Rehabilitation Technologies Application in Stroke and Traumatic Brain Injury Patients

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Abstract Neurorehabilitation plays a crucial role in the multidisciplinary management of brain injury patients. Emergent therapies based on rehabilitation technologies such as robots, bci, FES, and virtual reality could facilitate cognitive and sensorimotor recovery by supporting and motivating patients to practice-specific tasks on high repetitive levels during different stages of rehabilitation. Robots have become a promising task-oriented tool intended to restore upper limb function and a more normal gait pattern. Virtual reality environments by providing powerful sensorimotor feedback and increasing user interaction with a virtual scenario could improve gait, balance, and upper limb motor function. This chapter will provide an overview on

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the rationale of introducing rehabilitation technologies-based therapies into clinical settings and discuss their evidence for effectiveness, safety, and value for stroke and traumatic brain injury patients. In addition, recommendations for goal setting and practice of training based on disease-related symptoms and functional impairment are summarized together with reliable functional assessments.

1 Introduction

Stroke and traumatic brain injury (TBI) are major causes of long-term disability worldwide [\[32](#page-28-0)]. For each year, about 16 million people experience a first-ever stroke. This number is expected to rise to 23 million first-ever strokes in 2030 [\[135](#page-33-0)]. Globally, stroke is the second leading cause of death above the age of 60 years, and the fifth leading cause of death in people aged 15–59 years old [\[84](#page-31-0)]. An estimated 57 million people worldwide have been hospitalized with TBI [\[152](#page-34-0)], which is the leading cause of death and disability in children and adults from ages 1 to 44. At least 5.3 million Americans, 2% of the U.S. population, currently live with disabilities resulting from TBI [\[76](#page-31-1)]. This means that there is an increasing need for rehabilitation strategies to enhance recovery, improve functional status, and promote quality of life, a current challenge for healthcare sectors, industries, financial systems, and aging societies as a whole.

There is strong evidence suggesting that the damaged motor system is able to reorganize in the presence of motor practice [\[6,](#page-27-0) [65](#page-30-0), [74](#page-30-1)]. Further, recent research has shown that interventions that include high-intensity and repetitive task-specific practice are more effective than traditional approaches to enhance motor recovery after brain injury [\[75](#page-31-2)]. Relearning motor tasks requires an optimal set of practice conditions that promotes the maximum learning benefits [\[46](#page-29-0)].

Over the past decade, there has been an increasing interest in using technology for neurological rehabilitation [\[68\]](#page-30-2). The aim is to facilitate motor recovery by supporting and motivating individuals with impairments to practice-specific tasks on high repetitive levels. For example, robot assistance is able to support and alter ongoing movements by the application of forces through actuators. Robotic-assistive devices can also monitor performance and provide feedback to the user based on measurements made by the sensors within the system. Furthermore, in combination with virtual reality conveyed on a computer screen or head-mounted display, the technology can be used to convert repetitive movement practice into engaging functional tasks with game-like features. Overall, such developments have led to real-time multimedia exercise environments for clinical rehabilitation that are comparably or more effective than conventional therapy [\[74,](#page-30-1) [100](#page-32-0)]. Yet, in this still early stage of development, their full potential still remains to be determined.

1.1 Recovery After Stroke and Traumatic Brain Injury

The primary goals after stroke and TBI are to reduce brain tissue damage and promote maximal tissue preservation and recovery. Rapid detection and appropriate emergency medical care are essential in the acute phase [\[56](#page-30-3)]. Once a survivor is medically stable, the focus shifts to rehabilitation. The goals of the subacute phase include preventing secondary health complications, minimizing impairments, and achieving functional gains that promote independence in activities of daily living [\[35\]](#page-29-1).

Early and spontaneous neurological recovery is often attributed to the resolution of edema or return of circulation within the ischemic area and may continue for up to 8 weeks [\[7](#page-27-1), [55](#page-30-4), [81\]](#page-31-3). Later recovery, based on neural plasticity and reorganization, plays an important role in the restoration of function and reduction of impairment. Neural plasticity and reorganization of the brain leads to functional changes in the surrounding brain tissue and in remote locations that have structural connections with the injured area [\[48,](#page-29-2) [101](#page-32-1), [121\]](#page-33-1).

It has been reported that most neurological recovery occurs within the first 3 months post injury, and recovery may continue at a slower pace for at least 6– 12 months [\[58\]](#page-30-5). Progress toward recovery may plateau at any stage with only a very small percentage of individuals achieving full recovery [\[34,](#page-29-3) [39](#page-29-4), [58\]](#page-30-5). Recent clinical practice guidelines recommend that rehabilitation therapy should start as early as possible, once medical stability is achieved [\[35](#page-29-1)].

2 Clinical Problems: Disability and Recovery After Stroke and Traumatic Brain Injury

The types and degree of disability depend upon which area of the brain and degree of tissue damage. It is difficult to compare one individual's disability to another, since every patient can sustain damage in slightly different sections of the brain and in different amounts. In general, five types of disabilities can be defined: paralysis or problems controlling movement; sensory disturbances including pain; problems using or understanding language; problems with thinking and memory; and emotional disturbances.

Paralysis and motor control problems are the most common disabilities. Patients have difficulty with everyday activities such as walking or grasping objects, and some have problems with swallowing (dysphagia). Damage to a lower part of the brain, the cerebellum, can affect the body's ability to coordinate movement (ataxia), leading to problems with walking, balance, and body posture. Patients may also lose the ability to feel touch, pain, temperature, or position. Sensory deficits also may hinder the ability to recognize objects held and can even be severe enough to cause loss of the ability to recognize one's own limb. Some patients experience pain, numbness, or odd sensations of tingling accompanying paralyzed or weakened limbs

(paraesthesia). The loss of urinary continence is fairly common immediately after an event. Patients may lose the ability to sense the need to urinate or the ability to control bladder muscles. Patients frequently have a variety of pain syndromes resulting from damage to the nervous system (neuropathic or centrally mediated pain), e.g., shoulder pain. An injury to any of the brain's language-control centers can severely impair verbal communication (aphasia). The most severe form, global aphasia, is caused by extensive damage to several areas of the brain involved in language function, thereby patients lose nearly all their linguistic abilities; they cannot understand language or use it to convey thought. Stroke or TBI can cause damage to parts of the brain responsible for memory, learning, and awareness. Survivors may have dramatically shortened attention spans or may experience deficits in short-term memory. Individuals also may lose their ability to make plans, comprehend meaning, learn new tasks, or engage in other cognitive activities. For example, patients who develop apraxia (loss of ability to carry out a learned purposeful movement) cannot plan the steps involved in a multistep task and act on them in the proper sequence. Finally, many survivors feel fear, anxiety, frustration, anger, sadness, and a sense of grief sometimes related to their physical and mental losses. These feelings are a natural response to the psychological trauma or because of damage to mood control centers.

2.1 Upper Limb Impairment in Stroke and TBI

Severity of upper limb paresis in the first month after brain injury remains the best predictor of recovery of arm function and reflects the degree of damage in cortical motor areas and corticospinal tract. Depending on lesion location, there could be a different probability of recovery, for example, there is greater recovery from hemiparesis resulting from cortical lesions than subcortical or internal capsule located lesions, presumably due to convergence at this level of most axons coming from the primary motor cortex [\[130\]](#page-33-2). However, hemiparesis could be the result of a wide variety of lesion location and no correlation between specific kinematic and dynamic abnormalities with lesion location has been found [\[71](#page-30-6)].

Upper limb cortical mechanisms that control shoulder and elbow are integrated with those more distal-like wrist and hand, as part of a system subserving reaching, prehension, and manipulation. Early presence of proximal upper limb active motion could be determinant for functional recovery because upper limb proximal motor control is related to the sparing of crossed corticospinal tracts, which are considered crucial pathways for hand control [\[54](#page-29-5)]. This fact has important implications for clinicians in terms of pursuing upper limb proximal rehabilitation even in the absence of distal motor function that potentially could appear at a later time.

