interval series [10]. The three main time-domain features are the standard deviation of NN-intervals (SDNN), the square root of the mean squared differences of successive NN-intervals (RMSSD), and the percentage of interval differences of successive NN-intervals greater than 50 ms (pNN50).

The conversion of NN-intervals into time series provides input values for the power spectral density (PSD) calculation. The resulting PSD has two frequency bands of interest: the low-frequency band (LF) between 0.04 and 0.15 Hz related to sympathetic system activation and the high-frequency band (HF) between 0.15

and 0.4 Hz related to parasympathetic system activation. Three frequency-domain features are usually considered: the total power in the LF band (i.e., the integral of the PSD), the total power in the HF band, and the ratio between them (commonly referred to as the LF/HF ratio or sympathetic/parasympathetic balance).

SKIN CONDUCTANCE SIGNAL PHYSIOLOGICAL FEATURES

In a skin conductance signal, two components of skin conductance are characterized: tonic and phasic. The first, tonic skin conductance, is the slowly changing baseline level of skin conductance and is generally referred to as the skin conductance level (SCL). Each person has a different SCL that varies over time depending on the psychological state and autonomic regulation. Phasic skin conductance consists of rapid skin conductance increases followed by a return to the tonic level. These rapid increases are referred to as skin conductance responses (SCRs). Two features are derived, the SCR frequency and the mean SCR amplitude.

The skin conductance signal is initially filtered with a low-pass filter with $f_{cutoff}=5$ Hz for high-frequency noise removal [11]. Low-pass filtering with $f_{cutoff}=0.1$ Hz brings tonic skin conductance, while a high-pass filter with $f_{cutoff}=0.1$ Hz provides phasic skin conductance.

The mean SCL is calculated from tonic skin conductance. A transient increase in phasic skin conductance is detected as an SCR if its amplitude (from the start of the increase to the peak) exceeds 0.05 ms and the peak occurs within 5 s of the start of the increase.

RESPIRATION SIGNAL PHYSIOLOGICAL FEATURES

The signal obtained from the respiratory transducer has a periodic, nearly sinusoidal shape. Low-pass filtering with $f_{cutoff}=5$ Hz is adequate for reducing high-frequency noise. Peaks in the signal may be detected with a simple algorithm based on the signal derivatives. Respiratory period is computed by measuring the times between two peaks in the signal, while the mean respiratory rate is calculated as the reciprocal value of the mean respiratory period. In addition, respiratory rate variability may be calculated as the standard deviation of the reciprocal value of the respiratory period.

PERIPHERAL SKIN TEMPERATURE PHYSIOLOGICAL FEATURES

Peripheral skin temperature changes very slowly compared with the three other physiological signals. Responses to the stimuli are delayed by more than 15 s. High-frequency noise is removed with a low-pass filter whose $f_{cutoff}=1$ Hz. The skin temperature can be calculated as the mean value over the last 5 s [9].

AN EXAMPLE OF RECORDING PHYSIOLOGICAL SIGNALS

The physiological signals of a typical control subject during the baseline (rest), the physical control task, and a virtual rehabilitation (VR) task are shown in Fig. 2 [11]. In the baseline test, the subject remained quiet during rest; during the physical control

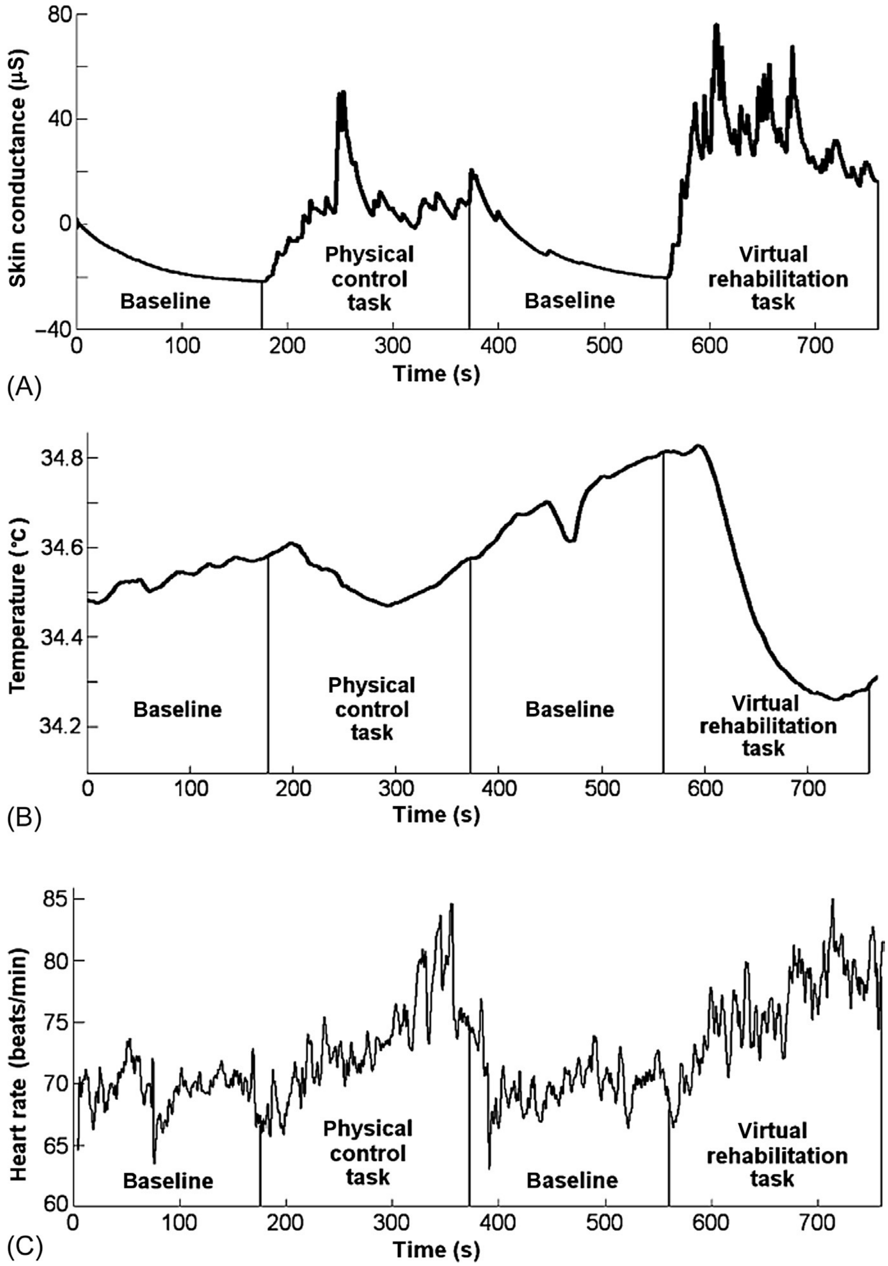

FIG. 2

A typical subject's (A) skin conductance, (B) skin temperature, and (C) heart rate.

From Novak D, Ziherl J, Olenšek A, Milavec M, Podobnik J, Mihelj M, et al. Psychophysiological responses to robotic rehabilitation tasks in stroke. IEEE Trans Neural Syst Rehabil Eng 2010;18(4): 351–361 with permission.

task, the subject moved the robot without the display and force feedback, while during the VR task, the subject combined the cognitively and motor-challenging reaching and grasping exercises using a robot and screen.

At the beginning of each activity, the skin conductance responds within seconds and increases during tasks, with this general increase being recognized as the mean SCL. Several brief increases in the skin conductance signal that appear during the two task periods represent a higher SCR frequency. Fig. 2B presents the skin temperature where a slight decrease during the physical control task is followed by a return to the baseline. Fig. 2C shows high heart rate variability during both the baseline and task periods, but clearly increases during the tasks. The increase is not as quick as in skin conductance.

PHYSIOLOGICAL RESPONSES

This section presents physiological responses to challenging robot rehabilitation tasks, including cognitive and motor activities with healthy subjects and patients after stroke. In general, human-robot interaction could be evaluated with self-support scoring, biomechanical parameters, physiological features, and task performance elements.

Fig. 2 gives opportunities to recognize some general trends of physiological signals [12]. The mean SCL increases during different tasks following the baseline rest periods. Skin temperature decreases during active tasks. The mean respiratory rate (not shown in the figure) significantly increases from the baseline during active periods. In a similar manner, heart rate increases from the baseline (Fig. 2C).

PHYSIOLOGICAL RESPONSES IN HEALTHY SUBJECTS

Intensive physical activity and various cognitive tasks cause a range of physiological signal responses. A virtual model of an inverted pendulum attached on top of a movable cart was presented to the person visually on the screen and haptically via a HapticMaster robot [10]. The challenges arising in such an environment are both cognitive and physical. The cognitive workloads were set in three levels: underchallenging, challenging, and overchallenging. In the easy underchallenging version, the pendulum had slow dynamics (reduced gravity) making the pendulum easy to balance. The medium-challenging level was made moderately difficult by increasing gravity. In the overchallenging case, the value of the gravity parameter was further increased (leading to faster dynamics); further, a half-second delay was also added between the time the cart was moved and the time the cart's movement affected the pole. All cognitive levels were tested at low and high physical load values. The high physical load required a subject to apply a five-time bigger force to achieve the same effect compared with the low physical load.

