

Review Article

Seven Capital Devices for the Future of Stroke Rehabilitation

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Stroke is the leading cause of long-term disability for adults in industrialized societies. Rehabilitation's efforts are tended to avoid long-term impairments, but, actually, the rehabilitative outcomes are still poor. Novel tools based on new technologies have been developed to improve the motor recovery. In this paper, we have taken into account seven promising technologies that can improve rehabilitation of patients with stroke in the early future: (1) robotic devices for lower and upper limb recovery, (2) brain computer interfaces, (3) noninvasive brain stimulators, (4) neuroprostheses, (5) wearable devices for quantitative human movement analysis, (6) virtual reality, and (7) tablet-pc used for neurorehabilitation.

1. Introduction

In the last decade, the manual conventional therapy for people affected by stroke has been often integrated with the use of technological devices specifically developed for increasing rehabilitative outcomes. Does the manual therapy really need this support? A study of 2008 showed that at dismissal from a hospital of rehabilitation, about half of patients with stroke are on wheelchair, whereas less than 15% are able to walk inside without aids, less than 10% are able to walk outside, and less than 5% are able in stair climbing [1]. Recovery of upper limb motor functions is even poorer, leading to suppose that upper limb recovery could be mainly intrinsic and slightly improved by therapy [2–4]. Furthermore, the need of more therapies performed in a more adequate and appropriate manner has been claimed [5]. In fact, the recovery has been shown to depend on the intensity of therapy, repetition of specified skilled movements directed towards the motor deficits and rewarded with performance-dependent feedback [6–8].

These are the main reasons for purposing the use of technological devices in order to increase intensity, repetitions, specificity, and feedback during rehabilitation. Many

reviews have already summarised the results of previous studies on the efficacy of these technologically supported treatments (for a recent one see Belda-Lois et al. [5]). In this paper, we provided our point of view on seven specific technological devices designed for supporting motor recovery after stroke. These technologies for rehabilitation of people affected by stroke are robots, brain computer interfaces, neuroprosthesis, noninvasive brain stimulators, wearable devices, virtual reality, and tablet-pc.

2. Robot

The English word robot was derived from the Czech word “robota”, meaning literally “serf labor” and figuratively “forced workers”; it is also used with the general meaning of “workers” in Russian and other Slavic languages [9]. The Robot Institute of America defined a robot as “a programmable, multi-functional manipulator designed to move material, parts or specialized devices through variable programmed motions for the performance of a variety of tasks” [9]. Three Ds were defined for identifying the most common tasks a robot is usually designed to perform: dull,

dirty, and dangerous [10]. These three Ds match neurorehabilitation in regards of the need of repetitive movements suggested as fundamental for sensorimotor relearning [11]. This task can be seen as dull and dangerous, for example, when a therapist is asked to support patient's weight during gait rehabilitation. Most recent approaches suggested that robots may also provide movement controllability and measurement reliability, two aspects that make robots ideal instruments to help medical doctors and therapists to address the challenges facing neurorehabilitation [12].

Robots for neurorehabilitation can be mainly divided in terms of the body functioning that they aim to rehabilitate or in terms of their design. In fact, the first division is primarily between robots for upper limbs and those for lower limbs, with a subdivision between bilateral and unilateral robots (especially for those aiming to upper limb recovery, whereas those for lower limb rehabilitation are usually bilateral because they focused on gait recovery). The second classification usually divided robots in exoskeletons and controller of endpoint trajectories. Typical examples of these robots are Lokomat as exoskeleton for lower limbs, Gait Trainer (or Gang Trainer) as end effector for lower limbs, ARMin III as exoskeleton for upper limb, and MIT-Manus as an end effector for upper limb, but many other commercial robots or specific prototypes exist.

Electromechanical devices, such as treadmill with body weight support or the above-cited Gait Trainer, are often referred to robot family in an improper manner. Furthermore, outcomes of rehabilitation supported with these devices are often analysed together with those of trainings conducted with robots. The adaptability allowed by the presence of "intelligent" sensors is the key point differentiating robots from electromechanical devices. However, in neurorehabilitation, this differentiation sounds picky, although the absence of an intelligent control may expose patients to some potential risks. It usually implies the continuous presence of a therapist during electromechanical trainings and limits the use of electromechanical devices. For example, for the Gait Trainer, the exclusion criteria include the presence of muscular contracture or presence of not healed bone fractures because of the absence of torque sensors able to assess the eventual joint resistance torque.

Are robots and electromechanical devices effective in stroke rehabilitation? An updated Cochrane review found that robotic-assisted gait training (Lokomat and Gait Trainer) in combination with conventional physiotherapy increased the odds of becoming independent in walking [13]. However, gait speed and walking capacity was not found significantly different between patients who received robotic versus conventional therapy alone. This Cochrane review included nonambulatory and ambulatory patients, those with subacute and those with chronic stroke, treated with Lokomat or Gait Trainer. More recently, Morone and colleagues suggested changing the question "Is robotic-assisted training effective?" into "Who may benefit from robotic training?" [14, 15]. The authors found that severely affected patients with subacute stroke are the ideal candidates for an increase of outcomes when conventional rehabilitation is accompanied by robotic training. Conversely, conventional

therapy alone and that supported by robotic training were found equivalent in less affected patients [14]. These differences were maintained also 2 years after dismissal [15].

However, we can paraphrase Clark when in 1997 he wrote: "Where are the artificial minds promised by 1950s science fiction and 1960s science journalism?" [16]: "Where are the robots promised by scientific literature able to restore motor functions after stroke?"

The high purchase cost, the confusion among robots and electromechanical devices, the still uncertainty about their efficacy, the absence of clear guidelines to achieve effective results, the need of trained therapists, and the scepticism by some members of the rehabilitation team are certainly contributing to limit the use of robots during inpatient care [14]. In fact, in this scenario, it still lacks a unified approach for integrating these devices into rehabilitation programs. Furthermore, the effectiveness of these devices therefore still depends heavily on the ability of the rehabilitation team to most effectively tailor the selection of motor parameters to each patient's needs and abilities [17].