In stroke and TBI patients, the upper limb may be hypotonic or flaccid without any volitional movement initially, or rigidly spastic later on. Moreover, undesired motor synergies could appear limiting independent control of single joints. There is scarce evidence about spasticity significantly interfering with voluntary movement, and in contrast no relationship has been found between spasticity, weakness, or loss of dexterity [\[132\]](#page-33-3).

However, other abnormalities after stroke cannot be explained by spasticity, weakness, or sensory loss. Thus, apraxia a cognitive and execution impairment is characterized by a loss of ability to perform a prior-learned action. It occurs more frequently in right hemispheric lesions but could occur on both sides of the body. Abnormalities in interjoint coordination are observed in these patients and seem not to be related to motor synergies, spasticity, or weakness. They are characterized by an imbalance between shoulder, elbow, and hand motions with deficit in transforming the planned trajectory into an appropriate motion, resulting in disorders of the kinematic and dynamic multijoint movements [\[10\]](#page-27-2).

Introducing a repetitive, intensive, and varied task-oriented therapy appears to be crucial to overcome these impairments and to increase generalization of new learned tasks. Impairment of upper limb sensory and proprioceptive function is a predictor of poor functional recovery even though motor function is intact or minimally impaired. This could be due to an interruption of projections from the cortical areas that represent upper limb dynamics [\[122\]](#page-33-4).

2.2 Gait Disorders in Stroke and TBI

Gait dysfunction is a common clinical manifestation of neurologic disorders in stroke and TBI. Patients usually show a gait pattern with loss of symmetry, decreased stance time and increased swing time for the affected limb, increased stance time on the unaffected side, and decreased step length. Swing phase appears delayed and could be associated to compensatory hip elevation (hicking), lateral trunk displacement, ankle equinus, and cincumduction movements (Fig. [1\)](#page-4-0). Speed of ambulation is decreased and influenced by weakness of hip flexors, knee extensors, and ankle plantar flexors [\[145\]](#page-34-1).

Fig. 1 Hemiparetic gait

TBI patients usually walk slightly faster than patients who had a stroke, with an increased step length. Compared to stroke in patients with TBI, the stance time for the affected limb is diminished, even though it remains increased for the unaffected limb [\[103\]](#page-32-2). Lesions affecting the frontal lobes can result in apraxic gait with a rigid pattern and the feeling of being stuck to the ground. This kind of gait is characteristically hypokinetic with slow-speed gait and limitation in limb advancement.

In summary, both patients with stroke and TBI can show a spastic hemiparetic gait pattern. Abnormal muscle activation pattern could lead to problems in motor coordination. In many cases, the cause of the deficits maybe related to spasticity but frequently this is accompanied by muscle weakness with decreased ability to recruit motor units, muscle atrophy, loss of muscle contractile properties, and agonist– antagonist cocontraction. All these factors may adversely impact the generation of functional movements during gait [\[102\]](#page-32-3).

3 Technology in Rehabilitation

3.1 Biofeedback in Neuroplasticity and Brain–Computer Interface (BCI)

After stroke, 80% of patients experience acute paresis of the upper extremity and only approximately one-third achieve full functional recovery [\[9\]](#page-27-3). Passive phenomena like reperfusion of the penumbra and resolution of brain oedema do account for some of the motor recovery post stroke or in traumatic brain injury. Nevertheless, recent discoveries that neurogenesis and neural reorganization can in fact occur in the adult after CNS injury have been revolutionary for the field of neurorehabilitation and contradict the dogma expressed by Santiago Ramon y Cajal back in the late nineteenth century. Evidence of such neuroplastic changes have been reproduced in both animal $\lceil 3 \rceil$ and human models $\lceil 150 \rceil$. Thence, research on how these neuroplastic phenomena can be exploited for motor recovery is currently a key focus, with neurochemical [\[11,](#page-28-1) [20,](#page-28-2) [134\]](#page-33-5) and neurophysiological [\[86,](#page-31-4) [139\]](#page-34-3) evidence of recovery-related neuroplasticity supporting the direction of this work.

A fundamental element in any process of learning is the presence of feedback. From a child who is learning to walk, to a gymnast who is training for a somersault, a real-time stream of multisensory data is continuously flowing to the brain during motor tasks. The integration of data from proprioceptive, visual, auditory, and sometimes even pain receptors helps the brain get a complete picture of the body's position, motion, and end result of any motor intention. Relaying of such data to the cerebellum, prefrontal, and motor cortices, over a repeated number of successful and failed attempts, forms the basis of motor skill learning [\[59](#page-30-7), [123](#page-33-6)].

Following stroke or traumatic brain injuries, this motor execution \rightarrow feedback loop is often disrupted. Damage to motor pathways, either at a cortical or subcortical level, leads to difficulty or complete inability to execute motor intention, which

thus breaks the feedback loop very early on. The core of most neurorehabilitation strategies is the aim of reclosure of this loop, either by aiding movement completion or by giving some form of feedback to the central nervous system that is coupled with the initial motor intention.

If one looks at even the most basic of physiotherapy strategies like passive arm movement, the assisted physiotherapist-guided motion is allowing for proprioceptive sensation and visual feedback to reach the brain. A more affective approach—and currently a gold standard in the physiotherapy field—is the use of repetitive, taskspecific training for relearning of motor skills needed for activities of daily living [\[118,](#page-33-7) [140\]](#page-34-4). This directly addresses one of the goals of neurorehabilitation as proposed in the latest clinical guidelines, which is to empower patients and families by helping motor function improvement and achievement of the highest level of independence in activities of daily living [\[99](#page-32-4)].

3.1.1 Electromyographic (EMG) Biofeedback

With this current knowledge on neuroplasticity in mind, one can start to appreciate the rationale behind the more recent technology-assisted strategies in the field of neurorehabilitation. One of the earliest technologies developed for biofeedback in the field of neurorehabilitation is EMG biofeedback. The mechanism behind this approach is the detection of attenuated electrical activity which occurs in paretic muscles upon motor intention and the conversion of this ineffective data to visual or auditory feedback to the patient—thus reclosing the loop. Research on such setups go as far back as the 1960s and within merely a decade it had become a standardized rehabilitation tool used commonly by physiotherapists [\[41](#page-29-6), [155\]](#page-34-5). A recent Cochrane review exploring the efficacy and benefits of EMG biofeedback in motor recovery post stroke has identified a number of trials publishing evidence of benefit for motor power, function, and gait recovery when this technology was added on to the standard physiotherapy regime but this has yet to reach statistical significance in view of the limited size of trials and robustness of results [\[157](#page-34-6)].

3.1.2 Brain–Computer Interface

Recent advances in neurophysiological signal acquisition and processing techniques have opened the way to a higher form of neurorehabilitative feedback approach, which can completely bypass the peripheral physiological outputs of the body *brain–computer interface (BCI)* [\[13](#page-28-3)]. Neurophysiological acquisition methods may range from noninvasive technologies like electroencephalography (EEG), magnetoencephalography (MEG), functional near-infrared spectroscopy (fNIR), and functional magnetic resonance imaging (fMRI) to invasive electrocorticography (ECoG). EEG technology still holds several limitations with respect to spatial resolution and quality of brain signal pick-up. Nevertheless, its safety, noninvasiveness, and excellent time resolution makes it one of the most popular signal acquisition media

Fig. 2 Brain–computer interface system and the feedback loop

for BCI. Among the earliest accomplishments in the world of BCI was Birbaumer et al.'s success in enabling two 'locked-in patients' to communicate using a BCI speller [\[12\]](#page-28-4). One of these patients was reported to have eventually learnt to use the BCI on his own to write letters and communicate with his friend [\[98](#page-32-5)].

Brain–computer interface systems take advantage of a number of different neurophysiological changes and patterns that have been noted to be associated with particular mental states and tasks [\[156\]](#page-34-7). Some of these modalities are dependent on the subject's intention and can be modulated actively through training. These include the *P*300 response (a positive EEG deflection 300 ms after a target stimulus is presented to the subject) and the *slow cortical potential* (SCP) (changes in amplitude that correlate with level of cortical activation). Both of these paradigms have been employed most notably for BCI spellers. Other BCI paradigms are based on passive, natural responses to present stimulus and need no training, like the *steady-state visual evoked potentials* (SSVEP) (change in the frequency of occipital cortex oscillations that matches the frequency of flashing light presented). These three modalities of BCI are mostly used for *assistive* purposes, substituting a function that was lost due to motor or speech impairment following conditions like stroke, amyotrophic lateral sclerosis, or traumatic brain injury (Fig. [2\)](#page-7-0).