For both physical load levels, the mean respiratory rate shows a statistically significant difference between the underchallenging and the other two conditions. The respiratory rate variability and final skin temperature determine the difference between the challenging and overchallenging conditions. Skin conductance was also indicative under the low physical load, but was relatively vulnerable to the effects of the high physical load. Although heart rate and heart rate variability did reveal differences between difficulty levels, those differences were most likely the result of the physical load [13].

Table 1 provides a summary of how each physiological parameter increased or decreased from the baseline during diverse cognitive and load levels obtained in different experiments [10,12,13]. Cases when the parameter significantly increases/decreases from the baseline to the task are marked with ↑ or ↓. Bigger arrows ↑ are used for $p < 0.01$, while asterisks * are used when $p < 0.05$, while no arrow indicates $p > 0.05$.

Arousal, valence, and physical activity can be evaluated according to the previously described criteria. None of the parameters reported in Table 1 could differentiate between the various difficulty levels of physical load. SCR frequency was found to relate to arousal, while SCR level links with physical activity. Both arousal and physical effort cause changes in the mean respiratory rate. Skin temperature is more related to valence.

PHYSIOLOGICAL RESPONSES IN A STROKE POPULATION

Motor rehabilitation is often performed with patients who have suffered damage to their autonomic nervous system; stroke patients, for instance, show long-lasting abnormalities in sweating and heart rate variability. Serious concerns arise from there concerning whether the physiological measurements discussed here may be a realistic indicator in this population. To investigate this, the virtual reaching and grasping exercise was implemented by using a HapticMaster and a large visual front projection. Psychophysiological measurements were then correlated with the results of a self-report questionnaire.

Skin conductance was found to be the most useful for state assessment in the group of hemiparetic persons and complementary healthy control group; for details, see [11,14]. The SCL differentiated between the physical baseline control task, the normal VR task, and the harder VR task. Due to the lack of studies on a larger stroke population able to confirm or counter these observations, further studies are requested to confirm this result.

Following these observations and considering the simplicity of the use of skin conductance sensors, skin conductance is the first candidate for a biocooperative rehabilitation robotics closed loop.

Skin temperature, unfortunately, shows different responses in the stroke and control groups. The response timing to stimuli is also much slower than skin conductance. Heart rate offers uncertain results with regard to psychophysiological responses.

USING PHYSIOLOGICAL RESPONSES TO CONDITION HUMAN-ROBOT INTERACTION

The task difficulty changes, entailed in upper- and lower-extremity multimodal rehabilitation, may be conditioned by several features associated with task

Table 1 Changes of physiological features during the cognitive task [12], simple arm activity [12], and the two levels of physical load

Signal	Parameter	Cogn. task	Arm activity task	Both tasks (cogn. + arm activity)	Low physical load (med. cogn.)	Low physical load (high cogn.)	High physical load (high cogn.)	Arousal	Increased stress/ valence	Increased physical activity
Skin conductance	Number of SCRs	↑	↑	↑	*	↑	↑	↑		↑
	Final SCL (μS)	↑	*	↑			↑			↑
Respiration	Mean resp. rate	↑	↑	↑	↑	↑	↑	↑		↑
	St. dev. of resp. rate		↓		↓	↓	↓	↓	↑	↓
Heart rate	Mean HR	*		↑		*	↑		↓	↑
	SDNN		*		↓	*	↓	↓		↓
Skin temperature	Final temperature	↓		*		*			↓	

From Munih M, Novak D, Bajd T, Mihelj M. Biocooperation in rehabilitation robotics of upper extremities, In: 2009 IEEE 11th international conference on Rehabilitation Robotics, Kyoto, Japan, pp. 425–430: 2009 with permission.

performance, biomechanical measurements, and physiological signals. Task performance (e.g., the number of objects caught) is related to the VR task itself. Biomechanical features describe the forces and movements applied by the subject, including parameters associated with position, velocity, acceleration, force, and work. The physiological signals—electrocardiogram, skin conductance, respiration, and skin temperature—enable several physiological features (some of them described above) to be calculated. All of these features can be used as inputs, while the algorithm defines one meaningful output variable that can be either continuous or stepwise. That output variable then adapts the complexity and modalities of the rehabilitation task by regulating the level of assistance and changing the type of task. Various methods have been studied and implemented extensively for this purpose; in general, there are two approaches: classification and estimation [15–18]. Some classification algorithms are nearest neighbors, the naïve Bayes classifier, Bayesian networks, discriminant analysis, support vector machines, radial basis functions, classification trees, artificial neural networks, fuzzy logic, hidden Markov models, relevance vector machines, large margin algorithm, and multiple classifier systems. Estimation has been used less frequently in the target problem, with example approaches being linear sums, linear regression, fuzzy logic, and artificial neural networks. It is very difficult, if not impossible, to compare the accuracy rate among the above methods since it depends on many factors, including study size, training set size, normalization method, dimension reduction method, and type of extracted future [15].

Badesa et al. in a study including seven healthy subjects found that a support vector machine with a radial basis function kernel model obtained the best result in terms of accuracy (91%) for classifying three different physiological states (relaxed, medium-stress, and overstressed level) [19]. Novak et al. in a recent study applied a biocooperative feedback loop to adjust the difficulty level of an upper-extremity rehabilitation task [9]. The accuracy rate, that is, the percentage of times the controller matched the subjects' preferences, was computed as a function of the training set size and for different types of input data (Fig. 3). Further, adaptive learning algorithms varied the internal properties according to the user responses. For a training set size of over 20, the best nonadaptive method showed that task performance was recognized as the most relevant type of data with an accuracy rate greater that 80%, while biomechanical data had a rate exceeding 75% in both 24 healthy subjects and 11 hemiparetic patients. Psychophysiological measurements yielded worse results with an accuracy rate of 60% for both healthy subjects and patients. The supervised adaptive methods were able to improve the accuracy rate of psychophysiological measurements up to 76% for healthy subjects and 68% for patients, but these results are still worse than the results obtained using task performance data. This suggests that by themselves, psychophysiological measurements may not be reliable in a biocooperative feedback loop, thereby making performance measures the first choice for task regulation.

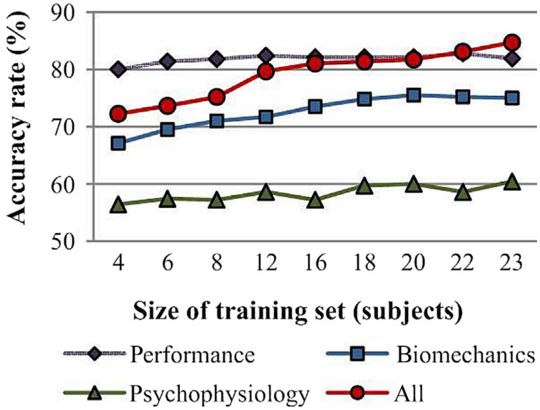

FIG. 3

Accuracy rate as a function of training set size for different types of input data in open-loop cross-validation; the data refer to healthy subjects. Accuracy rate is taken for the best nonadaptive method.

From Novak D, Mihelj M, Ziherl J, Olenšek A, Munih M. Psychophysiological measurements in a biocooperative feedback loop for upper extremity rehabilitation. IEEE Trans Neural Syst Rehabil Eng 2001;19(4):400–410 with permission.

BIOCOOPERATIVE LOOP CONTROL: STATE OF THE ART

Applications of the biocooperative loop control in rehabilitation robotics are nowadays still very limited. One of the very first demonstrations of human-in-the-loop-to-robot interaction based on affective information was demonstrated in 2006 by Liu et al. [20]. The robot was able to influence (lower) human anxiety in 11 out of 14 participants. A multimodal assistive robotic system during a drinking task that considered physiological signals and a force sensor was demonstrated in 10 healthy volunteers [18]. Human-to-robot interaction was also modulated in a group of 11 healthy persons [21]. Results of the popular reaching task of a falling droplet suggest that the method had a positive impact on the overall challenge/skill relationship.

A study conducted with five healthy subjects and four stroke patients showed the application of robot-assisted gait training using a biocooperative loop for adaptive regulation of the difficulty level of the task and including control of the cognitive load [22]. The study showed that a real-time, objective assessment and control of the cognitive load were possible by using a combination of psychophysiological measurements and task performance as a source of the state estimation. Finally, 10 healthy subjects and 6 hemiparetic patients participated in a study requesting the execution of upper-extremity reaching and grasping tasks and implementing a biocooperative feedback loop [9]. Also, in this study, the results suggested that psychophysiological measurements alone are partly reliable as a primary source in motor rehabilitation, but can provide supplementary information for task regulation.