Another issue recently raised up is the need to modify the "bottom-up" approach typical of many robots (and even more of electromechanical devices), based on the idea that moving passively the limbs of patients may enhance the recovery of limb functions. It is recently suggested to redesign or use robots on the basis of a top-down approach, for increasing the active participation of the patients during robotic training [5]. The other possible modification that may enhance the efficacy of robotic neurorehabilitation in the next years is the use of ambulatory exoskeletons. At the moment the most common robots are nonambulatory, even when based on motorized exoskeletons (as the Lokomat). Ambulatory exoskeletons may allow for more physiological trainings and allow patients to move in an environment similar to that they will find at their home returning.

3. Brain Computer Interfaces

Brain computer interfaces (BCIs) are a family of various devices aiming to translate measurements of brain activity into commands or messages. So, a BCI is a system directly measuring brain activity associated with the user's intent and translates by means of a computer the recorded brain activity into corresponding control signals for applications [18]. BCI could be used to provide the patient with real-time feedback, to allow for passive monitoring (assessing motor intention without providing real-time feedback), and to allow for active control of a computer and hence of many devices, by means of a computer. When the information is derived from the peripheral nervous system measuring neural activity, these devices are classified as Brain-Neural Computer Interface.

Limiting to brain activity, it is usually measured using electroencephalography (EEG) [18]. More recently, new noninvasive brain imaging techniques, such as functional near infrared spectroscopy (fNIRS), have been suggested to be used instead of EEG as a brain monitoring technique [19]. While EEG measures electrical activity, fNIRS measures

blood oxygenation levels in the brain, providing a different and complementary source of information about brain function [20].

In the last years, BCI devices have been designed as aids for patients, more than for the motor recovery. More recently, BCI systems are becoming more common in the context of neurorehabilitation. They can be used in combination with robotics-based therapy for enhancing the active participation of patients during their rehabilitation [5, 21–23].

In fact, a major problem with existing stroke robotic therapy is the low compliance and the typical bottom-up approach [5, 24]. On the contrary, active participation has been identified as an enhancer of rehabilitation outcomes, especially in the early phase of rehabilitative training [25]. People may find certain aspects of robotic therapy frustrating, exhausting, or boring or can be simply afraid or alienated by electromechanical devices. The use of BCI may hence contribute to increase directly rehabilitation effectiveness by means of the provided real-time feedback.

A new field in which BCI is used in neurorehabilitation is for supporting training based on motor imagery [26]. Recently, BCI has been combined with rehabilitative approaches based on motor imagery for stimulating the brain plasticity [27]. A study performed on 54 patients with stroke reported an accuracy of BCI systems on patients with stroke similarly to that of healthy subjects, despite the brain injury [27]. But the main problem is that effects of BCI devices are usually tested on few subjects, and further researches including large cohorts of patients are needed for proving its effectiveness. Moreover, our experience suggests that a good compliance of patient is required for using brain computer interface for the need of EEG and of a period of familiarization that could be sometimes too long, exhausting, and disaffecting for people with stroke.

4. Noninvasive Brain Stimulators

The activity of brain can be also enhanced or inhibited, not only monitored or used to control external devices. The use of electrical currents or magnetic fields can modify the functional activities of the brain, and it is known by almost two centuries, but in the last decade this approach, known as noninvasive brain stimulation (NIBS), has rapidly gathered a worldwide interest in therapeutic field.

The NIBS consists principally of two techniques: repetitive Transcranial Magnetic Stimulation (rTMS) and transcranial Direct Current Stimulation (tDCS). Globally concerning, NIBS aims to modulate motor cortical function, enhancing the brain plasticity by means of activation of long-term potentiation and long-term depression phenomena, even if definitive evidences in this sense are still lacking [28, 29]. However, both these techniques have showed potential benefits as adjunctive treatment of several psychiatric and neurological disorders, and now researchers are attempting new applications in other patient categories.

Because tDCS varies the spontaneous neuronal firing rates without producing action potentials, acting below the threshold of activation of potentials, it should be considered

as a neuromodulatory intervention rather than a stimulation [30]. This activity is dependent on the polarization of the electrodes. It is assumed that tDCS modulates the brain favoring the depolarization (and hence the activation by anodic stimulation) or hyperpolarizing (and hence the inhibition by cathodic stimulation) the resting membrane potential of neurons [31, 32].

If the application of electrical currents has been initially used to investigate the cortical functions, adding information about neuroanatomy and behavior, afterwards tDCS has gathered a role in the therapy. Used to treat depressive disorders in the 1960s and 1970s, the electrical stimulations are now proposed as treatment of many different diseases. Not only stroke, Alzheimer's and Parkinson's diseases and brain and spinal cord injuries, but also fibromyalgia, low back pain, and other chronic pain syndromes have been studied as possible target of treatment [33].

In stroke rehabilitation, the use of tDCS has regarded the recovery of motor and cognitive impairments. The preferential cortical target has been the primary motor cortex, the brain area in motor execution, memory formation, and consolidation of motor skills [34], enhancing the conviction that tDCS favors the brain plasticity through the strengthening of the synaptic connections, a mechanism similar to long-term potentiation [35]. Many studies have reported improvements in performance of complex ADL-like tasks with the paretic hand in patients with stroke after anodal tDCS [36]. It has been hypothesized that this mechanism involves an extensive network of brain regions. In fact, tDCS might be involved not only in the stimulation of the intended area, but also for adjacent cortical areas, due to the use of large electrode size [37].

There are no published studies reported seizure as adverse effect; on the contrary, pilot studies have attempted to use cathodal tDCS for the treatment of focal epileptic syndromes [38]. Only minor side effects, seldom occurring and not always perceived, may be mild headache, itching and erythema at the electrode site, fatigue, and nausea [32]. Therefore, this technique appears a safe treatment.

The treatment with tDCS can assist both the pharmacological and the rehabilitative treatments, preceding or following them. Sessions can last up to 30 min [39], close to the duration of a session of rehabilitative treatment, and can be administered in synchrony with motor rehabilitative protocols, strengthening the effects of motor rehabilitation [40].

However, some other studies reported that neither anodal nor cathodal transcranial direct current stimulation enhanced the effect of rehabilitation [41, 42]. Hence, although tDCS may appear one of the most potential technologies for the future improvement of therapies in the clinical setting, at the same time, many questions have still to be made to clarify certain aspects still not clear about its efficacy in enhancing motor rehabilitation, especially for patients with stroke in subacute phase. In fact, even if tDCS is widely used, research in this field is relatively young and in its early stages, with reduced sample sizes. The abiding efficacy of tDCS in the followup, the best patients' selection, and how the variation of parameters and a more accurate

focality (intensity, duration, and polarization) can influence a stable motor improvement need to be deeply studied. Nevertheless, the perspectives that widespread use of tDCS opens are very relevant, as the possibility of a continuous home-based therapy. In the clinical practice, advantages of tDCS in respect of rTMS or other technological devices are related especially to the fact that the stimulator is cheap, reduced in size, portable, simple to use, and painless.