The fourth major modality of BCI is based on motor imagery related changes in oscillatory activity like *event related (de)synchronization* (ERD/ERS). Desynchronization of EEG activity can be observed following both motor imagery and motor execution initiation, over the motor cortex, in the Mu and beta frequencies, followed by re-synchronization shortly after motor activity. This has become the modality of choice for BCI-based motor rehabilitation i.e., for *restorative* rather than assistive purposes [\[131\]](#page-33-8). Motor imagery (MI) itself has been shown to be associated with motor cortex activation [\[107,](#page-32-6) [128\]](#page-33-9). More importantly, repetitive MI tasks coupled with conventional (physiotherapy and occupational therapy) rehabilitation has been shown to have an added benefit in motor recovery [\[161\]](#page-35-0). This is of particular interest

when dealing with patients with negligible residual muscle function, in whom standard task-specific or constraint-induced therapy would not be possible.

Initial BCI studies in stroke and traumatic brain injury patients focused on control of mu rhythm via either motor imagery or motor execution in order to either move cursors on screen or move hand orthoses $[16]$. These assistive approaches were subsequently followed by restorative BCI systems, with or without the use of haptic devices [\[4](#page-27-5)] or functional electrical stimulation [\[29](#page-28-6)] for proprioceptive feedback. Two examples of BCI-based therapeutic setup with purely visual feedback will be briefly introduced next, while further technological devices will be discussed in subsequent sections.

The first is a computer game-based neurofeedback system developed by Prasad et al. [\[115\]](#page-32-7) for the rehabilitation of persons with chronic hemiplegic after stroke. The setup consisted of EEG signals acquired from C3 and C4 electrodes (overlying the motor cortex) which are processed online to translate into left and right movements of a ball on a computer screen. Subjects were required to maneuver the ball into a basket by imagining left- or right-hand movement according to the direction required (Fig. [3\)](#page-8-0). Performance throughout the sessions was based both on accuracy classification during the MI task and periodic motor function recovery scores as measured by action research arm test and grip strength. After a 6-week period, improvement in at least one modality of function was noted in all patients and every patient managed to operate the BCI successful with an average accuracy of 60–75%, suggesting feasibility of such a setup in the context of post-stroke rehabilitation. [\[115](#page-32-7)].

In a more recent publication by Cincotti et al. (2012), an elegantly designed BCI-based upper limb rehabilitation system for patients post-stroke is presented. The system is composed of a 32-channel EEG input, driving a BCI software that delivers two concurrent outputs when the patient's EEG signal is compatible with hand opening/closing motor imagery. The first output is intended for the assisting physician and is in the form of a moving cursor, representing the patient's mental activity. The second output is a visual feedback intended for the patient and is in the form of realistic images of moving hands, projected onto a white sheet that is placed over both of the patient's hands (Fig. [4\)](#page-9-0). In this way, attempts at hand movement

Figure 1 An illustration of a Brain-Computer Interface: (a) Main components of a BCI. (b) Timings of a ball-basket game paradigm.

Fig. 3 A computer game-based neurofeedback system driven by EEG-based brain–computer interface*—Reproduced with permission from* Prasad et al. [\[115\]](#page-32-7).

Fig. 4 EEG-based BCI upper limb rehabilitation system, giving both motor imagery information to the therapist and visual realistic hand motion feedback to the patient—*Reproduced with permission from* Morone et al. [\[94](#page-31-5)]

lead to the visual illusion of the paretic hand moving, as projected onto the screen superimposed on the paralyzed hand. This system was installed in a rehabilitation ward and tested on 29 stroke patients in whom increased alpha and beta reactivity was noted post training, along with moderate increases in functional outcome measures when compared to control subjects testing non-BCI MI practice.

3.1.3 Conclusion

As its name implies, brain–computer interface is merely a new interface that can translate a person's intentions into numerous outputs of various forms. Thus, the present challenge in neurorehabilitation research is the development of useful BCI applications and platforms that can offer more effective and efficient motor recovery to patients suffering from stroke and traumatic brain injury.

To date, most studies explore the benefits of MI-BCI rehabilitation in conjunction with standard physiotherapy, and so robust statistical evidence of superiority of MI-BCI-driven rehabilitation over standard active motor training is still difficult to prove and further randomized trials need to take place. Confounding factors to the observed beneficial effects of MI-BCI rehabilitation—albeit desirable themselves—include the increased willingness and time spent by patients doing active motor training within the BCI setup itself when compared to those in the standard, repetitive tasktraining groups.

The potentials for BCI in this context are various: visual, proprioceptive or, any other output that is coupled with motor imagery/intention can reinforce biofeedback to the patient and provide valuable information to the clinician regarding the patient's engagement and performance in these previously invisible MI tasks. Finally, innovative outputs and applications driven by MI-BCI can increase patient's motivation and engagement in his rehabilitation process, through the use of media like video games, engaging work-out sessions, or simply through the confidence-boosting sight of his arm actually moving on command, made possible only through BCI-driven robotics or functional electrical stimulation.

"If I can't do it once, why do it a hundred times?" Quote from a severe hemiplegic patient on conventional table exercises - Reinkensmeyer and Housman, 2007

3.2 Virtual Reality-Based Rehabilitation

Rehabilitation technologies such as virtual reality are based on motor learning principles and could be implemented in order to compensate, restore, and recover cognitive impairment and loss of sensorimotor function caused by stroke and TBI.

Virtual reality can be defined as an approach to user–computer interface that involves real-time simulation of an environment, scenario, or activity that allows for user interaction via multiple sensory channels [\[17\]](#page-28-7).

The rationale for using virtual reality training on brain injury rehabilitation is because during therapy a repetitive massed practice of relevant functional tasks based on imitation and movement observation could be useful to facilitate targeted brain networks and potential neuroplastic changes. Functional and motor recovery observed during virtual reality task-oriented therapy may be linked to induced neuroplasticity changes with a mirror-neuron system activation, reorganization of damaged motor cortex, decreased aberrant cortical hyperexcitability on unaffected hemisphere, and at synaptic level synthesis of neurotrophic factors (BDNF) that encourage axonal sprouting and dendritic spine formation [\[15](#page-28-8), [109,](#page-32-8) [159](#page-35-1)].

Virtual environments are characterized as immersive, where a three-dimensional environment is displayed allowing to change visual perspective with head movements (head-mounted visual displays, virtual caves), semi-immersive with threedimensional fixed visual perspective presentations, or nonimmersive in the case of two-dimensional presentations displayed on a screen with or without interface devices as keyboard, computer mouse, or a joystick. There are some commercially available devices such as the IREX system (from GestureTek, Canada), Nintendo Wii , Sony Playstation EyeToy, Microsoft Kinect (Fig. [5\)](#page-11-0). Furthermore, there has been virtual reality systems designed to be coupled to haptic and robotic devices to provide interaction forces and sensorimotor feedback between the user and the virtual environment. Examples of combined robotic and haptic systems include the Rutgers Ankle Rehabilitation system, Cybergrasp, CyberGlove, Gentle-S, PneuWrex , Mit-Manus, and Armeo Power. They all have been used with the purpose of increasing the feeling of immersion and user interaction into the virtual scenario. Haptic devices add precision to tracking motion, providing a powerful multisensory feedback that contributes to improve real-world activity level motor outcomes [\[19](#page-28-9)].