CONCLUSION

The task performance parameters, biomechanical measurements, and physiological responses can provide biofeedback capabilities useful for task regulation and difficulty-level adaptation during robot-assisted rehabilitation. The physiological signals alone can enable a general estimate of a user's emotional state. In order to adapt the delivered therapy to the specific needs and demands of the patient, the combination of several physiological parameters is required, and regulation should be supported by the use of adaptive learning algorithms.

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CHAPTER

Muscle synergies approach and perspective on application to robot-assisted rehabilitation

23

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INTRODUCTION

The comprehension of the control mechanisms underlying muscle coordination during daily motor activities is a fascinating challenge in neuroscience. Several fundamental questions concerning, for example, how animals (including humans) move or how they interact with the environment are still debated in the literature [1], highlighting the complex attitude of the central nervous system (CNS) to manage the huge redundancy of the musculoskeletal system [2].

One of the most common approaches to investigate the fundamental roles underlying the coordinated activity of the redundant muscles leading to the movement is the analysis of "muscle synergies." In more details, the term "muscle synergy" has been used by many authors to define a set of coactivated muscles, which activation level is characterized by a specified gain [3,4]. The tendency of a set of muscles to "work together" corroborates the hypothesis that the production of the movement results from spinally organized muscle groupings that generate specific motor outputs [3,5,6]. This organization would thus reduce the computational workload and, consequently, would help to solve the ill-posed problem of motor control concerning the redundant number of actuators leading a movement [2].

HOW TO EXTRACT MUSCLE SYNERGIES FROM MUSCLE ACTIVITY

The analysis of muscle synergies consists in identifying the latent structure underlying the activity of a large set of muscles in order to highlight the common features among them, in terms of timing of activation and enrollment of muscle groups.

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From the mathematical point of view, this analysis is achieved by decomposing a set of preprocessed electromyographic (EMG) signals as the weighted summation of primitive functions reflecting the common concomitance of activity among several muscle groups (i.e., timing of activation; see [7] as a review) and their modulation (i.e., enrollment of muscle groups) [8]. To this aim, two main approaches have been adopted:

- The linear transformation of the matrix of preprocessed EMG signals [7,9]
- The decomposition of the matrix of preprocessed EMG signals in time-varying activation waveforms [8,10]

For the sake of simplicity and because of its larger adoption, we only refer to the former approach in this book chapter.

More specifically, the extraction of muscle synergies consists in decomposing a set of EMG signals as the weighted summation of primitive functions, as described by the following equation:

$$M = W \times C + Res \tag{1}$$

where M is the $m \times t$ matrix of a set of m preprocessed (i.e., rectified and filtered) EMG signals recorded over a t long time base window, W is an $m \times n$ matrix of weight coefficients describing the enrollment of muscle groups with n the number of muscle synergies, C is an $n \times t$ matrix of activation coefficients constituting the basic components or primitive functions, and Res is an $m \times t$ matrix of residuals (Fig. 1).

Several algorithms, relying on different assumptions, have been adopted to implement Eq. (1) (see [7] for a review). Among those, the most common are the principal component analysis (PCA), the factor analysis (FA) with *varimax* rotation, and the nonnegative matrix factorization (NNMF). PCA and FA are multivariate data reduction techniques that do not require specific features of the input dataset, but they map it in different ways: the output of the former method consists of orthogonal components; the output of the latter consists of latent variables not necessarily orthogonal. The NNMF can be used under the assumption that input and output are nonnegative and rely on the hypothesis that muscle activity and neural control signals (see M and C in Eq. (1)) are inherently nonnegative as well [11]. Accordingly, previous authors suggest that a set of positive weight coefficients (see W in Eq. (1)) allow for a more intuitive interpretation of the results [11].

Overall and whatever the factorization algorithm is, if $n < m$ and residual term (Res) is negligible (i.e., the product $W \times C$ likely resembles M), then it is possible to state that the initial dataset can be mapped into a lower-dimensional space. Accordingly, the low-dimensional space would reflect the output of the CNS leading to the behavior of the high-dimensional muscle-related space. If $n = m$, the result of the factorization will provide the exact reconstruction of the original dataset.

In general, n is determined as the minimum number of muscle synergies able to capture the structural variation of the dataset, so that, by adding one more synergy, it

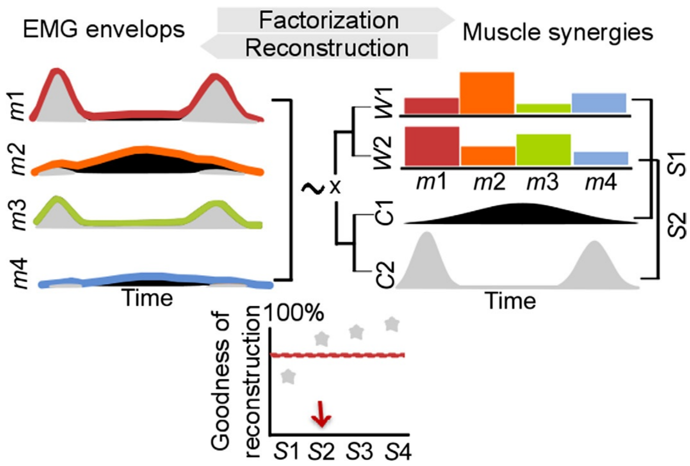

FIG. 1

Schematic representation of the muscle synergy extraction process. In this example, *M* the matrix of the EMG envelops includes four muscles (*m*1–*m*4), and it is represented on the left. The selected factorization algorithm provides a satisfactory level of reconstruction with two synergies (which threshold is represented with a line in "Goodness of reconstruction," bottom panel). The two muscle synergies, *S*1 and *S*2, are represented on the right as a combination of two weight (*W*1 and *W*2) and activation coefficients (*C*1 and *C*2). The matrix of residual is not reported. The schematic drawing is proposed to explain the concept, and it is not based on real data.

will only add noise to the reconstructed dataset [8]. The standard approach to achieve this purpose consists in assessing the validity of the decomposition using measures of goodness of approximation or reconstruction, taking into account the dependence of the amount of explained variance on the number of extracted synergies. Examples of these methods are the latent root criterion [9,12], the mean square error [13], and the variance accounted for [14].

Recent works have pointed out that some methodological aspects should be carefully considered before factorizing datasets in order to allow for a meaningful interpretation of the outcome of these algorithms [15]. Specifically, before factorizing, EMG signals usually undergo the cascade of band-pass filtering, rectification, low-pass filtering, and resampling processes. These steps strongly modify the frequency content of the dataset [16] and may impair the detection of oscillatory input to the muscles [17]. In addition, all factorizing algorithms require specific criteria to separate the systematic behavior underlying muscle activity from random fluctuation [5,9], that is, they achieve a further filtering of the information of the decomposed EMG dataset. As a matter of fact, Hug and colleagues [18] recently showed that smoothing the EMG signals with different cutoff frequencies can influence the number of extracted muscle synergies.

Therefore, it is important to remark that some preliminary choices underlying the implementation of all factorization algorithms should be carefully considered because they can tremendously affect the outcome of the analysis, thus reducing the overall meaning underlying the interpretation of muscle synergies.

MUSCLE SYNERGIES EVIDENCES IN HUMANS AND THEIR IMPLICATION FOR REHABILITATION

Several behavioral studies on animals and humans [8,9,19–21] have shown that muscle synergies can reveal underlying patterns in muscle activity that may reflect different levels of neural functions [22].

Despite the physiological origin and meaning of muscle synergies is still debated, it is certain that the coordinated activity of many muscles during motor tasks can be described by a limited number of muscle synergies [23] likely describing neural functions from the noninvasive and relatively simple measure of muscle activity [24]. Remarkably, even when motor patterns are highly variable across repetitions, movements, and individuals, as it is the case for neurological patients, muscle synergies are characterized by a consistent motor structure [23].

In particular for disorders of the CNS such as stroke, spinal cord injury (SCI), Parkinson's disease (PD), and multiple sclerosis (MS), all commonly characterized by several motor deficits resulting from an impaired muscle activity and coordination, muscle synergy analysis reveals interesting correlates of motor impairments.

Here, we summarize how stroke, SCI, PD, and MS influence the organization and activation of muscle synergies in human adults, and we provide insights on the potential of this analysis for neurorehabilitation.

MUSCLE SYNERGIES IN STROKE

Stroke is a neurological accident caused by the interruption of blood supply to the brain. After a stroke, the cortical damage interferes with the flow of descending signals to the interneuronal structures of the spinal cord often causing an abnormal orchestration of muscle synergies [25].

It has been observed that, in this population, the organization (number and structure) of muscle synergies depends on the level of impairment and on the onset of the cerebrovascular accident [14,15,26,27]. In particular, the number of muscle synergies in the affected side can be preserved, reduced, or augmented due to the preservation, merging, or fractionation of the muscle synergies [14,27].