Similar to the tDCS, rTMS has showed to be effective in the treatment of many neurological and psychiatric conditions, despite a major variability. Differently by the direct current, rTMS operates on neurons via brief pulses of high-intensity magnetic field by an inductive coil. Use of repetitive stimulations entails a persistent modulation of neural excitability. The induced current is able to depolarize neurons both directly at the axon hillock or indirectly via depolarization of interneurons. Classic use of rTMS implies trains of pulses at specific frequencies. Stimulator consists of a large electrical capacitance that is attached to a coil of several turns of copper wire. This implies a modulation of cortical excitability as well as of other physiological, metabolic, and behavioral measures [43]. Although rTMS has been studied much more than tDCS, also for rTMS it is not well clear how it delivers the immediate clinical benefit, even if the association of neuromodulators and growth factors release is supposed to be over the above-cited mechanism of neuroplasticity [29]. Differently from tDCS, rTMS entails a wider intersubject and intersession variability [44], conditioning the effect because of the broad variety of experimental procedures and parameters utilized. In fact, several different protocols have been proved, but no definitive evidence has been established.

In neurorehabilitation, clinicians have tested rTMS, in order to drive the adaptive plasticity and to facilitate the process of recovery. Several small investigations have shown functional improvements. Most of the results have been obtained by inhibitory approaches, both for motor (performances) and cognitive (speech) impairments [45, 46].

In conclusion, despite some encouraging studies, the use of NIBS is promising but needs to be delved deeper. Protocols should be standardized worldwide and multicenter-controlled clinical trials should be set up to provide definitive evidence in neurorehabilitation. In addition, studies about the economic benefits from a continuous use of these techniques should be taken into consideration (i.e., cost-effective home therapy versus inpatient rehabilitation). At the same time, many therapeutic opportunities based on NIBS are open for researchers worldwide.

5. Neuroprosthesis

Neuroprosthesis (or neural prosthesis) is a general term referring to devices that cannot only receive output from the nervous system (such as BCI), but can also provide input, with the possibility to interact with the peripheral and central nervous systems [18]. Furthermore, neuroprosthesis is a device that substitutes, completely or in part, a motoneural

function at peripheral level. Cochlear and retinal implants are examples of neuroprosthesis [18].

In neurorehabilitation field, electronic devices may directly stimulate muscles or nerves that should in turn stimulate muscles (this second possibility needs the integrity of peripheral nerves).

Some neuroprostheses are based on the principle of functional electrical stimulation (FES), and in the recent years it has been used in stroke rehabilitation. For example, during locomotion, FES can be timed with the swing phase of the gait cycle to stimulate the ankle dorsiflexor muscles, usually weaker in patients with stroke. Recently it has been shown that the use of FES for 3 months increases the maximum voluntary contraction and the motor-evoked potentials [47].

FES has been used as surface or as implanted stimulation. A possible example of gait FES is based on a tilt sensor which measures the orientation of the shank, controlling when to turn the stimulator of tibialis anterior on and off [48]. Another example is based on the use of a pressure attached below the foot, allowing to know if the heel is in contact with the ground or not for controlling ankle joint movements [49].

Regarding FES efficacy recent findings showed that FES may improve active movements and strengthen muscles, improving gait velocity and endurance, preventing falls [50], reducing spasticity, and providing better functional recovery [51–53]. So, in the field of gait rehabilitation, neuroprosthesis may provide more potential benefits than common orthoses, as reported by rehabilitative outcomes [54] and patients' comments [48, 55].

6. Virtual Reality

Similar to the use of the term robot, also the expression virtual reality is sometimes used improperly in neurorehabilitation. In many studies a computer-based technology providing visual stimuli on a monitor is generally called virtual reality. But with the expression virtual reality (VR) we should refer to a high-end user-computer interface involving real-time stimulation and interactions of an embedded subject through multiple sensorial channels (visual and auditory, sometimes haptic, smell and taste if possible), based on a synthetic environment in which the subject feels his presence [56]. Similar to the three Ds of robotic works, VR is based on three Is defining its features: immersion, interaction, and imagination [56]. So, a computer videogame should not be considered as VR because of the absence of immersion in a virtual environment. However, with the more wide use of tridimensional visual stimuli also in video games, this difference is going to be reduced in the early future.

Both VR and computer-based stimulation are supposed to have the potential to greatly increase the ways in which people are trained during rehabilitation. There are many advantages provided by VR at the basis of this idea: the synthetic environment is easily changeable, allowing for designing an optimal individualized therapy, VR can provide functional, rich stimuli and motivating context, increasing

the active participation of the subject in his rehabilitation (a fundamental aspect to increase the rehabilitative outcomes [25]), and then the data can be collected for monitoring and evaluating rehabilitation progress.

In the last few years there have been an increase in the application of virtual reality and computer-interface-based systems to the rehabilitation of a variety of deficits resulting from lesions of the nervous system [57, 58]. The main area is probably the rehabilitation of patients with stroke, in particular with respect to the function of the upper extremities.

Several virtual reality systems for upper limb rehabilitation have been developed and tested worldwide following different methods and therapeutic concepts including systems used to train reaching movements through imitation of a virtual instructor [59, 60]; systems based on haptic devices [61]; systems for training individual hand and finger properties such as range of motion and strength by means of intense practice of skilled movements [62, 63]; systems to train general upper limb movements by mental rehearsal and the imitation of movements of the nonparetic arm [64].

It has been shown that, after VR training, there is a cortical reorganization due to neuroplasticity in which cortical activation was reorganized from contralesional (before VR) to ipsilesional (after VR) activation; that is, there is a shift in cortical organization of the affected limb from the ipsilateral hemisphere to the contralateral hemisphere after the VR intervention. It is probably due to the fact that VR may have motivated and promoted practice-dependent reorganization resulting from the increased amount of use of the affected limb in relevant motor tasks [65].