Feedback is crucial for user's engagement, motivation, and concentration during virtual therapy and has been determined essential to increase effect . In addition to visual and auditory feedback, tactile and force feedback provided by haptic devices

Fig. 5 A kinect-based virtual reality system. With permission of Complejo hospitalario de Toledo-Spain

increases the user interaction with the virtual environment and objects. Augmented feedback also could be implemented during sessions using knowledge of results (KR) or knowledge of performance (KP- desirable/ undesirable movement patterns). Usually, virtual reality therapies are applied to patients with low or moderate spasticity (Ashworth scale score equal or less than 2), and mild or moderate upper limb paresis. The presence of certain degree of active movements and manipulation ability (active wrist extension above 20°, metacarpophalangeal finger extension above 10^o, and approximately between 30 and 42 points in upper extremity Fugl-Meyer assessment) seem to be necessary for participation in virtual therapy programs. Hand dexterity scores lower than 45in Box and block test could be also considered a criterion for therapy admission.

Treatment sessions can vary widely in terms of number and duration between different studies. Duration of 40 min to 1 h, delivered 3–5 days a week along a three– four week period, is common [\[83](#page-31-6)].

Usually, patients with both types of stroke, ischaemic, or hemorrhagic are included in virtual reality therapy. A recent study has shown, in line with previous data with more classical interventions [\[104](#page-32-9)] a differential response depending on etiology of stroke. Although all participants achieved motor improvements, patients affected by hemorrhagic stroke improved significantly more on FIM scores and kinematic parameters compared to ischaemic stroke patients [\[64\]](#page-30-8).

Majority of patients are treated predominantly during a subacute or chronic phase (greater than 3–6 months) after brain injury, because in many cases acute phase deliver of this therapy results in impractical due to an unstable medical condition or severe plegia.

Virtual reality therapy is typically applied to patients without cognitive impairments, but many times stroke and TBI patients show cognitive and perceptual disorders. The minimal cognitive and perceptual requirements to use virtual rehabilitation in an effective manner still remain unidentified.

3.2.1 Virtual Reality for Upper Limb Rehabilitation in Stroke and TBI

An increased number of studies have been proposed in the last decade to evaluate the scientific evidence for the effectiveness of virtual reality in upper limb rehabilitation after TBI or stroke.

Regarding virtual reality effectiveness for upper limb motor recovery in stroke patients, a moderate beneficial effect has been reported. In a systematic review by Henderson et al., the authors found that compared to conventional therapy, there is a moderate level of evidence (2b) on the effectiveness of using nonimmersive virtual reality training for upper limb rehabilitation [\[50\]](#page-29-7).

In a meta analysis that reviewed five randomized controlled trials about virtual reality therapy for subacute and chronic stroke patients (daily sessions, 5 days a week, during 4–6 weeks), authors found improvements on upper limb motor function, with increasing Fugl-Meyer scale scores between 13.7–20%, at the end of treatment when compared to controls $(3.8-12.2\%)$ treated with conventional occupational therapy [\[124\]](#page-33-10).

A recent Cochrane review [\[78](#page-31-7)] analyzed 19 studies with 565 participants. In three of them (101 participants), they achieved significant statistically differences regarding ADLs performance in patients with virtual reality therapy (standardized mean difference 0.81; IC 95% [$0.39-1.22$]). However, authors concluded that there was insufficient evidence about the effectiveness of virtual reality therapies to significantly increase grip strength.

A recent review of current state of post-stroke virtual rehabilitation [\[42](#page-29-8)] analyzed eight studies of upper limb and concluded that virtual reality could induce a moderate improvement on upper limb motor function with a small additive effect in terms of real-world activity daily living motor outcomes in subjects performing intervention with haptic feedback.

Another recent study [\[79\]](#page-31-8) reviewed ten studies examining effectiveness of virtual reality-based rehabilitation regarding upper limb and hand fine motor skills in chronic stroke patients. Significant improvements were found in finger fractionation, finger tracking, and time from peak hand velocity at the moment an object was lifted from a table. Moreover, in five of the ten studies of this review, significant improvements were reported regarding transfer of virtual reality gains to real-world tasks when assessed by the Jebsen Taylor hand function test.

In a recently published systematic review and metaanalysis, twenty six upper and lower limb controlled trials compared virtual reality to conventional therapy in stroke patients [\[82](#page-31-9)], demonstrating a moderate effect in favor of virtual reality therapy. Time post-stroke and type of virtual therapy intervention (commercial gaming, semi-immersive, immersive virtual environments) did not significantly affect the outcomes. In addition, virtual reality therapy induced significant improvements across domains of International Classification of Function, Disability, and Health. (ICF-World Health Organization. Geneva, 2001). For body function level, there was a significant benefit of virtual reality therapies compared to conventional therapy, with an overall effect size $G = 0.48, 95\%$ CI [0.27,0.70]. For activity level outcomes, they found the same benefit with an overall effect size $G = 0.58$, 95% CI [0.32, 0.85],

whereas for participation level outcomes, the overall effect size was $G = 0.56, 95\%$ CI [0.02,1.10]. However, authors accept that results should be interpreted with caution due to considerable variability within interventions.

The evidence in favor of using virtual reality for upper limb rehabilitation in TBI patients to improve motor function still is very limited.

In a four-patient study, [\[52\]](#page-29-9) used a virtual reality system consisting of a computer, software, and a motion-tracking device. Prerecorded arm movements of a virtual "teacher" and the patient arm movements using a motion-tracking capture system were displayed on a computer screen. The patient was asked to mimic the virtual teacher movements, and the difference between movement trajectories provided augmented feedback. In this study, three out of the four patients improved upper limb function, and movement trajectories were smoother, straighter, and more accurate after the therapy. Moreover, patients achieved higher Fugl-Meyer scale scores and were able to generalize learned skills to real-world performance.

Virtual reality systems for TBI patients seem to improve accuracy of movement for both hands (left $p = 0.01$; right $p = 0.02$), speed and efficiency for right hand ($p = 0.01$) and $p = 0.002$, respectively), and bilateral hand dexterity assessed by Box and Block Test [\[95\]](#page-31-10).

Appropriate arm-postural coordination is crucial to perform reach and grasp activities without abnormal compensatory strategies (trunk displacement) and to carry out activities of daily living in standing position (bathing, dressing, cooking).

A study of a virtual reality system for arm-postural coordination using the World Viz Vizard software (Santa Barbara CA), integrated with a six-camera system for motion capture and a custom-made 3D- immersive videogame. Patients use large arm movements to control their avatar trying to reach the maximum number of targets. Participants with mild-to-moderate TBI using this virtual system improved arm movement time, arm postural coordination and movement trajectory, forward reach, and single-leg standing [\[143](#page-34-8)]. There was no follow-up to assess retention and duration of improvements.

3.2.2 Virtual Reality for Lower Limb Rehabilitation in Stroke and TBI

Efficacy of virtual reality technology to improve walking and balance for post-stroke and TBI patients has been studied for its clinical application during the last ten years. Hardware and software of virtual reality systems created for this purpose ranged from fully immersive systems combining motion platforms, instrumented treadmills, motion capture systems, and surround sound systems (i.e., Computer-Assisted Rehabilitation Environment-CAREN) to nonimmersive gaming-based commercially available systems (i.e., Nintendo Wii), and virtual reality systems coupled to haptic or robotic devices (i.e., Rutgers Ankle Rehabilitation System).

Improvements on balance and ambulation could be due to task-specific training and the virtual reality elements that simulate real-world environments and motivate patients to practice.

For stroke patients, most studies have been carried out during the chronic phase post stroke. In this population, combining virtual gait training with conventional therapies seems to be more effective than application of virtual training alone.

Some studies show that chronic stroke patients who received additional 30 min per session of virtual reality walking therapy added to conventional physical therapy achieved significant improvements on balance, gait velocity, cadence, and step length, compared to controls without virtual therapy [\[24](#page-28-10), [63\]](#page-30-9). Therefore, even a short time of virtual training a day could yield significant gait improvements.

A differential effect in terms of biomechanics and functional outcomes has been found between nonimmersive and immersive haptic–robotic virtual systems. A positive impact on gait biomechanics has been shown when patients are trained with a force-feedback robot interfaced virtual reality system. In a single-blind randomized control study, subjects in the robot interfaced virtual reality group demonstrated significantly larger increase in ankle power generation, ankle range of motion (ROM),

and knee ROM during swing phase of gait, compared to controls [\[93](#page-31-11)].