In severely impaired chronic stroke subjects, it is possible to observe these three behaviors in the lower and upper limb [14,26–28]. The merging and fractionation may be interpreted as a possible compensatory or adaptive reorganization of brainstem and spinal controls [27]. While slight modifications of the level of participation of the muscles in the muscle synergies seem to occur in a short time period, the separation and the degree of the redifferentiation (i.e., the fractionation) of merged synergies seem to require more time, so they are evident only in chronic individuals [27]. The degree of merging seems to be related to the degree of motor and functional deficit [14,27] and associated with the poststroke cocontractions of muscles [29,30], a fusion of the muscle synergies [14], and the couplings of shoulder and elbow actions [29] that might induce a reduction of joint motion and limb functionality [23,27]. In severely chronic poststroke individuals, the number of muscle synergies is correlated with spasticity [25], reduced walking speed, clinical measures of balance and walking function, biomechanical measures such as propulsion asymmetry and step length asymmetry [14,26], and Fugl-Meyer assessment [27] even better than gait and balance function [14].

In subacute or mildly impaired stroke subjects, muscle synergies are usually preserved in the affected lower and upper limbs [30–32], with the exception of the synergies dominated by the activation of shoulder muscles that are generally altered [28,33]. It has been observed that both normal and abnormal synergies are correlated with perilesional high gamma identified with subdural electrocorticography signals. According to this observation, perilesional spiking may organize synergies after stroke [34].

Muscle synergies can be modified by the stroke lesion, the consequent motor reorganization and recovery, and the rehabilitative treatment [33]. However, the ability to develop new synergistic patterns as a response to maladaptive compensatory strategies might occur just in severely chronic stroke patients with intact sensorimotor cortex. Indeed, it has been observed that the ones without intact sensorimotor cortex show a high preservation of muscle synergies and that the preservation of muscle synergies correlates positively with hand functionality in patients with intact sensorimotor cortex and subcortical lesions only [25].

MUSCLE SYNERGIES IN SPINAL CORD INJURY

SCI affects corticospinal connectivity and the organization of the spinal cord below the site of the lesion; consequently, it can affect the encoding and recruitment of muscle synergies [3,23,35].

The few investigations of muscle synergies in persons with SCI suggest that the plasticity induced by the lesion and by the training after the lesion leads to a reorganization of the connections of the interneuronal networks that induces a modification or creation of new muscle synergies [15,36,37]. The reorganization of muscle synergies occurs both in upper and lower extremities [36,38], while, in some cases, it is also possible to observe the alteration of the number and of the activation of the motor modules [39].

As for stroke, muscle synergies are able to highlight differences between healthy subjects and patients with SCI, and the number of muscle synergies is considered as a biomarker to assess patient's condition throughout the gait recovery process [40]. While the first attempt to relate the disruption of upper-limb muscle synergies to the functional grasping abilities was not meaningful [38], the degree of similarity in the number and structure of muscle synergies with the healthy reference presents significant correlations with walking performance [40].

MUSCLE SYNERGIES IN PARKINSON'S DISEASE

PD is characterized by motor deficits resulting from the degradation of dopaminergic neurons in the basal ganglia [41], such as increased coactivation of antagonistic muscles and reductions in amplitude of the distal lower-extremity musculature activation [23,42].

Only two studies explored muscle synergies in this population so far [43,44]. The results show a moderate decrease in the number of motor modules compared with healthy individuals and a slight alteration of the activations and the preservation of weight coefficients during gait [43].

Similarly to stroke, the simplified neuromuscular control is related to a decreased walking speed in PD [43]. Though gait speed increases significantly after dopaminergic medication that enhances basal ganglia function, it does not affect neuromuscular complexity [44].

In PD, the structure and recruitment of motor modules seems not as severely impaired as in incomplete SCI and stroke, probably because spinal and cortical structures remain primarily intact [23,43].

MUSCLE SYNERGIES IN MULTIPLE SCLEROSIS

MS leads to a diffuse inflammatory demyelination and neurodegeneration in the brain and spinal cord. A frequent consequence is the reduction of fiber conduction capacity, which can also alter the sensory feedback, resulting in impairments such as muscle weakness, sensory deficits, spasticity, and fatigue interfering with many activities of daily living.

Muscle synergies have been recently explored in this population as well. Specifically, Lencioni et al. [45] investigated lower-limb muscle synergies of 17 persons with MS while walking. During gait, MS patients have synergies' dimensionality as healthy persons. Their neurological deficit alters the modular control through modifications of the timing activation profiles rather than the weight composition, and these changes are associated with their main walking impairment, muscle weakness, and prolonged double support [45].

Other authors reveal that MS leads to significant changes in multidigit synergies and feed-forward adjustments of the synergies prior to a quick action that might imply a possible contribution of subcortical structures to the impaired synergic control [46].

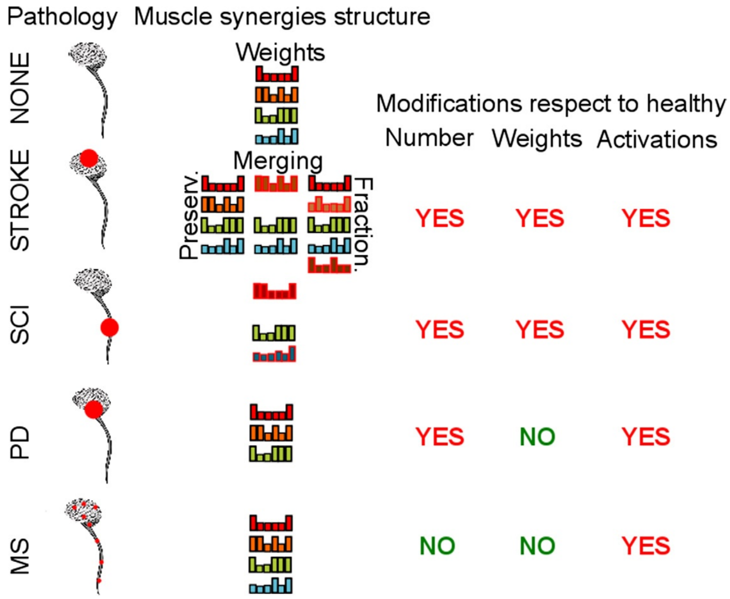

FIG. 2

Schematic summary of the modifications of muscle synergies in stroke, spinal cord injury (SCI), Parkinson's disease (PD), and multiple sclerosis (MS) according to the literature reported in this chapter. On the left, a representative location of the lesion is showed as dots on a draw of the CNS. In the center, a schematic representation of muscle synergies structure is proposed. The weight coefficients as number and composition are proposed just to explain the concept, and they are not based on real data. The weight coefficients modified in the specific neuropathology with respect to the healthy reference case (first row) are reported with a not-black contour. On the right, YES is used if the specific muscle synergy feature (number, weight, or activation) is modified with respect to the healthy reference and NO if it is preserved.

While stroke seems to fully impact muscle synergies, the diffuse central and spinal neuronal damage and atrophy characteristic of MS seems to preserve the independence of neural control signals [47] and impacts their activations [45] (Fig. 2).

MUSCLE SYNERGIES DURING ROBOT-ASSISTED REHABILITATION

The analysis of muscle synergies shows a great potential for neurorehabilitation because they can:

- quantify individual-specific motor impairments [14,15,23,24,26,27],
- assess the effects of rehabilitation [15,23,24,33],

- provide a framework for the development of targeted therapies to enhance neural plasticity and induce motor recovery [15,23,27],
- improve the understanding of the neural mechanisms of motor plasticity [15,23,24,27].

This great potential can be exploited in particular for robot-assisted rehabilitation. On one hand, robots represent excellent platforms to provide an intense and quantifiable motor therapy [48] and/or a controlled and reproducible environment for functional assessment and for motor control studies. On the other hand, muscle synergies are an accessible window to CNS functions. Nowadays, the two approaches can be combined since last end-effector robots and exoskeletons are characterized by limited weight and encumbrance, allowing extensive superficial EMG activity recording during the use of the device for myocontrol and continuous muscle assessment.

Here, we report on some studies in human adults using muscle synergies to assess the effectiveness of robot-aided rehabilitation and for the design and test of the control strategies provided by the robots.

MUSCLE SYNERGIES AS A QUANTITATIVE ASSESSMENT FOR ROBOT-AIDED REHABILITATION

Robot-aided motor training impacts upper-limb muscle synergies, and the latter can document the effect of the conjunction between the natural ongoing of the pathology and the intense robot-mediated treatment in subacute poststroke patients [33].

During a pilot study [33], six subacute poststroke subjects underwent robot-mediated therapy with the InMotion2 robot (Interactive Motion Technologies, Inc. Cambridge, Massachusetts) that allows the execution and assistance of movements in the horizontal plane. The robot provided an assisting force when subjects were not able to reach the targets. The robot also provided forearm support to compensate for the action of the gravity. The robot-aided treatment was administrated for 1 hour, 5 days per week, for 6 weeks.

During the treatment, the severity of the impairment was evaluated using clinical scales; in addition, the end-effector trajectory and muscle activity from 10 upper arm and shoulder muscles was analyzed to monitor the effectiveness of the ongoing therapy.