A recent Cochrane review analysed 19 studies involving 565 patients with stroke, putting together the use of VR with video-gaming therapy for stroke rehabilitation [66]. Positive results were found in terms of recovery of arm function and increase in independence in activities of daily living, and few and mild adverse effects were sporadically reported, whereas no evidence was found for improvements in global functions, grip strength, or gait speed. However, this Cochrane review suggested caution in interpretation of results because studies on VR effects in rehabilitation generally enrolled a small sample of subjects, and interventions and outcome measures varied, limiting the comparisons among studies. Then, because the intervention approaches in the included studies were predominantly designed to improve motor function rather than cognitive function or activity performance, there was no evidence for cognitive improvement after VR training. Finally, the majority of participants in VR rehabilitation were young people with chronic stroke, relatively active (in many researches they should be able to move a joystick), then the positive effects were found soon after the end of the treatment, and it is not clear whether the effects are long-lasting.

Although further trials involving larger numbers of participants and longer-term followup are required, VR and video-gaming therapy could be further developed on the basis of the recent development and the progressive cost reduction of 3D televisions, combined with markerless system for movement analysis [67] or accelerometric devices

for controlling video games [68]. These technologies could bring at home of patients new rehabilitative tools in the early future.

7. Wearable Devices

The instrumented movement analysis is a systematic manner to investigate motor abilities of a subject, involving measurements, descriptions, and assessments of quantities characterizing human biomechanics and locomotor control [69, 70]. It is a fundamental tool for assessing pathological conditions and compensatory motor strategies and for evaluating the improvements during rehabilitation, in a more sensible and objective manner than ordinal scores of clinical scales [71].

Through instrumented movement analysis, the kinematic and kinetic parameters of human movements can be determined, and musculoskeletal functions can be quantitatively evaluated. As a result, instrumented movement analysis has been employed in sports, rehabilitation, and health diagnostics. It is sometimes called “gait analysis” because most of these studies are related to human locomotion.

Research on instrumented movement analysis has been conducted since the late 19th century, and its widespread application in biomedical engineering began with the availability of video camera systems [72–74]. A standard laboratory of gait analysis is formed by a multicamera motion capture system and force platforms with the capability of measuring ground-reaction forces [75]. However, this standard gait analysis requires specialized laboratories, expensive equipment, and lengthy setup and postprocessing times, with limitations in terms of the moving area and gait cycles.

In the last decade, an alternative gait analysis method was developed based on wearable sensors. Some of the potential benefits of using wearable device to assess movements in clinical settings could include the low cost compared with more commonly used gait analysis equipment, the small dimensions and light weight, and no limitation of the testing environment to a laboratory, enabling subjects to walk relatively unrestricted [76, 77].

Wearable devices for motion sensing can be accelerometers [76, 77], force sensors [78, 79], goniometers [80], inclinometers [81], gyrosensors, and strain gauges, and they can be worn or attached to various parts of the body [82].

Particular interest has been devoted to the use of accelerometers for assessing human locomotion [76]. In fact, the ability of a subject to maintain balance during walking can be properly assessed by measuring upper-body accelerations [83, 84]. A large and growing body of the literature has investigated the use of this technique in healthy subjects [85–88], patients with stroke [77, 89], children with cerebral palsy [90], people with low-back pain [91], and those with cognitive impairments [92].

With the development of motion-sensing technology, an increasing number of wearable sensors will be developed for gait analysis in the future, increasing the use of wearable sensors in the clinical field [82]. Even clothes formed by fibers

and yarns made in conducting and piezoresistive materials able to record vital signals have been developed as a really wearable device [93].

The development of wireless wearable sensors has also been facilitating the development of wearable ambulatory robotic exoskeletons. More of them are still in prototypal version, such as those developed in projects financed by the European Community as, for example, Tremor (extended title: An ambulatory BCI-driven tremor suppression system based on functional electrical stimulation) [94] and Better Projects (extended title: BNCI-driven robotic physical therapies in stroke rehabilitation of gait disorders) [5]. However, some commercial products have recently been delivered, such as EKSO (Ekso Bionics, Richmond, CA, USA) and ReWalk (Argo Medical Technologies Inc., Marlborough, MA, USA) exoskeletons. These devices are primarily developed as orthoses especially for subjects with spinal cord injury [95], but it is arising the idea to use ambulatory exoskeletons also during stroke rehabilitation [5, 96].

8. Tablet-PC

The last but not the least technology that merits a mention in this paper is a new technology that is changing our life, modifying the way we interact and communicate: the multi-touching tablets. This is evident through the widespread use of smartphones and tablet-pc. The ease of downloading and using applications (apps), many of them free, is changing our life style, allowing to do many things in new forms, from reading newspaper, playing, communicating with friends, getting weather updates, to finding the closest supermarket. It is hence clear that this technology can have potential benefits also in healthcare and rehabilitation fields [97]. Particularly tablet-pc, with its many apps, seems to have potentialities for enhancing therapy, offering speech to text options, handwriting enhancements, and options for motor skill development, and so forth. First of all, tablet may increase the possibilities of augmentative and alternative communication interventions [98]. Then, it could be helpful for assessing deficits of fine movements at hand level and hence for assessing rehabilitation outcomes [99]. Finally, specific rehabilitative programs for upper limb rehabilitation can be developed on this simple tool, with all the advantages above reported for the video-game-based therapy.

When returning home, people with stroke may use these tablets for improving their hand abilities. This opportunity is offered by the multitouching technology. Furthermore, tablets, similar to virtual reality and video-game-based therapies, may allow to collect data of patients' improvements. It is also possible to imagine that these data can be shared in real time via internet with therapists, medical doctors, and other members of rehabilitative staff. So, although at the moment the evidence that tablets can be effective for enhancing stroke rehabilitation is still lacking, and only few studies investigate this aspect, the potentiality of this tool and its wide diffusion suggest that tablet will enter soon in neurorehabilitation [98, 99].

9. Conclusions

At the lights of the above researches, the seven technologies reported in this paper seem to have potentialities to increase the effectiveness of rehabilitation in patients with stroke. However, according to Morone and colleagues [14, 15], the question about their efficacy on rehabilitation should be changed into which patients may benefit more from the use of these devices. Robotic therapy seems to be more effective when used in severely affected patients, whereas virtual reality video-game-based therapy is probably more effective in less affected patients. We expect similar target patients for Tablet-pc. Also other aspects, such as compliance and psychological features, should be taken into account for defining the best target population. The last potentiality of these new technologies is their possible combination. For example, brain stimulation was performed during robotic training in patients with stroke in subacute [41, 100] and chronic [101] phases. Accelerometric assessment was performed during sessions of electromechanical training to obtain online information about the patients' recovery and the goodness of parameter selection [17]. As reported above, the use of wireless wearable devices could be combined with robotic technologies for the development of ambulatory exoskeletons [93, 94]. Also brain computer interface could be combined with robotic training for a top-down approach [5].