In contrast, a randomized controlled trial [\[44](#page-29-10)] showed that chronic post-stroke patients that followed balance and gait training with a nonimmersive video-gaming system did not achieved significant improvements on Fugl-Meyer assessment, Berg balance test, time up and go, and 6-min walk test compared to controls that continued with normal activity without receiving any special intervention. However, additional studies are needed to establish real efficacy of nonimmersive commercially available devices for virtual gait training.

Evidence about virtual reality therapy for gait and balance recovery in acute stroke patients is still limited. In a recent randomized controlled trial [\[91](#page-31-12)] that studied 59 acute stroke patients, the treatment group $(n=30)$ received standard rehabilitation plus virtual reality therapy (10–12 sessions, 30 min per sessions, 3 weeks) that included some exercises that challenged balance while standing (soccer, snowboarding). The control group $(n=29)$ received the same conventional rehabilitation plus identical exposure to virtual therapy without balance challenging exercises (performed sitting). Patients in virtual training balance exercises achieved after therapy greater improvements on 2-min walk test and time up and go test, diminishing lower limb impairment assessed by Chedoke-McMaster Leg domain compared to controls.

Studies with acute TBI patients and virtual reality-based gait training are also scarce, but at least for chronic patients some studies had shown feasibility and efficacy of this therapy, with improvements on gait and balance confidence [\[138](#page-34-9), [141](#page-34-10)].

For mild-to-moderate chronic TBI patients, arm–leg coordination movements and dynamic postural stability gains have been found using an Xbox Kinect sensor with an interactive customized virtual reality games and scenarios [\[144\]](#page-34-11).

In addition to this evidence of efficacy, studies point to the feasibility of virtual therapy implementation. Thus, nonimmersive virtual training added to conventional therapy could lead to improvements on walking distance, gait speed, and balance compared to usual therapy, with high therapy compliance and patients attending the majority of sessions without any reports of adverse events [\[89\]](#page-31-13).

3.2.3 Conclusions

At the present time, studies indicate moderate evidence about the effectiveness of virtual reality technology to improve gait, balance, and upper limb motor function in stroke and TBI patients. Combined interventions adding virtual training to conventional rehabilitation appear to yield better motor and functional outcomes than a single intervention.

There are still some challenges to attain effective translation of learned motor skills in virtual environments to real-world activities of daily living performance. Emerging evidences suggest some progress in this issue, as represented by the positive impact found with virtual therapies across ICF domains.

Nevertheless, outcomes obtained from different studies should be interpreted with caution due to considerable variability within interventions (dosage, intensity, duration), small sample sizes, variable design quality of studies, and lack of detail provided about "conventional therapy." Finally, reports of cybersickness or adverse side effects (dizziness, headache, pain) after using virtual reality are scarce or minimal. Future studies should be considered to determine whether virtual reality training could affect patients condition, facilitate recovery, or interfere directly or due to adverse effects with functional recovery.

3.3 Robotics and Haptic Devices

Robotics in the medical field requires the convergence of expertise in robotics, medicine, and computer science, and the identification of specific robotic system design demands is in various stages of development.

In recent years, there have been significant developments in the design of robotic system for applications in surgery, rehabilitation, prosthetics, and assistance directed at the elderly or the disabled.

In particular in the field of rehabilitation, robotic systems may have the potential to reduce the demands.

Human operators in order to cope with the increasing growth demand and potential for injury by reducing the staff effort introduce more effective rehabilitation protocols.

Robotic systems are also called upon to address the demands for home care for the elderly, especially in relation to the execution of repetitive tasks.

Robotic technology can provide support to rehabilitation therapy [\[146](#page-34-12)]. Early robotics, starting in the late 1950s, focused on large manipulators to replace workers in factories who were performing dirty, dangerous, and undesirable tasks. The rehabilitation robots were based on previous designs in the field of prosthetics, where devices have been developed for the substitution of function of upper and lower limbs, some of which are in widespread use in rehabilitation clinics. This chapter will focus on devices for the rehabilitation of the upper limb and review some of the most used.

3.3.1 Robotics Devices

Robots for upper limb rehabilitation generally consist of robotic arms with several degrees of freedom, the end of which is connected to the hand or arm of the patient. Many research groups have developed robotic devices for upper limb rehabilitation, for example, Massachusetts Institute of Technology (MIT) Manus [\[69\]](#page-30-10), Assisted Rehabilitation and Measurement (ARM) Guide [\[116\]](#page-32-10), Mirror Image Motion Enabler (MIME) [\[18\]](#page-28-11), Bi-Manu-Track [\[51\]](#page-29-11), GENTLE/S [\[26\]](#page-28-12), Neurorehabilitation Robot (NeReBot) [\[120\]](#page-33-11), REHAROB [\[142](#page-34-13)], Arm Coordination Training 3-D (ACT^{3D}) [\[136\]](#page-33-12), and ARMin [\[97](#page-32-11)].

Generally, you can follow on the computer screen a representation of the movements of the robot. The interaction between patient motion and movement of the robot can be done in various ways. The robot can drive limb movements of the subject completely, without any subject active participation; or you may demand a greater participation by the user, who must strive to make the move. The user must prioritize positioning task performance, e.g., move the robotic arm so that its position in space, represented graphically on the computer screen, coincides with a desired position, also shown in the form of a 'target' on the screen. The task of the robot, in these scenario, is to encourage parallel movement of the patient, e.g., applying guiding resistance in the event of deviations from the desired trajectory, or to apply assistance if the patient has difficulty initiating or continuing the movement. The utility of these robot systems is shown by numerous clinical studies [\[114](#page-32-12)].

3.3.2 Haptics Devices

Haptics is a term that was derived from the Greek verb "haptesthai" meaning "of or relating to the sense of touch." It refers to manual sensing and manipulation of surrounding objects and environments through the sense of touch. The "touching" of objects and or environment can be made through these devices and the objects and environments can be real, virtual, or a combination of both. Also, the interaction may or may not be accompanied by other sensory modalities such as vision or audition [\[38\]](#page-29-12).

The training with these devices is based on exercise therapy modalities that the literature and/or clinical practice indicate may help restore upper limb motor control and function [\[37](#page-29-13)].

There are two modalities to restore mobility, passive, and active mobilization. In the passive mode, the robotic device moves the patient's arm. In the active mode, the movement is either partially assisted by the robotic device, or resisted by the robotic device. An example of passive motion intervention is a system that provides bimanual mobilization, where the movement of the unaffected arm is mirrored by simultaneous passive movement of the affected arm provided by the robotic device.

For example, the device Phantom permits simulation of fingertip contact with virtual objects. A pen-like stylus tracks the pitch, roll, and yaw and x, y, and z Cartesian coordinates of the virtual point probe. Its actuators communicate forces

back to the user's fingertips as it detects collisions with virtual 3-D objects, simulating the sense of touch [\[88](#page-31-14)]. Other haptics devices are Omega3 [\[45](#page-29-14)], Falcon [\[87\]](#page-31-15), and haptic knob for rehabilitation of hand function [\[72](#page-30-11)].

For ambulation rehabilitation, the science behind exercise in persons with neurologic disease supports treadmill training over "conventional therapy [\[33](#page-28-13)]. What constitutes "conventional therapy" is highly variable and not well described in the literature. This area only recently has been given more study attention [\[30](#page-28-14)]. Traditionally, the conventional physiotherapy approach focuses on strengthening and practicing single selective movements or various neurofacilitation techniques. Conventional therapy methods, however, do not specifically emphasize the activity of ambulation. Limited evidence exists to support the effectiveness of these techniques in the restoration of walking ability [\[47](#page-29-15), [67,](#page-30-12) [80,](#page-31-16) [148](#page-34-14)].

Many rehabilitation paradigms have been developed to promote recovery of lower extremity function and walking through task-specific training. Walking on the treadmill alone [\[77,](#page-31-17) [119](#page-33-13)] or in combination with body weight support (i.e., body weight supported treadmill training [BWSTT]) [\[27](#page-28-15), [149](#page-34-15)] has become an increasingly popular option in the past several years. Although recent reviews of the literature have not demonstrated different outcomes of BWSTT for patients who have had a stroke [\[31,](#page-28-16) [36](#page-29-16)] based on task-specific approach, gait training is the best way to improve the walking pattern [\[28\]](#page-28-17). Such repetition is thought to facilitate the integration of remaining and altered sensorimotor systems in persons with either an acute or chronic brain injury [\[53](#page-29-17), [137\]](#page-34-16).