The robot-aided therapy led to a reduction of the impairment of the hemiparetic limb and to an improvement of motor performance in all patients, as shown by the trend of clinical scores and of all robotic related metrics throughout the therapy.

From a qualitative point of view, muscle synergies related to poststroke patients were similar to those of the healthy control group. However, the structure of those underlying shoulder flexion/extension (in particular due to the abnormal contribution of the deltoid heads) was slightly altered before the robotic therapy. After the treatment, the improvement of motor performance was achieved in conjunction with a slight, even though not statistically significant, restoring of the coordination of the activity of muscle groups crossing the elbow.

In summary, in subacute poststroke subjects, muscle synergies underlying shoulder control can reflect the functional deficit induced by the pathology; they can be modified by the rehabilitative treatment, and the improvement of motor performance can be achieved in conjunction with a slight restoring of the coordination of the activity of elbow muscle groups. These results support the hypothesis that muscle synergies reflect the injury caused by the cerebrovascular accident and that they could document the effects of the functional recovery resulting from a suitable robotic treatment.

MUSCLE SYNERGIES FOR THE DESIGN OF CONTROL STRATEGIES FOR REHABILITATIVE DEVICES

Understanding the effect of assisted movements on the induced muscle activity helps to optimize the use of robotic devices. Robots are mainly employed in the motor rehabilitation of lower and upper extremities to provide support against gravity and assistance during movement execution. Muscle synergies were used to understand how these two therapeutic strategies impact on upper-limb muscle organization and coordination.

The effect of gravity compensation was investigated on upper extremities in a group of nine healthy subjects [49]. They performed 3-D arm reaching movements with five different levels of arm-weight support provided by the Armeo Boom (Hocoma AG, Zurich, Switzerland). The characteristics of kinematics and of the activity of 14 upper-limb muscles were analyzed. While kinematics features varied across weight support conditions without distinct trends, the level of activation of upper-limb muscles and of the timing activation of muscle synergies progressively decreased as the level of arm-weight support increased. These results suggest that the analysis of muscle synergies can be used as a possible marker for identifying an optimal level of arm-weight support for rehabilitation.

The effect of upper-limb passive mobilization provided with the arm light exoskeleton (Wearable Robotics srl) was also assessed during 3-D point-to-point reaching movements [50,51]. Movement execution and muscle activities of 16 upper-limb muscles in healthy subjects were recorded. The results revealed that passive arm movements were able to elicit a significant muscle activity in most of the muscle groups. As expected, the activity was lower than during active reaching, but the main structure of muscle synergies was preserved.

Remarkably, both trajectories and speed profiles influenced muscle activity and coordination in the passive training. In particular, the execution of trajectories acquired from (other) healthy subjects promoted the activation of two muscle synergies more than in case of linear trajectories with a muscle synergy structure more similar to the natural one [50]. The same effect was produced when proposing complex speed profiles rather than adopting a constant speed [51]. Indeed, linear trajectories executed according to a minimum jerk speed profile seemed to elicit a muscle organization more similar to the natural one than in case of constant speed [51].

Overall, these results suggest that upper-limb muscle activity and synergies are influenced by the trajectory and speed profile of the assisted reaching movement; therefore, they should be carefully considered when designing passive robot-mediated rehabilitative training.

CONCLUSIONS AND FUTURE TRENDS

Muscle synergies constitute not only a fascinating motor control hypothesis but also a practical framework to study muscle coordination. In this respect, the analysis of muscle synergies is prone to be particularly helpful in neurorehabilitation. The results of the clinical and scientific studies reported here highlight the ability of muscle synergy analysis to quantify motor impairments, to quantitatively assess the effects of rehabilitation, and to drive the design of more effective robot- and technology-aided motor therapies.

Noticeably, few very recent studies indicate how muscle synergies could also be used to drive the development of robotic treatments aimed at acting, impacting, challenging, modifying, perturbing, and/or correcting muscle synergies [15] by integrating musculoskeletal models in the control of the robot and the task [52], by adopting force fields, or through myoelectric controls [53]. In the future, muscle synergies could also drive muscle stimulation provided in combination with robotics. Indeed, the combination of the two technological approaches reinforces the ability of robotic devices to finely control movements with an additional therapeutic effect resulting from direct muscle activation. In this sense, muscle synergies may provide a framework to develop and drive targeted therapies to enhance neural plasticity.

However, further investigations are still necessary to bring muscle synergies into neurorehabilitation. In particular, due to the limited number of studies so far, it is not yet clear if neuromotor recovery is best achieved with the reconstruction of the lost original muscle synergies or with the creation of new adaptive and compensatory synergies [15]. As a consequence, more research and clinical investigations on larger populations of neurological patients are required. It is necessary to both characterize muscle synergies within different populations and focus on single individuals, following the evolution of their muscle synergies during recovery and comparing the effect of different rehabilitative strategies. For this purpose, robot- and technology-aided treatments play a very important role since they can "structure" the rehabilitative treatment and improve its quantification and repeatability. Finally, the methodological procedure for the analysis of muscle synergies needs more attention [15]. Indeed, the high variability of tasks, the kinds and numbers of muscles included in the analyses, and the processing of EMG signals prevent a direct comparison of the literature so far. Studies aimed at comparing these variables and their impact on muscle synergy analysis will favor a better comprehension of old and new results helping the translation of muscle synergies analysis into clinics.

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CHAPTER

Telerehabilitation Robotics: Overview of approaches and clinical outcomes

24

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INTRODUCTION AND IMPETUS FOR TELEREHABILITATION ROBOTICS

Best practice for successful rehabilitation often involves intensive, repetitive practice that actively engages the participant in goal-oriented and task-specific activities to regain functional capacities in upper and lower extremities [1]. As other chapters in this volume have discussed, recent advances in robot-assisted therapy have greatly increased the capacity for improving voluntary UE movement and LE strength and locomotor function. Several studies have observed that robot-assisted therapy demonstrates equivalent outcomes compared with one-on-one therapy, even when delivered in the home environment [2,3]. The results of these studies indicate that robot-assisted therapy provides reliable, reproducible treatment while measuring performance without the need for real-time human oversight [4]. Although there is ample evidence for the effectiveness of robot-assisted therapy and there is great potential to improve access and reduce cost, unfortunately, these technologies are underutilized in the home environment.

The US Department of Veterans Affairs pioneered telemedicine deployment to overcome geographic barriers that emerged as veterans returned home. Since the initial usage, demand for high-quality health care at an affordable price provides pressure for further development, which now includes provisions for rehabilitation services at a distance or telerehabilitation (TR) [5,6].

Telerehabilitation robotics (TRR) is a relatively new subdiscipline of health care and clinical science that bridges established features of robot-assisted rehabilitation and telehealthcare to provide efficacious services at a distance using information and communication technologies. Rehabilitation at home, most often by a spouse or child, was the standard for many people recovering from injury prior to the twentieth century. With the advent of the World War II and a nationwide polio epidemic during the early 1900s, demand for hospital-based rehabilitation rose. However, providing therapy in one's own residence has been revitalized in recent years due to several factors including advances in technology, shortage of licensed therapists, and patient preference all in an environment of ever increasing cost containment. Technological advancement and adoption of

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new health-care models will change the way we practice rehabilitation medicine and facilitate the effective transition to home rehabilitation in select populations. The purpose of this chapter is to provide an overview of the current approaches and detail the available data on clinical outcomes and improved access to services.

SURVEY OF TECHNOLOGY

Changes in the health-care environment have led to the emergence of robotic devices that are aimed at improving the quality, reproducibility, and cost-effectiveness of rehabilitation. Additionally, research teams are working to weave the principles of motor learning and neuroplasticity into device construction to improve clinical outcomes [7]. Comprehensive reviews of currently available devices for upper [8] and lower extremities [9] have recently appeared in the literature.

Many devices are aimed at rehabilitation delivery. However, a limited number have demonstrated clinical efficacy and few are currently used for patient care in clinical settings. Due to the recent creation of the TRR field, only a handful of robotic devices have been investigated. Most devices tied to TRR are in the feasibility stage of development. Only two TRR devices (e.g., Hand and Foot Mentor [10,11] and SCRIPT [12]) have been fully deployed in the home environment. Several devices have shown promise for application to TRR delivery but have either focused on remote monitoring [13–15] or home deployment [16,17] but not both simultaneously. Both features are necessary to progress to a fully integrated TRR deployment; however, a distinction must be made to differentiate devices that have encountered the unique set of challenges associated with full TRR delivery including home deployment, connectivity, and remote monitoring.

Notwithstanding the relatively small numbers of TRR devices, substantial heterogeneity in robotic device construction, control protocol, and user interface exists. Despite these differences, all devices share the common capability to sense and record movement (e.g., position, velocity, torque, and various performance metrics). Additionally, devices share the capability to aid with user movement, typically through electric, pneumatic, or passive actuation. For a detailed discussion of design, control architecture, or general robotic devices, please refer to previous chapters. In this section, we will discuss the level of user involvement, remote assessment, treatment targets, and construction of various devices utilized in TRR application.