References

- [1] S. Paolucci, M. Bragoni, P. Coiro et al., "Quantification of the probability of reaching mobility independence at discharge from a rehabilitation hospital in nonwalking early ischemic stroke patients: a multivariate study," *Cerebrovascular Diseases*, vol. 26, no. 1, pp. 16–22, 2008.
- [2] A. Heller, D. T. Wade, and V. A. Wood, "Arm function after stroke: measurement and recovery over the first three months," *Journal of Neurology Neurosurgery and Psychiatry*, vol. 50, no. 6, pp. 714–719, 1987.
- [3] D. T. Wade, R. Langton Hewer, and V. A. Wood, "The hemiplegic arm after stroke: measurement and recovery," *Journal of Neurology Neurosurgery and Psychiatry*, vol. 46, no. 6, pp. 521–524, 1983.
- [4] J. Carr and R. Shepherd, *Neurological Rehabilitation: Optimizing Motor Performance*, Butterworth-Heinemann, 1998.
- [5] J. M. Belda-Lois, S. Mena-Del Horno, I. Bermejo-Bosch, J. C. Moreno, J. L. Pons, D. Farina et al., "Rehabilitation of gait after stroke: a review towards a top-down approach," *Journal of NeuroEngineering and Rehabilitation*, vol. 13, pp. 8–66, 2011.
- [6] A. Karni, G. Meyer, C. Rey-Hipolito et al., "The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 95, no. 3, pp. 861–868, 1998.
- [7] J. W. Krakauer, "Motor learning: its relevance to stroke recovery and neurorehabilitation," *Current Opinion in Neurology*, vol. 19, no. 1, pp. 84–90, 2006.
- [8] M. C. Cirstea and M. F. Levin, "Improvement of arm movement patterns and endpoint control depends on type

- of feedback during practice in stroke survivors,” *Neurorehabilitation and Neural Repair*, vol. 21, no. 5, pp. 398–411, 2007.
- [9] M. Xie, *Fundamental of Robotics: Linking Perception to Action*, World Scientific, Singapore, 2003.
 - [10] P. Lin, K. Abenay, and G. A. Bekey, *Robot Ethics: The Ethical and Social Implications of Robotics*, The MIT Press, Cambridge, Mass, USA, 2012.
 - [11] P. Langhorne, J. Bernhardt, and G. Kwakkel, “Stroke rehabilitation,” *The Lancet*, vol. 377, no. 9778, pp. 1693–1702, 2011.
 - [12] V. S. Huang and J. W. Krakauer, “Robotic neurorehabilitation: a computational motor learning perspective,” *Journal of NeuroEngineering and Rehabilitation*, vol. 6, no. 1, article 5, 2009.
 - [13] J. Mehrholz, C. Werner, J. Kugler, and M. Pohl, “Electromechanical-assisted training for walking after stroke,” *Cochrane Database of Systematic Reviews*, no. 4, Article ID CD006185, 2007.
 - [14] G. Morone, M. Bragoni, M. Iosa et al., “Who may benefit from robotic-assisted gait training? A randomized clinical trial in patients with subacute stroke,” *Neurorehabilitation and Neural Repair*, vol. 25, pp. 636–644, 2011.
 - [15] G. Morone, M. Iosa, M. Bragoni et al., “Who may have durable benefit from robotic gait training?: a 2-year follow-up randomized controlled trial in patients with subacute stroke,” *Stroke*, vol. 43, no. 4, pp. 1140–1142, 2012.
 - [16] A. Clark, *Being There: Putting Brain, Body, and World Together Again*, MIT Press, Cambridge, Mass, USA, 1998.
 - [17] M. Iosa, G. Morone, M. Bragoni et al., “Driving electromechanically assisted gait trainer for people with stroke,” *Journal of Rehabilitation Research and Development*, vol. 48, no. 2, pp. 135–146, 2011.
 - [18] B. Graimann, G. Pfurtscheller, and B. Allison, *Brain-Computer Interfaces: Revolutionizing Human-Computer Interaction*, Springer, Dordrecht, The Netherlands, 2010.
 - [19] S. M. Coyle, T. E. Ward, and C. M. Markham, “Brain-computer interface using a simplified functional near-infrared spectroscopy system,” *Journal of Neural Engineering*, vol. 4, no. 3, pp. 219–226, 2007.
 - [20] E. Buch, C. Weber, L. G. Cohen et al., “Think to move: a neuromagnetic brain-computer interface (BCI) system for chronic stroke,” *Stroke*, vol. 39, no. 3, pp. 910–917, 2008.
 - [21] Y. Fuchino, M. Nagao, T. Katura et al., “High cognitive function of an ALS patient in the totally locked-in state,” *Neuroscience Letters*, vol. 435, no. 2, pp. 85–89, 2008.
 - [22] G. Pfurtscheller, G. R. Müller-Putz, R. Scherer, and C. Neuper, “Rehabilitation with brain-computer interface systems,” *Computer*, vol. 41, no. 10, pp. 58–65, 2008.