Positive changes in larger cortical representation have been demonstrated in patients with a TBI [\[60](#page-30-13), [105\]](#page-32-13). Rehabilitation efforts that promote motor recovery of ambulation activity through task specificity and repetition for persons with a TBI can be complicated by a number of different factors: (1) the potential for multiple motor impairments, both of a pyramidal and extrapyramidal nature; (2) the presence of cognitive or communication impairment; (3) the need for a high number of repetitions as part of the training; and (4) the high level of manual assistance required to help the patient during gait training. These factors combine to make task-specific training for persons who have sustained a TBI very labor intensive, time consuming, and costly. To address some of these limitations, locomotor therapy with a robotic device has been introduced as a task-specific technique to apply precise movement training that may increase the efficiency and/or effectiveness of this type of intervention. Some of the benefits of robotic-assisted treadmill training include more intensive and prolonged training modes, consistent movements, and a reduction in manual labor required from the therapist. Although considerable literature exists on the effectiveness of locomotor training with robotic-driven therapy on spinal cord injury populations [\[25](#page-28-18), [57,](#page-30-14) [153\]](#page-34-17), surprisingly little published research is available regarding persons with a brain injury. In some studies of persons who had a stroke, investigators found better outcomes with robotic-assisted training compared with conventional training [\[127\]](#page-33-14).

A Cochrane Review [\[92\]](#page-31-18) on patients who had a stroke found that RATT in combination with physical therapy improves some gait parameters but not others. As for research on patients with a TBI who were treated with robot-assisted therapy, only a

few studies are available using this training modality or comparing the effectiveness of the different interventions [\[40,](#page-29-18) [43\]](#page-29-19). In a randomized study with 16 subjects with TBI, there was evidence that BWSTT with manual and robotic assistance at participants' preferred walking speed and adjustments made on the basis of their velocity gains are an effective approach to increase self-selected and maximal walking velocity. RATT-trained participants had significant improvement in step length symmetry. Participants in both groups expressed significant improvement in their mobility. On the basis of between-group differences, no training technique appears to be superior to the other; however, the Lokomat required fewer staff and less manual effort from the staff was reported, with decreased staffing costs. Although the literature has demonstrated that gait training with either manual or robotic BWSTT is equivalent in persons who have had a stroke, this study provides the first reported evidence of this finding in the TBI population [\[40](#page-29-18)].

3.3.3 Guidelines

Robot therapists must present certain features that are crucial if they are to be really effective [\[21\]](#page-28-19). Some of these are summarized below. Robot interventions must

- i. Have a high level of compliance; a highly compliant robot that is a system that can be easily moved even with a very small force is applied and, at the same time, that does not oppose the movement of the patient but facilitates it by means of gently modulated forces [\[21](#page-28-19)].
- ii. Have a wide range of forces; in skilled therapeutic treatment, it is necessary to find the right combination of guiding and resisting forces, according to the individual's performance and the nature of the task.
- iii. Adhere to a minimal force assistance-level criterion; This criterion is motivated by the requirement of compatibility with the schema theory of "assist as needed principle" of motor learning [\[21](#page-28-19)] or the "minimal assistance strategy" [\[154\]](#page-34-18).
- iv. Promote improvement of proprioceptive awareness; considering the fact that motor deficits are highly associated with proprioceptive deficits or deficits of spatial representations that affect the integration of the body schema. In many cases, such deficits are even more disabling than the purely motor deficits, but are not adequately considered [\[21\]](#page-28-19).
- v. Have a high degree of system intelligence; the figure below Fig. [6](#page-19-0) illustrates the basic elements that characterize information flow: (1) a haptic robot; (2) a force field generator; (3) a performance evaluator; and (4) an adaptive controller. In other words, an efficient therapeutic robot must not be a purely executive electromechanical device but must provide the patient with a rich interactive environment.
- vi. Be designed in a modular way; the complexity of the therapeutic robot, in particular the number of degrees of freedom employed, should be as small as possible and selected based on each patient need [\[21\]](#page-28-19).

vii. Facilitate synergy between physiotherapy and therapeutic robot; the general principle is that robot therapy and physiotherapy should be synergistic and cooperative. The appropriate division between robot and human therapy can, in general terms, be formulated as follows: (i) the robot therapist trains the patient to improve basic motor coordination; and (ii) the human therapist exploits the improved coordination in a functional context by challenging the patient with tasks that require increasingly skilled actions [\[21](#page-28-19)].

3.4 Neuromuscular Electrical Stimulation in Rehabilitation of Upper Extremities

Electrical stimulation of the peripheral nervous system (PNS) can be used as a therapy and/or assistive devices for patients with TBI and stroke [\[8](#page-27-6), [23](#page-28-20), [113](#page-32-14)]. Neuromuscular electrical stimulation (NMES) refers to electrical stimulation of intact lower motor neurons hereby eliciting contractions of the otherwise paretic or paralyzed muscles [\[14\]](#page-28-21). Functional electrical stimulation (FES) is the use of NMES to activate muscles in a precise sequence and intensity, mimicking efferent signals from the central nervous system (CNS), in order to accomplish functional tasks [\[106\]](#page-32-15).

NMES is applied as waveforms of electrical current which are characterized by stimulus frequency, pulse amplitude, and width. The quantity of recruited muscle fibers depends on the pulse amplitude and width of the stimulation, whereas temporal summation is reliant on the stimulation frequency. Thus, the strength of the elicited muscle contraction is tuned by adjustment of the stimulus parameters [\[106,](#page-32-15) [129](#page-33-15)]. Normally, stimulation frequencies in the range of 12–16 Hz is used in upper extremity applications in order to achieve muscle responses, without generating muscle fiber fatigue and rapid decline in contractile force [\[129\]](#page-33-15). It has been documented that NMES can improve neuromuscular function in stroke and TBI patients by strengthening of atrophied muscles, moderation of spasticity, decreasing pain, increasing motor control, and range of motion [\[111](#page-32-16), [126](#page-33-16)]. Further, it has been suggested that NMES leads to relearning of motor function through the same mechanisms as conventional repetitive movement training [\[129\]](#page-33-15) where afferent input is increased during

the training [\[126](#page-33-16)]. In such case, NMES is denoted as therapeutic electrical stimulation (TES) [\[111](#page-32-16)[–113,](#page-32-14) [126](#page-33-16)].

NMES devices are classified according to their mode of current application and the stimulation parameters utilized. Three modes of current application are described:

- Surface NMES systems where surface electrodes are placed over the motor point or the nerve innervating the target muscle and the entire system is external to the body.
- Implantable NMES systems where electrodes (e.g., cuff-, epimysial, or intramuscular electrodes) are placed around the nerves that innervate the targeted muscles, or at the motor point of the targeted muscles. An implantable stimulator is placed in the vicinity of the electrodes, and controlled via a control unit which is placed external to the body.
- Percutaneous NMES systems where needle- or wire- electrodes are inserted close to the motor point of the targeted muscles and the remaining part of the system is external to the body [\[106](#page-32-15)].

Similarly, three stimulation methods exist:

- Cyclic NMES where stimulation parameters are preprogrammed and triggered via the NMES system without any concurrent voluntary contraction of the target muscles by the subject.
- Electromyography (EMG)/biofeedback-mediated NMES where stimulation is triggered by EMG or positional feedback of the upper extremity obtained directly from the subject, which is actively participating in the rehabilitative exercise.
- Neuroprostheses where NMES in combination with the prostheses is used to facilitate functional and meaningful behavioral tasks [\[23](#page-28-20), [70](#page-30-15), [129\]](#page-33-15).

Each of the NMES modalities has their own strengths and weaknesses which are going to be described in detail in the following sections.