LEVEL OF USER INVOLVEMENT/ASSISTANCE

Rehabilitation robots can act as passive modalities (e.g., moving the extremity without active contraction); however, providing too much or a predictable amount of assistance may have negative consequences for learning, that is, encourage lassitude. This can occur when someone learns to provide only the amount of force needed to trigger the assistance. To avoid this, controls for rehabilitation robotic devices have primarily drawn concepts from rehabilitation, neuroscience, and motor learning that determine the level of initiation, user involvement, and control of actuation. With this information, many devices provide active-assist interaction. Active-assist provides help to the user as needed to accomplish the task. This takes advantage of the device's ability to decrease task difficulty and encourage participation while capitalizing on active initiation of movements, which have been shown to increase cortical activity compared with passive motion [18].

The Hand Mentor and Foot Mentor devices (Motus Nova LLC, Atlanta, Georgia) (Fig. 1A and B) were designed for use by individuals with residual upper and lower extremity impairments with the goal of improving active range of motion (AROM) and strength in the distal musculature. Participants use their affected wrist or ankle to complete gamelike training programs to challenge motor control. A software algorithm constantly monitored patient performance and modifies the level of difficulty. Initially, performance required only a small degree of wrist or ankle voluntary motion. As user's motor control improves (8 successes in 10 attempts), the robotic device progressively increases the difficulty level, requiring greater AROM to achieve the goal. Conversely, if the user experiences difficulty (2 or fewer successful attempts out of 10), the device decreases the difficulty level. The Mentor systems provide visual and auditory feedback of the target location and summaries of trial-by-trial performances. Remote monitoring is available via a clinician dashboard.

Much like the Mentor systems, the home-based Computer-Assisted Arm Rehabilitation (hCAAR) [17] provides active assistance. In one study, the hCAAR was deployed in the home for 8 weeks and provided 17 stroke survivors with active assistance in the completion of task-specific goals. The hCAAR has a feature that allows the unaffected limb to signal the device to provide assistance. Although the hCAAR system was deployed in stroke survivor's homes, the authors did not report remote monitoring of patient performance. Instead, the hCAAR consistently monitors performance and adjusts the level of assistance according to the performance and baseline assessment.

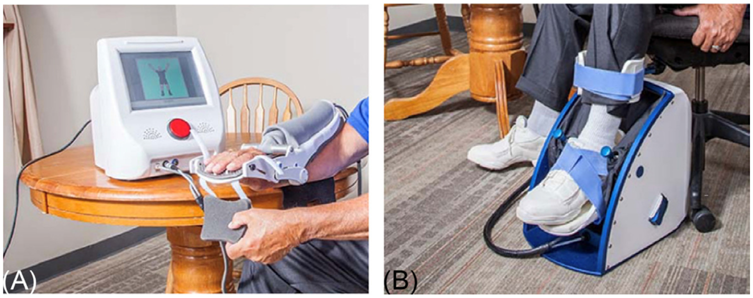

FIG. 1

Shown in (A) and (B) are the Hand and Foot Mentor air muscle assemblies utilized for telerehabilitation robotics. The setups shown display the typical usage of the devices when deployed in patient's homes. Both devices are compatible for right- and left-sided use and are designed for easy donning and doffing with elastic and Velcro attachments. The control unit (A) is compatible with both the Foot and Hand Mentor and displays the visual exercise interface for the patient.

Unlike the devices described above, the SCRIPT project evaluated both a passive and active control devices, ultimately using a passive dynamic assistance mechanism called SPO (SCRIPT passive orthosis) to aid with wrist and finger extension. A passive assistance mechanism simplifies the construction of software algorithms required to control the SPO and likely decreases the cost of deployment. Although the SPO provides passive actuation, the device provides an interactive environment much like that seen in the hCAAR and Mentor systems.

TREATMENT TARGET

The unique challenges that face TRR device deployment in the home environment have provided uncommon pressures not seen by general rehabilitation devices such as space, size, cost, and ease of use limitations. Due to these constraints, all the TRR devices have focused on rehabilitation of either the upper or lower extremity.

Contemporary robot-assisted rehabilitation focuses primarily on the proximal upper extremity [19]. As a result, initial research into whether the focus of treatment should target proximal and/or distal segments suggested that early involvement of distal arm movements is favorable over proximal training. The authors cite an increase in the transfer of treatment effects to the untrained arm segments [20]. The observed transfer effects can be partially explained by the inherent complexity of training distal motor control (e.g., grasping and manipulating objects) that automatically involved coordinating proximal segments. This great potential for distal targeted devices to improve clinical and kinematic performance in combination with generally smaller constructions makes these types of devices uniquely suited for TRR deployment. Both the SPO and the HM devices target the distal upper extremity. Unlike the Hand Mentor, which focuses intervention to the wrist, the SPO afforded individual extension assistance to individual digits and the wrist. Much like the HM™, the upper extremity portion of the assisted movement with enhanced sensation (AMES) was directed at assisting wrist motor control during its preliminary home deployment without remote monitoring.

TRR devices that do not focus on distal extremity control generally operate on an end-effector construction, resulting in targeting the proximal muscles. The hCAAR [21], Java Therapy [22], Jerusalem TeleRehabilitation System [14], MEMOS [15], and others [13,23] all share common lineage with the MIT-MANUS. Although these devices utilize the entire upper extremity to interact with the user interface and complete the interventions, the joystick design often constrained the distal upper extremity to grasp an end effector, thus driving the focus of the intervention to the proximal musculature.

IMPLEMENTATIONS

DEPLOYMENT

Telerehabilitation robotic interventions present challenges to researchers and clinicians needing to deploy robotic devices in the home. To date, there are two primary deployment strategies that have been utilized: home delivery and remote deployment. Many TRR interventions in the literature have utilized some version of home delivery, where a clinician, trained in robot-assisted therapy, arranges an in-home delivery, setup, and training for the user and caregivers. The home delivery methods afforded treating clinicians the additional benefit of information regarding the user's home environment and allow tailoring of future interventions to the user's specific needs. Additionally, baseline functional assessments can be completed in the home reducing travel time for users that have transportation difficulties. Although this strategy provides the users with geographic or travel restrictions the most tailored care, this deployment strategy shifts the cost of travel onto the clinician. The significant drawback to the home delivery model was initially deemed obligatory due to the complexity of device setup and training. However, as devices become more commercialized and user friendly (Fig. 1A and B), the remote deployment strategy is becoming more feasible. With remote deployment, the device is shipped to the user's home, and training is handled through video modules, which are produced in advance or with direct web-based interaction with support staff trained in setting up the intervention.

While the home delivery method has not been directly assessed, a second method has been utilized that circumvents a portion of the travel demand for both parties, thus bridging the gap to remote delivery. The so-called clinic-based deployment adds TRR device setup and training to a previously scheduled clinic visit. While the patient is seen in the clinic for traditional rehabilitation, the TRR device is introduced, and a clinician trained in robot-assisted rehabilitation provides the preliminary training, so the user and caregiver can independently set up the device when they return home. Once the user and caregivers have demonstrated proper and safe use, devices are dispensed in the clinic. Trained staff can monitor the device setup remotely and provide support over the phone or through a web-based interface.

INTERVENTION PROTOCOLS, STRATEGIES, AND DOSING

The innovative development of Java Therapy in 2001 prescribed TRR dosing of approximately 1 h per day over the course of a 4-week study [22]. Java Therapy involved a simple, force-feedback joystick that physically assisted or resisted upper extremity movement, while quantitative feedback of performance informed caregivers of progress through an Internet connection. While the intervention showed efficacy in improving kinematic motor performance, no clinical outcomes were assessed. Many TRR intervention strategies have been derived from validated studies investigating clinically successful neurorehabilitation dosing and intensity for the patient population of interest. Although there is little consensus on the ceiling effects of dosing and intensity for traditional rehabilitation, there does appear to be a dosing threshold (60 min per day) that must be surpassed in order to have meaningful improvements in functional outcomes [24]. However, the majority of TRR interventions derive daily dosing as a fraction of the study length, meaning the shorter the experimental protocol the higher the daily dosing parameters and vice versa for longer studies. Preliminary studies from Wolf et al. anchor their TRR interventions on previous evidence from 2-week constraint-induced therapy studies that showed clinical efficacy with dosing up to 6h per day [25]. For their longer-term TRR interventions, dosing was often prescribed for 5 days a week 3h per day totaling to 120h. More recently, our laboratory introduced an incremental approach to dosing. We progressively increased the volume and intensity of exercise to reduce fatigue [10]. The TRR interactive interface has been shown to improve exercise compliance. For our 3-month intervention, users were encouraged to start at lower daily activity levels and slowly progressed to the prescribed 2h therapy dosage within 2 weeks.