 - [23] C. Enzinger, S. Ropele, F. Fazekas et al., “Brain motor system function in a patient with complete spinal cord injury following extensive brain-computer interface training,” *Experimental Brain Research*, vol. 190, no. 2, pp. 215–223, 2008.
 - [24] M. J. Matarić, J. Eriksson, D. J. Feil-Seifer, and C. J. Winstein, “Socially assistive robotics for post-stroke rehabilitation,” *Journal of NeuroEngineering and Rehabilitation*, vol. 4, article 5, 2007.
 - [25] S. Paolucci, A. Di Vita, R. Massicci et al., “Impact of participation on rehabilitation results: a multivariate study,” *European Journal of Physical and Rehabilitation Medicine*, vol. 48, no. 3, pp. 455–466, 2012.
 - [26] V. Kaiser, I. Daly, F. Pichiorri, D. Mattia, G. R. Müller-Putz, and C. Neuper, “Relationship between electrical brain responses to motor imagery and motor impairment in stroke,” *Stroke*, vol. 43, no. 10, pp. 2735–2740, 2012.
 - [27] K. K. Ang, C. Guan, K. S. Chua et al., “A large clinical study on the ability of stroke patients to use an EEG-based motor imagery brain-computer interface,” *Clinical EEG & Neuroscience*, vol. 42, no. 4, pp. 253–258, 2011.
 - [28] M. A. Nitsche and W. Paulus, “Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation,” *Journal of Physiology*, vol. 527, no. 3, pp. 633–639, 2000.
 - [29] E. M. Wassermann and S. H. Lisanby, “Therapeutic application of repetitive transcranial magnetic stimulation: a review,” *Clinical Neurophysiology*, vol. 112, no. 8, pp. 1367–1377, 2001.
 - [30] D. P. Purpura and J. G. Mcmurtry, “Intracellular activities and evoked potential changes during,” *Journal of Neurophysiology*, vol. 28, pp. 166–185, 1965.
 - [31] T. Wagner, F. Fregni, S. Fecteau, A. Grodzinsky, M. Zahn, and A. Pascual-Leone, “Transcranial direct current stimulation: a computer-based human model study,” *NeuroImage*, vol. 35, no. 3, pp. 1113–1124, 2007.
 - [32] A. P. Arul-Anandam, C. Loo, and P. Sachdev, “Transcranial direct current stimulation—what is the evidence for its efficacy and safety?” *F1000 Medicine Reports*, vol. 1, article 58, 2009.
 - [33] M. A. Nitsche and W. Paulus, “Transcranial direct current stimulation—update 2011,” *Restorative Neurology and Neuroscience*, vol. 29, no. 6, pp. 463–492, 2011.
 - [34] J. Reis, H. M. Schambra, L. G. Cohen et al., “Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation,” *Proceedings of the National Academy of Sciences of the United States of America*, vol. 106, no. 5, pp. 1590–1595, 2009.
 - [35] M. A. Nitsche, A. Schauenburg, N. Lang et al., “Facilitation of implicit motor learning by weak transcranial direct current stimulation of the primary motor cortex in the human,” *Journal of Cognitive Neuroscience*, vol. 15, no. 4, pp. 619–626, 2003.
 - [36] F. C. Hummel and L. G. Cohen, “Non-invasive brain stimulation: a new strategy to improve neurorehabilitation after stroke?” *The Lancet Neurology*, vol. 5, no. 8, pp. 708–712, 2006.
 - [37] M. A. Nitsche, L. G. Cohen, E. M. Wassermann et al., “Transcranial direct current stimulation: state of the art 2008,” *Brain Stimulation*, vol. 1, no. 3, pp. 206–223, 2008.
 - [38] S. W. Yook, S. H. Park, J. H. Seo, S. J. Kim, and M. H. Ko, “Suppression of seizure by cathodal transcranial direct current stimulation in an epileptic patient—a case report,” *Annals of Rehabilitation Medicine*, vol. 35, no. 4, pp. 579–582, 2011.
 - [39] M. B. Iyer, U. Mattu, J. Grafman, M. Lomarev, S. Sato, and E. M. Wassermann, “Safety and cognitive effect of frontal DC brain polarization in healthy individuals,” *Neurology*, vol. 64, no. 5, pp. 872–875, 2005.
 - [40] F. Hummel and L. G. Cohen, “Improvement of motor function with noninvasive cortical stimulation in a patient with chronic stroke,” *Neurorehabilitation and Neural Repair*, vol. 19, no. 1, pp. 14–19, 2005.
 - [41] S. Hesse, A. Waldner, J. Mehrholz, C. Tomelleri, M. Pohl, and C. Werner, “Combined transcranial direct current stimulation and robot-assisted arm training in subacute stroke patients: an exploratory, randomized multicenter trial,” *Neurorehabilitation and Neural Repair*, vol. 25, no. 9, pp. 838–846, 2011.
 - [42] C. Rossi, F. Sallustio, S. Di Legge, P. Stanzione, and G. Koch, “Transcranial direct current stimulation of the affected