3.4.1 Surface NMES

Surface NMES most often are voltage regulated in order to avoid tissue damage due to the changing resistance of the electrode–skin interface. Voltage regulation though might lead to variable motor responses due to decreased current induction as a function of increased impedance of the electrode–skin interface [\[129](#page-33-15)]. Surface systems are especially well suited for short-term rehabilitative use due to their lowcost, simplicity, and ease of use $[106]$ $[106]$. However, lack of deep muscle selectivity, potential skin irritation and pain, and unappealing esthetics are drawbacks of the surface systems. Choosing the optimal electrode dimensions and position in order to avoid pain and skin irritation while trying to recruit the appropriate muscles is a very complex task [\[110\]](#page-32-17). As a consequence, surface systems are most often utilized in the clinic, where skilled personnel secures repeated placement of the electrodes in the appropriate positions [\[106](#page-32-15)]. As a result of the aforementioned, surface NMES systems are considered to be temporal systems.

3.4.2 Implantable NMES

In implantable NMES systems, it is possible to use current-regulated stimulation due to elimination of skin resistance which results in a more homogeneous electrode– tissue interface [\[129\]](#page-33-15). By doing so, it is possible to achieve consistency and repeatability in the elicited motor responses with less pain [\[129](#page-33-15)]. Implantable NMES systems are intended for long-term use and since none of the leads of the system need to protrude the skin they can be made larger and more durable [\[106](#page-32-15)]. The implant is powered via batteries (rechargeable or disposable) or through radio fre-quency telemetry link from an external control unit (see Fig. [1\)](#page-4-0) [\[106](#page-32-15)].

Cuff electrodes, used in implantable NMES systems, can either have a spiral or tube shape, and the geometric dimensions (e.g., internal diameter, longitudinal length) of the electrode are made to fit the targeted nerve [\[49](#page-29-20), [110](#page-32-17)]. Cuff electrodes are made of polymer, and can be fabricated with various mono-, bi-, and tri-polar configurations [\[110](#page-32-17)].

Epimysial electrodes are disk-shaped electrodes which are surgically placed on the muscle near the motor point [\[110](#page-32-17)], and are well suited for activation of broad superficial muscles [\[129\]](#page-33-15).

Intramuscular electrodes are wire or needle electrodes which are inserted into the target motor point using a hypodermic needle. They allow high degree of stimulation selectivity and can recruit deeper muscles [\[106](#page-32-15)].

3.4.3 Percutaneous NMES

Similar to implantable NMES systems, percutaneous systems most often are current regulated. The advantages of percutaneous NMES systems are that they can recruit deeper muscles, and have high muscle selectivity and repeatable responses over time. The intramuscular electrodes are inserted by a hypodermic needle through the skin [\[106,](#page-32-15) [110\]](#page-32-17) and the leads of the electrodes exit the skin and are connected to an external stimulator unit. A large surface electrode is used as anode (see Fig. [1\)](#page-4-0). Percutaneous stimulation is less likely to be painful since the stimulation pulses bypass the afferent receptors in the skin [\[106](#page-32-15)]. As with surface systems, percutaneous NMES systems are considered to be temporal systems, because there is a risk of breakage or displacement of the electrodes over time, and risk of infection at the point of electrode leads entry. As a consequence, use of percutaneous electrodes is limited to less than 3 months when it needs to be replaced [\[129](#page-33-15)].

3.4.4 Cyclic NMES

Cyclic NMES consists of electrical stimulation of the paretic or paralyzed muscles, whereby muscle contractions are elicited. Cyclic NMES is applied while the subject is passive, but it has been shown that the effect of this type of stimulation can be enhanced by instructing the subject to actively accompany the movement via thought and, if the subject has any voluntary control of the limb, by actively tensing of the muscles [\[126](#page-33-16)].

3.4.5 EMG/Biofeedback-Mediated NMES

EMG or biofeedback-mediated NMES requires larger degree of cognitive investment, since the subject is actively taking part in the rehabilitative exercises. In EMGmediated NMES, stimulation is initiated when volitionally generated EMG activity exceeds a predefined threshold, whereas for biofeedback-mediated NMES, joint translation resulting from voluntary muscle contractions can be used as a threshold for initiation of NMES stimulation [\[70\]](#page-30-15). Specifically, NMES stimulation is triggered after the subject has performed the initial part of the predefined movement and NMES helps complete the remaining part of the movement [\[129\]](#page-33-15). Feedbackmediated NMES is believed to result in larger rehabilitative gains than cyclic NMES, due to the cognitive involvement in the exercises which can facilitate neural plasticity. Firm scientific evidence of greater rehabilitative gains through feedback-mediated NMES though still is lacking and has the additional prerequisite of some degree of voluntary control of the affected limb [\[23,](#page-28-20) [70](#page-30-15), [129](#page-33-15)].

3.4.6 Neuroprostheses

Neuroprostheses are developed with focus on augmenting the independence of the user by safely and efficiently facilitating the completion of functional tasks [\[23,](#page-28-20) [110\]](#page-32-17). Neuroprostheses are mainly for patients with severe paralysis where motor relearning strategies are thought to have limited potential [\[23\]](#page-28-20). Neuroprostheses can have different sources of control signals to trigger or adjust the stimulation patterns. Some examples of sources of control are

- Contralateral hand joysticks.
- Wrist movement.
- EMG activity of agonistic muscles.
- Switches located on various places on the body [\[110\]](#page-32-17).

Several neuroprostheses for grasping have been developed, and they are mostly designed as bracelets (e.g., the Handmaster [\[1](#page-27-7), [2](#page-27-8)]) where NMES is applied through surface, percutaneous, or implantable electrodes [\[110](#page-32-17)].

3.4.7 Rehabilitative Effect of Neuromuscular Electrical Stimulation

In general, the literature supports that the most effective approach when aiming at restoring motor functions is to begin NMES as soon as possible [\[14,](#page-28-21) [113](#page-32-14)], since the rehabilitative effect of NMES appears to be more pronounced and enduring for acute stroke survivors. Furthermore, there are indications that patients with milder impairments have a greater benefit from NMES than those with severe involvement [\[23,](#page-28-20) [129](#page-33-15)]. This may be related to the patients with milder impairments being able to take active part in the rehabilitation [\[23](#page-28-20)]. Based on the current knowledge about motor relearning and post-stroke recovery, [\[70\]](#page-30-15) stated that rehabilitative NMES training should include the following key elements: should be repetitive, intensive, attention demanding, task-oriented, and provide feedback. This implies that the NMES system should be highly flexible and adjustable in order to be adapted to the progress and actual needs of the patient. In this way, [\[113](#page-32-14)] suggests that the early use of NMES should be conducted with surface systems since these provide sufficient flexibility to change stimulation parameters and electrode position. In relations to surface electrodes, a novel electrode array with 64 channels has been developed and presented in [\[62](#page-30-16)]. The electrode array is embedded in a garment which can be applied to the arm. Real-time switching of the location and number of active electrodes is possible, hereby making the array very flexible and adjustable while avoiding the need to physically readjust electrode positions [\[61\]](#page-30-17).

The appropriate stimulation paradigm would be based on the subject's clinical condition. If the subject is severely involved, cyclic NMES is preferred in order to facilitate muscle strengthening, range of motion, moderation of spasticity, decreasing pain, and increasing motor control $[113]$ $[113]$. Afterward, functional training is introduced preferably using EMG/biofeedback-mediated NMES [\[113\]](#page-32-14), since there is indication that this type of stimulation might have a better effect than cyclic NMES [\[70\]](#page-30-15). In case voluntary movement of the upper extremity is present at initiation of rehabilitation, EMG/biofeedback-mediated NMES might be initiated at the beginning of rehabilitation.

Recently, [\[66\]](#page-30-18) has suggested contralateral controlled NMES denoted as contralateral controlled functional electrical stimulation (CCFES) as a novel approach to improve recovery of volitional hand function in patients with stroke. The source of control signals and triggering is a glove which is worn on the unaffected hand and detects the degree of hand opening. The degree of hand opening then translates to a stimulation pattern which elicits finger and thumb extension of the paretic hand. In this way, movements mimicking the unaffected hand are elicited in the paretic hand. The preliminary findings from subacute post-stroke patients suggest that CCFES produces larger improvements than cyclic NMES [\[66](#page-30-18)], and in this way CCFES might be a future alternative to cyclic NMES as the initial intervention.