MONITORING/OVERSIGHT

Monitoring and oversight are essential components of any successful rehabilitation paradigm, and that is especially true when the remote nature of TRR precludes physical interaction with a clinician. Several strategies have been used to monitor patient usage and performance during a study and can be categorized as “store and forward” and “real-time monitoring.” In 2001, Reinkensmeyer et al. published an early report on real-time monitoring and interaction with hemiparetic patients using a TRR interface [22]. Testing began with real-time oversight, while patients performed TRR interventions in a local outpatient clinic and progressed to home deployment. Further advancements were made when real-time monitoring began to include “remote control” of the TRR device by study clinicians. In the event difficulties occurred or modifications of the rehabilitation paradigm were required, the clinician was able to remotely take control of the device and provide assistance [15]. Carignan and Krebs described this innovation as “cooperative telerehabilitation” in which the clinician and user interacted directly with each other [26]. Cooperative telerehabilitation affords the advantage of remote, direct physical evaluation and assessment, while the user and clinician interacted in a graphical interface.

While these advancements in TRR devices and systems addressed concerns over remote rehabilitation, they do not address staffing challenges that are facing healthcare systems. More recent clinical studies investigating TRR applications have sought to address the staffing concerns by eliminating active remote monitoring in favor of a “store-and-forward” model that does not require real-time oversight by clinicians [3,10,11,27]. The store-and-forward model affords significant advantages of scheduling flexibility to both clients and clinicians. The advantage of scheduling flexibility is amplified when dosing is taken into consideration. Many protocols prescribed two or more hours of rehabilitation per day, which would present a significant scheduling constraint to clinic-based therapy. For in-home users, the scheduling flexibility of TRR allows them to complete their prescribed robotic rehabilitation in any permutation that suits their lifestyle. This autonomy is not without complete oversight and required monitoring. The HM and FM devices record and store the following variables: overall active time, time in each training module, percent success for each training module, minimum and maximum wrist angle, and a measure of force (pneumatic pressure). These data are encrypted, stored, aggregated, and forwarded (telephone,

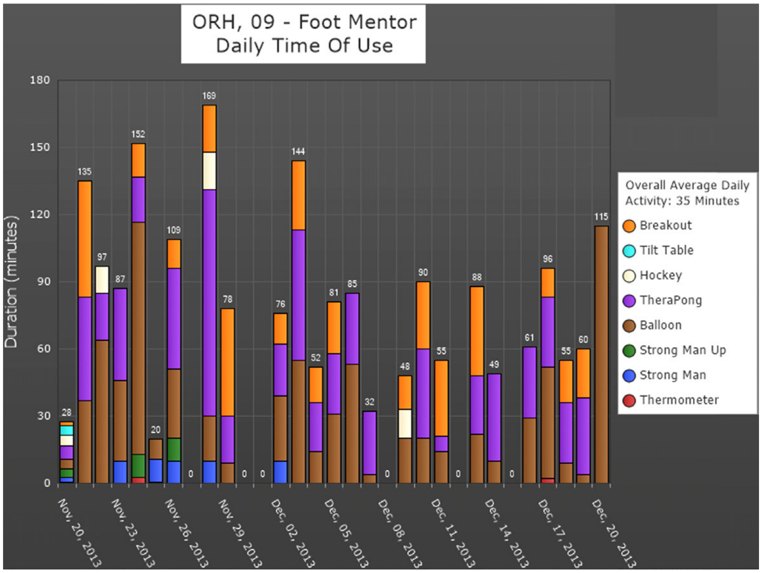

FIG. 2

Example of clinician interface presents graphic usage data in minutes of therapy provided by the FM for each type of game played over the course of study.

internet, and cellular connection), so the clinician can access all relevant user data, such as total time performing therapy (Fig. 2).

Users of the HM and FM devices are provided real-time feedback through a graphical user interface of their extremity position, force, and success rate. Each time a participant completes a training module, a summary for that session is displayed on-screen. Although real-time oversight is not required for the store-and-forward delivery model, highly individualized training programs are achieved by computer algorithms that continually monitor user performance and adjust difficulty based on performance. In short, changes in difficulty are based on success rate; above 80% the difficulty level is automatically increased. Progression requires an increase in the ROM to achieve the target. Conversely, if user success falls below 20% success rate, the difficulty level decreases [10].

One concept that unifies both active, remote monitoring and the store-and-forward model is the ability to monitor multiple patients at a time and effectively equate to TRR acting as a work-force multiplier of clinician hours. Although not directly practical for cooperative TRR applications described above, both general paradigms can take advantage of clinicians monitoring multiple users at a time. As demand for rehabilitation increases and evidence accumulates on the efficacy of life-long care following neurological damage, the importance of increasing clinician efficiency is paramount.

OUTCOMES

CLINICAL

The proposition that TRR can contribute to superior clinical outcomes is based on evidence that augmented exercise, particularly that of a minimum of 16 h in the first 6 months after stroke [28], improves functional recovery. Additionally, utilization of TRR through distributed practice is associated with better retention of performance [7]. These key benefits of TRR serve to rebalance the current mismatch with conventional therapy services that typically utilize massed practice due to limited clinic schedules and staff. Research has shown that during intensive rehabilitation stays, patients spend only 13% of their time with activities that could improve mobility [29]. As such, TRR can play an important role in the recovery of distal hand and finger function, which is often the last to show signs of improvement.

To date, two TRR systems for stroke have been investigated for home deployment. The SCRIPT project deployed a passive dynamic wrist and hand orthosis (SPO) [30] that provides extension forces via passive metal springs that are used in combination with a SaeboMAS for proximal support. The gaming exercises are displayed on a touch screen computer and controlled by arm/hand movements including wrist and finger flexion/extension, pronation and supination, and reaching in all directions [30]. The SCRIPT intervention consists of 6 weeks of self-administered distal arm training in the home with custom-designed games. Participants are monitored remotely and have weekly in-home follow-up visits to adjust the SPO so that the participant can actively open the hand to grab a 2.5-cm cube [30].

In 2014, investigators studied the use of the SPO with chronic stroke participants with limited arm/hand function (having at least 15 degrees active elbow flexion and quarter range of active finger flexion, but not full active ROM). They reported significant changes in both the Fugl-Meyer (FM) and the Action Research Arm Test (ARAT) after 6 weeks of a home-based training. Positive correlations in usage time and improvement on the ARAT were shown across the group. Although participants were encouraged to use the device for an hour each day, the investigators found that participants averaged 15 min of self-selected usage of the device daily [31].

Our lab has investigated the Hand Mentor (HM) and Foot Mentor (FM). These devices are composed of a hand or foot peripheral component controlled by a pneumatic pump (i.e., McKibben muscle) to assist with wrist extension or ankle dorsiflexion. Training programs are designed to increase active wrist and finger flexion and extension and improve accuracy and motor control through variations in speed and graded movements to on-screen targets [10,11,27]. Participants with chronic stroke must demonstrate at least a trace of volitional wrist or finger extension in the extremity to use the device. The current protocol for the HM/FM studies provides the device in the home for 12 weeks with a custom exercise prescription/game selection for strengthening and/or motor control improvement. All participants are remotely monitored via a clinical dashboard. Clinicians also make weekly calls with participants to ensure continued compliance and progression of therapeutic activities.

Participants enrolled in Mentor™ system studies were instructed to complete up to two 1 h sessions daily over the course of a 12-week protocol. In 2014, our lab documented statistically significant improvements of 7.7 points ($p = 0.01$) on ARAT scores compared with baseline. Further, the improvements observed following the TRR intervention surpassed the previously validated minimally clinical important difference (MCID), indicating that participants achieved clinically relevant improvements [10]. In a follow-up study in 2016, we confirmed our 2014 findings in a larger population [11]. We observed significant improvement in ARAT scores (30%, $p = 0.046$) among users with the average improvement again surpassing MCID of 5.7 points, indicating a clinically meaningful change in upper extremity function. The protocol when used with FM demonstrated a 29.03% increase in gait speed, from 0.31 to 0.40 m/s, correlating to a change from home ambulation status to limited community ambulation status per validated stratification of gait speed [32].

An evaluation of three studies that used different robotic systems showed no significant difference with respect to improvement in ADL measures (i.e., FIM score). Comparisons at the level of abnormal structure and function have not been made, nor between training in one or two planes of joint motion. To date, no studies have directly compared the SPO and HM/FM robotic system, but differences can be expected based on motor control principles.

One limitation of the HM, FM, and SPO devices is the requirement that users have some degree of volitional movement, often excluding those clients who are categorized as being severely impaired. Future research into the design and instrumentation of robotic devices is needed for the inclusion of severely impaired distal segments. To date, robotic devices and orthosis, such as the Java Therapy and AMES used in feasibility studies, have been too large and burdensome for deployment to homes or add to caregiver burden in terms of donning and setting up the therapy device.

SATISFACTION AND QUALITY OF LIFE

Patient satisfaction is an important and commonly used indicator for measuring the quality of health care. Patient satisfaction affects clinical outcomes and patient retention and is an effective indicator to measure the success of a rehabilitation intervention.