- hemisphere does not accelerate recovery of acute stroke patients," *European Journal of Neurology*. In press.
- [43] A. Pascual-Leone, J. Valls-Sole, E. M. Wassermann, and M. Hallett, "Responses to rapid-rate transcranial magnetic stimulation of the human motor cortex," *Brain*, vol. 117, no. 4, pp. 847–858, 1994.
 - [44] A. Hiscock, S. Miller, J. Rothwell, R. C. Tallis, and V. M. Pomeroy, "Informing dose-finding studies of repetitive transcranial magnetic stimulation to enhance motor function: a qualitative systematic review," *Neurorehabilitation and Neural Repair*, vol. 22, no. 3, pp. 228–249, 2008.
 - [45] M. A. Naeser, P. I. Martin, E. Treglia et al., "Research with rTMS in the treatment of aphasia," *Restorative Neurology and Neuroscience*, vol. 28, no. 4, pp. 511–529, 2010.
 - [46] C. G. Mansur, F. Fregni, P. S. Boggio et al., "A sham stimulation-controlled trial of rTMS of the unaffected hemisphere in stroke patients," *Neurology*, vol. 64, no. 10, pp. 1802–1804, 2005.
 - [47] D. G. Everaert, A. K. Thompson, Su Ling Chong, and R. B. Stein, "Does functional electrical stimulation for foot drop strengthen corticospinal connections?" *Neurorehabilitation and Neural Repair*, vol. 24, no. 2, pp. 168–177, 2010.
 - [48] D. J. Weber, R. B. Stein, K. M. Chan et al., "BIONic WalkAide for correcting foot drop," in *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, vol. 6, pp. 4189–4192, 2004.
 - [49] J. M. Hausdorff and H. Ring, "The effect of the L300 neuroprosthesis on gait stability and symmetry," *Journal of Neurologic Physical Therapy*, vol. 30, no. 4, article 198, 2006.
 - [50] R. B. Stein, S. Chong, D. G. Everaert et al., "A multicenter trial of a footdrop stimulator controlled by a tilt sensor," *Neurorehabilitation and Neural Repair*, vol. 20, no. 3, pp. 371–379, 2006.
 - [51] S. K. Sabut, C. Sikdar, R. Kumar, and M. Mahadevappa, "Improvement of gait and muscle strength with functional electrical stimulation in sub-acute & chronic stroke patients," in *Proceedings of the IEEE Engineering in Medicine and Biology Society*, vol. 2011, pp. 2085–2088, 2011.
 - [52] S. K. Sabut, C. Sikdar, R. Kumar, and M. Mahadevappa, "Functional electrical stimulation of dorsiflexor muscle: effects on dorsiflexor strength, plantarflexor spasticity, and motor recovery in stroke patients," *NeuroRehabilitation*, vol. 29, no. 4, pp. 393–400, 2011.
 - [53] G. Morone, A. Fusco, P. Di Capua et al., "Walking training with foot drop stimulator controlled by a Tilt Sensor to improve walking outcomes: a randomized controlled pilot study in patients with stroke in subacute phase," *Stroke Research and Treatment*. In press.
 - [54] R. van Swigchem, H. J. van Duijnhoven, J. den Boer, A. C. Geurts, and V. Weerdesteyn, "Effect of peroneal electrical stimulation versus an ankle-foot orthosis on obstacle avoidance ability in people with stroke-related foot drop," *Physical Therapy*, vol. 92, no. 3, pp. 398–406, 2012.
 - [55] C. Bulley, J. Shiels, K. Wilkie, and L. Salisbury, "User experiences, preferences and choices relating to functional electrical stimulation and ankle foot orthoses for foot-drop after stroke," *Physiotherapy*, vol. 97, no. 3, pp. 226–233, 2011.
 - [56] G. C. Burdea and P. Coiffet, *Virtual Reality Technology*, John Wiley & Sons, Hoboken, NJ, USA, 2nd edition, 2003.
 - [57] M. K. Holden, "Virtual environments for motor rehabilitation: review," *Cyberpsychology and Behavior*, vol. 8, no. 3, pp. 187–211, 2005.
 - [58] F. D. Rose, B. M. Brooks, and A. A. Rizzo, "Virtual reality in brain damage rehabilitation: review," *Cyberpsychology and Behavior*, vol. 8, no. 3, pp. 241–262, 2005.
 - [59] M. D. Holden and T. Dyar, "Virtual environment training: a new tool for neurorehabilitation," *Neurology Report*, vol. 26, pp. 62–71, 2002.
 - [60] L. Piron, T. Paolo, F. Piccione, V. Laia, E. Trivello, and M. Dam, "Virtual environment training therapy for arm motor rehabilitation," *Presence*, vol. 14, pp. 732–740, 2005.
 - [61] J. Broeren, M. Rydmark, A. Björkdahl, and K. S. Sunnerhagen, "Assessment and training in a 3-dimensional virtual environment with haptics: a report on 5 cases of motor rehabilitation in the chronic stage after stroke," *Neurorehabilitation and Neural Repair*, vol. 21, no. 2, pp. 180–189, 2007.
 - [62] A. S. Merians, H. Poizner, R. Boian, G. Burdea, and S. Adamovich, "Sensorimotor training in a virtual reality environment: does it improve functional recovery poststroke?" *Neurorehabilitation and Neural Repair*, vol. 20, no. 2, pp. 252–267, 2006.
 - [63] D. Jack, R. Boian, A. S. Merians et al., "Virtual reality-enhanced stroke rehabilitation," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 9, no. 3, pp. 308–318, 2001.
 - [64] A. Gaggioli, F. Morganti, R. Walker et al., "Training with computer-supported motor imagery in post-stroke rehabilitation," *Cyberpsychology and Behavior*, vol. 7, no. 3, pp. 327–332, 2004.
 - [65] H. J. Sung, S. H. You, M. Hallett et al., "Cortical reorganization and associated functional motor recovery after virtual reality in patients with chronic stroke: an experimenter-blind preliminary study," *Archives of Physical Medicine and Rehabilitation*, vol. 86, no. 11, pp. 2218–2223, 2005.
 - [66] K. E. Laver, S. George, S. Thomas, J. E. Deutsch, and M. Crotty, "Virtual reality for stroke rehabilitation," *Cochrane Database of Systematic Reviews*, vol. 7, no. 9, Article ID CD008349, 2011.
 - [67] B. Lange, C. Y. Chang, E. Suma, B. Newman, A. S. Rizzo, and M. Bolas, "Development and evaluation of low cost game-based balance rehabilitation tool using the Microsoft Kinect sensor," in *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, vol. 2011, pp. 1831–1834, 2011.
 - [68] G. Saposnik, R. Teasell, M. Mamdani et al., "Effectiveness of virtual reality using wii gaming technology in stroke rehabilitation: a pilot randomized clinical trial and proof of principle," *Stroke*, vol. 41, no. 7, pp. 1477–1484, 2010.
 - [69] J. Perry, *Gait Analysis: Normal and Pathological Function*, Slack Incorporated, 1992.
 - [70] S. Ghoussayni, C. Stevens, S. Durham, and D. Ewins, "Assessment and validation of a simple automated method for the detection of gait events and intervals," *Gait and Posture*, vol. 20, no. 3, pp. 266–272, 2004.
 - [71] M. Iosa, C. Mazzà, R. Frusciantè et al., "Mobility assessment of patients with facioscapulohumeral dystrophy," *Clinical Biomechanics*, vol. 22, no. 10, pp. 1074–1082, 2007.
 - [72] D. M. Gavrila and L. S. Davis, "3-D model-based tracking of humans in action: a multi-view approach," in *Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition*, pp. 73–80, San Francisco, Calif, USA, June 1996.
 - [73] A. Cappozzo, U. Della Croce, A. Leardini, and L. Chiari, "Human movement analysis using stereophotogrammetry.