In the chronic phase after stroke or TBI when the initial rapid improvements caused by spontaneous recovery and rehabilitation have taken place, it might be beneficial to use percutaneous or implantable NMES systems in order to diminish the risk of pain and skin irritation caused by surface stimulation [\[113](#page-32-14)].

Rehabilitation in the chronic phase could be conducted with the use of EMG/biofeedback-mediated NMES and/or via use of a neuroprosthesis. A neuroprosthesis is potentially very useful for the patient once in the chronic phase since he/she might not benefit further from the NMES rehabilitation. In such case, the neuroprosthesis can function as assistive devices to assist in activities of daily living (ADL) [\[113](#page-32-14)].

3.4.8 Conclusion

NMES can be used to improve post-stroke and TBI rehabilitation, by initially strengthening muscles, augmenting range of motion, moderating spasticity, decreasing pain, and increasing motor control. Furthermore, it is suggested that NMES provides intensive traffic of neural information toward the brain promoting neural plasticity and motor relearning and resulting in enduring improvement of motor function.

The optimal NMES system for a given patient depends on the severity of the injury and how much time has elapsed since the injury. In general, rehabilitation should be initiated as quickly as possible in which case surface NMES is preferred due to a its flexibility with adjustable stimulation parameters and electrode positions. In less compromised patients who have voluntary movement of the affected upper extremity, EMG/biofeedback-mediated NMES is initiated in early phase, whereas severely affected patients should use cyclic NMES rehabilitation. The 64-channel electrode array developed by Keller and the contralateral controlled NMES system suggested by Knutson could be very beneficial additions to NMES systems for use during the acute phase after TBI and stroke rehabilitation.

Percutaneous and implantable NMES systems can be used to reduce pain and skin irritation commonly observed when using surface stimulation systems. Although percutaneous and implantable systems should first be used after the initial rapid recovery of function has declined, they are not as flexible as surface NMES system and thus not allow the same adjustability to respond to changes in the patient condition. Similarly, neuroprostheses can be used in the chronic phase as an assistive device to perform ADL.

4 The "Wish List"

4.1 Game on!—delivering technology to the golden years.

The last couple of decades have been revolutionized by the power of personal computers, smart phones, game consoles, and other technologies that are now used by people from all walks of life on everyday basis. This new phenomenon has important implications in shaping the needs and expectations of the patients of today and tomorrow. With every passing year, increasing proportions of older adults and elderly are becoming technology oriented, connected to the virtual world and dependent on gadgets for communication, information, and recreation. Today, more than 90% of people over 65 years of age report the use of internet at least weekly [\[133](#page-33-17)]. This goes against the traditional image of elderly patients with nonexistent computer literacy and a tendency to drift into nostalgic trips to simpler lives.

A shift in perception toward the use of technology with the elderly has become crucial. The integration of technological applications into activities of daily lives of

older patients is soon becoming a necessary step in order to engage patients, leading to a more driven and effective course of recovery. A promising niche in this context is the use of video games in stroke rehabilitation.

Today, between 40 and 50% of the elderly population report weekly use of computer games [\[133](#page-33-17)]. This is only expected to rise with each passing year. Research on the use of computer games by the elderly has early roots [\[151\]](#page-34-19) yet the rise—and availability—of more active gaming platforms like the Nin-tendo Wii[®] [\[125\]](#page-33-18) and Microsoft Kinect[®] [\[73\]](#page-30-19) has heightened the interest in their use for neurorehabilitation.

The vision is that in the near future, such technology-based rehabilitation tools and games become common house-hold gadgets. The aim is to have a rehabilitative platform that is engaging and enjoyable, instigating higher number of hours in rehabilitative training and making the process of motor recovery more efficient and less burdensome. With increased affordability, more versatile applications, and broadening of target population in the marketing phase, these "exergaming" devices $[147]$ could ultimately find their way into the homes of the general elderly population, with more seamless transitioning between maintenance and rehabilitation of motor function and fitness.

4.2 Virtual Reality Technology

Application of virtual reality technology for motor and functional recovery in stroke and TBI patients seems promising. A more extended use of virtual reality systems coupled to haptic devices that increase user interaction with the virtual environment and objects could be important for functional recovery in terms of obtaining better real-world activity level outcomes. In the next future, patients with severe upper and lower limb paresis could also be treated using hybrid virtual reality systems coupled to brain computer interfaces (BCI), and exoskeleton or robotic devices, but at the present time, cost-effectiveness and a probably greater time of training remain as potential limitations to extent application of these systems in clinical settings. Finally, many virtual reality applications designed as rehabilitation tools are still expensive and compatibility between different hardware, software, drivers, and protocols is a problem that still remains unsolved. It would be desirable that gaming industry introduces changes in design of gaming consoles in terms to be more user-friendly for disability people, allowing them to play at different speeds or difficulty levels, developing as well on line available games for telerehabilitation and home use.

4.3 Technological Wishes from a Rehabilitation Clinician

Still at present, neurological rehabilitation is more an art than a science. Most of evaluation metrics are based on observational charts and therapies depend on the personal experience and education of the single physiotherapist. Technology today can provide sensors of many types capable of monitoring virtually all relevant characteristics of movement. Muscular activity, force, kinematics, balance, and activity of the cerebral cortex are all parameters that can be collected and processes while performing rehabilitation exercise. Through these sensors, patient participation, as well as brain and muscular changes associated with the exercise, can be monitored and used to measure the effects of the interventions and to guide the rehabilitation therapy. On the other hand, robotic device can provide support for any movement and function. Although already theoretically possible, a robotic rehabilitation based on multisensory human–machine interactions has been only seldom applied and only in laboratory conditions. On the other hand, also in this highly technical environment, results have been more of importance for the understanding of neurophysiological and recovery mechanisms than for clinical applications. The hope is that through simplification of the technical approaches and through development of technology-based evaluation and of treatment, protocols will became a part of the routine in neurological rehabilitation. Neuroengineering-based tools will then leave the research lab, becoming the everyday companion of neurological rehabilitation professionals.

5 Conclusions

Stroke and TBI are disabling diseases with high social costs and neurological rehabilitation is the best approach to reduce disabilities. Once considered only necessary in the early months after brain damage, evidences are summing up in indicating that neurological rehabilitation is a lifelong endeavor needed to reduce disability and to improve function even years after the lesion [\[5\]](#page-27-9). Within this framework, the need to provide cost-effective rehabilitation is becoming mandatory. Neuroengineering has the potential to provide effective intensive rehabilitation at a lower cost. In spite of these promises, more than a decade of research and clinical applications have provided limited impact on everyday treatments. Nevertheless, much work has been completed to demonstrate the value of robotic-mediated rehabilitation for upper and lower limb in patients after stroke and TBI. Advantages of using this technology include reduce staff utilization, and increase intensity of therapy and subject engagement with either equivalent or better results than traditional care in most cases. Other modalities such as electrical stimulation combined with robotic therapy appear to

offer further advantages but only small trials are available to support these findings. Comparative trials of different robots are spars and additional studies should be considered.

Collaborative development by engineers and clinicians of robots that are simpler in design, more directly linked to functional use, and with less cost will allow further deployment of the technology to a larger section of patient population that may benefit and eventually allow development of wearable robots that can easily be used at home, altogether allowing increased time use with resulting benefits for this population.

Another aspect of high expectation relates to the understanding of the biological substrate of recovery and most importantly the capacity to directly link rehabilitation exercises with brain changes. This is already feasible in laboratory condition. By recording different biological signals from muscle or brain, it is possible to follow changes in activation and connectivity patterns linking them with treatment and recovery [\[90,](#page-31-19) [108\]](#page-32-18). These findings may serve to guide the correct timing for the exercise intervention by the physiotherapist as well as by a robot [\[158\]](#page-35-2).

All these findings are promising and are helping to close the knowledge gap between rehabilitation interventions and induced brain changes. Controlling and quantifying the biological effects of a rehabilitation protocol will allow to base neurological rehabilitation on solid scientific ground.

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