Satisfaction of the HM/FM devices was studied using a 14-question survey to assess user satisfaction, progress, ease of use, and appropriateness of the intervention for their needs. Based on 12 stroke participant responses, overall satisfaction with the Mentor intervention was high [10]. In a follow-up study published in 2016, survey responses from 19 stroke participants again showed high overall satisfaction with the Mentor intervention [11]. When asked what they would change about the device, participants requested adding games of greater difficulty, making the computer component smaller and easier to handle, and improving ease of donning/doffing the peripheral device. Overall satisfaction was consistently expressed in terms of an appropriate therapy for their condition from both participants and a survey of clinicians.

In a qualitative design study, 10 chronic stroke participants who used the HM device reported overall positive benefits in the following areas: increased mobility, a sense of control over their therapy and scheduling, increased independence, and an outlet for physical and mental tension and anxiety [33]. TRR therapy allowed users to feel "in control of their therapy" and supported the idea of patient-centered delivery of care [34].

Incident rates for depressive symptoms in persons post stroke have been reported to be as high as 41%–52% [35]. Additionally, stroke patients with depression have a higher utilization of health-care services [35] and higher health-care costs [36]. Depression is a predictor of poor functional outcomes [37] leading to an additional cascade of health-care service utilization and increased costs. In the comparison of home-based TRR with the Mentor device with traditional therapy services in an 8-week intervention at 6 months post stroke, Linder et al. found that participants in robot plus home exercise program (HEP) group demonstrated comparable significant gains (a decrease in reported depressive symptoms) on the Center for Epidemiologic Studies Depression Scale (CES-D) and Stroke Impact Scale (SIS) domain scores. Similar studies found a decrease in reported depressive symptoms on the CES-D after a 12-week HM/FM intervention [10,11].

INCREASE UTILIZATION

Protocol recommendations for at-home use of the TRR devices have wide variability in the literature ranging from 30 to 120 min. Chronic stroke survivors in the SCRIPT project were asked to use the SPO device for 30 min a day, 6 days a week and were otherwise left free in their choice of when and how long to use the device. Participants were monitored remotely and visited weekly by a supervising clinician to progress exercises on a case-by-case basis. Ten patients used the system on an average of 94.4 (±43.6) min/week, averaging 14 min of self-administered training each day [34].

Recommendations for use of the Mentor system were significantly higher than those of the SPO. The Mentor devices were issued with the instruction to complete exercise for up to two 1 h sessions daily. Our analysis of usage determined that participants averaged 90.6 min of daily usage, over 30.6 therapy sessions, across the 106-day episode of care [11].

COST

One of the major drivers behind the proliferation of TRR practices is the potential to positively impact resource allocation while reducing health-care expenditures. Under certain conditions, robotic rehabilitation can provide even larger doses of therapy than would otherwise be completed in one-on-one therapy, especially in a labor-strapped health-care field. Unfortunately, high-quality evidence regarding the impact on resource allocation and health-care expenditures is still needed.

Despite the current limitations, promising findings have emerged. Tousignant et al. estimated 17% savings per patient during a 12-session intervention, compared with the estimated cost of home visits [38]. Larger cost savings (58%) were reported by Kortke et al. for 3 months of home-based cardiac rehabilitation, compared with the 3-week inpatient rehabilitation [39]. In agreement with the magnitude of savings Kortke et al. reported, a more comprehensive cost analysis comparing TRR with clinic-based rehabilitation in the VA health-care system [11] documented an average of $2352 (64.97%) less costs than equivalent clinic-based stroke therapy (Fig. 3).

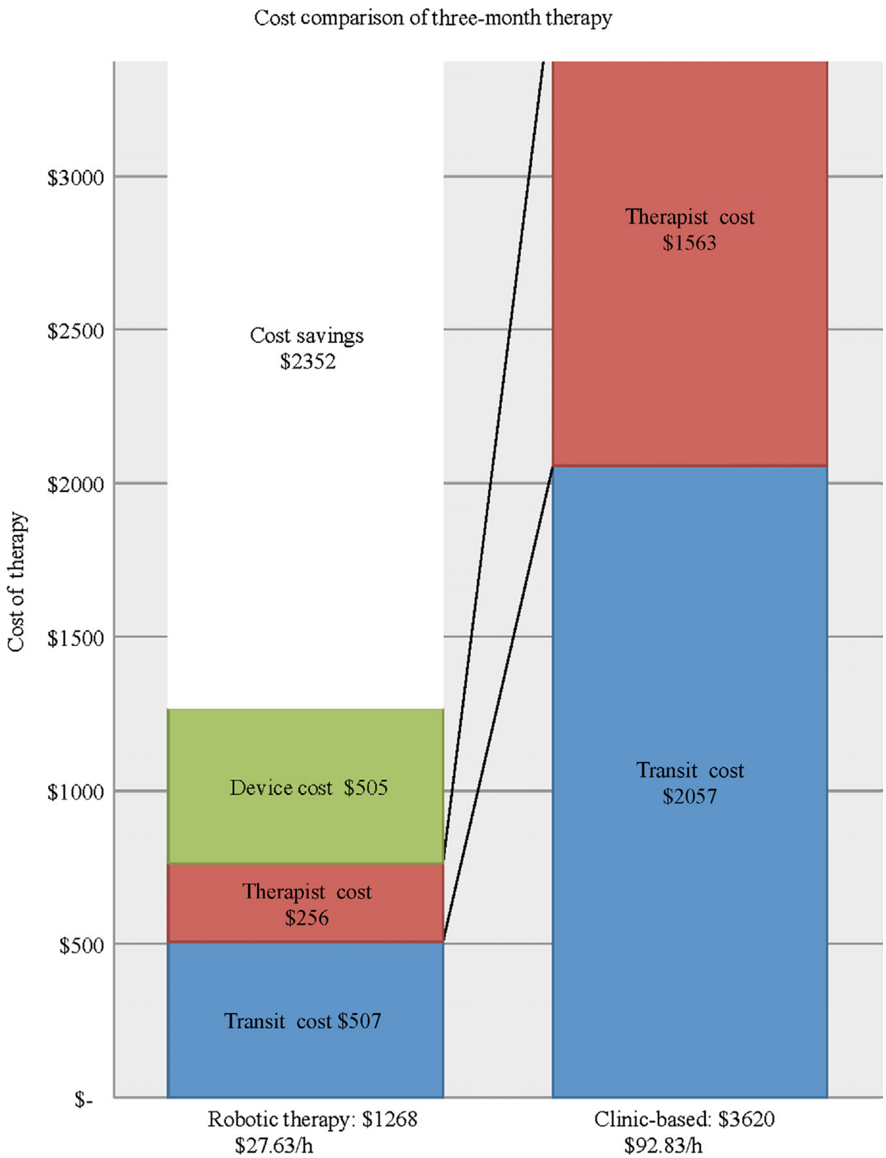

FIG. 3

Three-month cost of home-based, robotic telerehabilitation compared with clinic-based outpatient therapy, based on three, 1 h weekly physical therapy sessions in the outpatient clinic. Hourly costs are based on robotic therapy receiving an average of 30.6 sessions for 90 min compared with clinic-based therapy receiving an estimated three, hour-long sessions per week during the study.
Figure reproduced with permission from Housley S, Garlow A, Ducote K, Howard A, Thomas T, Wu D, et al. Increasing access to cost effective home-based rehabilitation for rural veteran stroke survivors. Austin J Cerebrovasc Dis Stroke 2016;3(2):1.

TRR costs included device, deployment costs (home delivery, support, connection, and pickup based on average round-trip distance), monthly maintenance, server connection costs, therapist monitoring of patient progress, and telephone-based follow-up calls. These elements were totaled across the treatment period and compared with projected clinic-based physical therapy of three 1 h sessions held weekly at the closest VA medical center.

In summary, future trials including TRR should incorporate cost analyses (cost per dosage), associated with clinical findings (cost per effect size). The main advantage of TRR is the possibility to reliably increase dosing and intensity of rehabilitation while providing interactive user interfaces that consequently motivates users. Although the evidence is gradually emerging regarding the positive impact of TRR on health-care costs, the lack of studies evaluating costs from similar perspectives and accounting for similar elements deters any definitive conclusions.

CONCLUSION AND FUTURE DIRECTIONS

This chapter has reviewed a large body of work with the aim of introducing the historical context and impetus for the development of TRR, provides an overview of the current approaches, and presents the data on clinical outcomes and improved access to services. It is reasonable to expect that a fuller understanding of TRR will enhance our understanding and increase our ability to design better approaches to neurological rehabilitation, especially for those affected by motor loss.

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REHABILITATION ROBOTICS

TECHNOLOGY AND APPLICATION

Edited by Roberto Colombo and Vittorio Sanguineti

A comprehensive view of the field of rehabilitation robotics, from neuroscience and engineering concepts to clinical applications.

Rehabilitation Robotics provides a comprehensive view of the robot technologies available for neurorehabilitation and their application to different pathologies. The design, implementation, and modalities of intervention of rehabilitation robots incorporate findings from behavioral studies on sensorimotor adaptation and motor skill learning and their neural substrates.

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