- Part 1: theoretical background," *Gait and Posture*, vol. 21, no. 2, pp. 186–196, 2005.
- [74] L. Chiari, U. Della Croce, A. Leardini, and A. Cappozzo, "Human movement analysis using stereophotogrammetry. Part 2: instrumental errors," *Gait and Posture*, vol. 21, no. 2, pp. 197–211, 2005.
- [75] C. M. Kim and J. J. Eng, "Magnitude and pattern of 3D kinematic and kinetic gait profiles in persons with stroke: relationship to walking speed," *Gait and Posture*, vol. 20, no. 2, pp. 140–146, 2004.
- [76] J. J. Kavanagh and H. B. Menz, "Accelerometry: a technique for quantifying movement patterns during walking," *Gait and Posture*, vol. 28, no. 1, pp. 1–15, 2008.
- [77] M. Iosa, A. Fusco, G. Morone et al., "Assessment of upper-body dynamic stability during walking in patients with subacute stroke," *Journal of Rehabilitation Research and Development*, vol. 49, no. 3, pp. 439–450, 2012.
- [78] H. H. C. M. Savelberg and A. L. H. D. Lange, "Assessment of the horizontal, fore-aft component of the ground reaction force from insole pressure patterns by using artificial neural networks," *Clinical Biomechanics*, vol. 14, no. 8, pp. 585–592, 1999.
- [79] A. Forner Cordero, H. J. F. M. Koopman, and F. C. T. van der Helm, "Use of pressure insoles to calculate the complete ground reaction forces," *Journal of Biomechanics*, vol. 37, no. 9, pp. 1427–1432, 2004.
- [80] S. K. Ng and H. J. Chizeck, "Fuzzy model identification for classification of gait events in paraplegics," *IEEE Transactions on Fuzzy Systems*, vol. 5, no. 4, pp. 536–544, 1997.
- [81] H. J. Luinje and P. H. Veltink, "Inclination measurement of human movement using a 3-D accelerometer with autocalibration," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 12, no. 1, pp. 112–121, 2004.
- [82] W. Tao, T. Liu, R. Zheng, and H. Feng, "Gait analysis using wearable sensors," *Sensors*, vol. 12, no. 2, pp. 2255–2283, 2012.
- [83] D. A. Winter, "Human balance and posture control during standing and walking," *Gait and Posture*, vol. 3, no. 4, pp. 193–214, 1995.
- [84] J. J. Kavanagh, R. S. Barrett, and S. Morrison, "Upper body accelerations during walking in healthy young and elderly men," *Gait and Posture*, vol. 20, no. 3, pp. 291–298, 2004.
- [85] C. Mazzà, M. Iosa, F. Pecoraro, and A. Cappozzo, "Control of the upper body accelerations in young and elderly women during level walking," *Journal of NeuroEngineering and Rehabilitation*, vol. 5, article 30, 2008.
- [86] D. S. Marigold and A. E. Patla, "Age-related changes in gait for multi-surface terrain," *Gait and Posture*, vol. 27, no. 4, pp. 689–696, 2008.
- [87] C. Mazzà, M. Iosa, P. Picerno, and A. Cappozzo, "Gender differences in the control of the upper body accelerations during level walking," *Gait and Posture*, vol. 29, no. 2, pp. 300–303, 2009.
- [88] C. Mazzà, M. Zok, and A. Cappozzo, "Head stabilization in children of both genders during level walking," *Gait and Posture*, vol. 31, no. 4, pp. 429–432, 2010.
- [89] C. Mizuike, S. Ohgi, and S. Morita, "Analysis of stroke patient walking dynamics using a tri-axial accelerometer," *Gait and Posture*, vol. 30, no. 1, pp. 60–64, 2009.
- [90] M. Iosa, T. Marro, S. Paolucci, and D. Morelli, "Stability and harmony of gait in children with cerebral palsy," *Research in Developmental Disabilities*, vol. 33, no. 1, pp. 129–135, 2012.
- [91] C. J. Lamoth, O. G. Meijer, P. I. Wuisman, J. H. van Dieën, M. F. Levin, and P. J. Beek, "Pelvis-thorax coordination in the transverse plane during walking in persons with nonspecific low back pain," *Spine*, vol. 27, no. 4, pp. E92–E99, 2002.
- [92] C. J. Lamoth, F. J. van Deudekom, J. P. van Campen, B. A. Appels, O. J. de Vries, and M. Pijnappels, "Gait stability and variability measures show effects of impaired cognition and dual tasking in frail people," *Journal of NeuroEngineering and Rehabilitation*, vol. 8, no. 1, article 2, 2011.
- [93] R. Paradiso, G. Loriga, and N. Taccini, "Wearable system for vital signs monitoring," *Studies in Health Technology and Informatics*, vol. 108, pp. 253–259, 2004.
- [94] E. Rocon, J. M. Belda-Lois, A. F. Ruiz, M. Manto, J. C. Moreno, and J. L. Pons, "Design and validation of a rehabilitation robotic exoskeleton for tremor assessment and suppression," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 15, no. 3, pp. 367–378, 2007.
- [95] A. Esquenazi, M. Talaty, A. Packel, and M. Saulino, "The reWalk powered exoskeleton to restore ambulatory function to individuals with thoracic-level motor-complete spinal cord injury," *American Journal of Physical Medicine & Rehabilitation*, vol. 91, no. 11, pp. 911–921, 2012.
- [96] S. H. Kim, S. K. Banala, E. A. Brackbill, S. K. Agrawal, V. Krishnamoorthy, and J. P. Scholz, "Robot-assisted modifications of gait in healthy individuals," *Experimental Brain Research*, vol. 202, no. 4, pp. 809–824, 2010.
- [97] S. Marceglia, S. Bonacina, V. Zaccaria, C. Pagliari, and F. Pincirol, "How might the iPad change healthcare?" *Journal of the Royal Society of Medicine*, vol. 105, no. 6, pp. 233–241, 2012.
- [98] M. Flores, K. Musgrove, S. Renner et al., "A comparison of communication using the Apple iPad and a picture-based system," *Augmentative and Alternative Communication*, vol. 28, no. 2, pp. 74–84, 2012.
- [99] D. Haubenberger, D. Kalowitz, F. B. Nahab et al., "Validation of digital spiral analysis as outcome parameter for clinical trials in essential tremor," *Movement Disorders*, vol. 26, no. 11, pp. 2073–2080, 2011.
- [100] S. Hesse, C. Werner, E. M. Schonhardt, A. Bardeleben, W. Jenrich, and S. G. B. Kirker, "Combined transcranial direct current stimulation and robot-assisted arm training in subacute stroke patients: a pilot study," *Restorative Neurology and Neuroscience*, vol. 25, no. 1, pp. 9–15, 2007.
- [101] D. J. Edwards, H. I. Krebs, A. Rykman et al., "Raised corticomotor excitability of M1 forearm area following anodal tDCS is sustained during robotic wrist therapy in chronic stroke," *Restorative Neurology and Neuroscience*, vol. 27, no. 3, pp. 199–207, 2009.