Rehabilitation Technologies for Cerebral Palsy

Deborah Gaebler-Spira, Elisabetta Peri, Francesca Lunardini, Fernando Sanchez-Santed, Margaret Duff, Mary Kay Ballasiotes and Rafael Raya

Abstract Cerebral palsy (CP) is the most common motor disorder of childhood. It is characterized by abnormal muscle tone and is caused by a nonprogressive injury to the developing brain. The hallmark of abnormal posture and movement occurs as the child develops fundamental motor skills. Thus, it is critical to make opportunities for infants and young children to interact with the environment. It is recognized that assistive technology can improve the functional capabilities limited by CP. In this chapter we will explore four distinct current innovative strategies that promote rehabilitation functional outcomes. The first two will focus on the output side of treatment that of robotic control systems with virtual reality to increased practice performance in locomotion and activity of daily living. The second contribution describes the state of the art of wearable sensors providing feedback for improving motor performance including communication. The third will focus on noninvasive

D. Gaebler-Spira (\boxtimes) · M. Duff Rehabilitation Institute of Chicago, Chicago, USA e-mail: dgaebler@ric.org

M. Duff e-mail: mrduff@asu.edu

E. Peri · F. Lunardini Politecnico di Milano, Milan, Italy e-mail: elisabetta.peri@polimi.it

F. Lunardini e-mail: francesca.lunardini@polimi.it

F. Sanchez-Santed University of Almeria and InPaula, Almeria, Spain e-mail: fsanchez@ual.es

M.K. Ballasiotes International Alliance for Pediatric Stroke, Charlotte, USA e-mail: mkballasiotes@gmail.com

R. Raya

Spanish National Council for Science Research, Madrid, Spain e-mail: rafael.raya@csic.es

© Springer International Publishing Switzerland 2016 J.L. Pons et al. (eds.), *Emerging Therapies in Neurorehabilitation II*, Biosystems & Biorobotics 10, DOI 10.1007/978-3-319-24901-8_4

brain stimulation for CP rehabilitation. The next contribution provides analogues strategies used with stroke research that may be translated to children. Finally, we summarize the assistive devices for rehabilitation of people with CP from a parents perspective describing the challenges achieved and the future work required.

1 Introduction

The challenges of applying robotics and studying rehabilitation in childhood are complex but not insurmountable. The hallmarks that distinguish children are development, an acquisition of skills and growth a change in size. These two processes create a moving target when utilizing adult robotics and in turn analyzing movement, motor control, and functional outcome. The maturing brain and musculoskeletal system are in flux during childhood with critical periods and growth spurts. Critical periods of brain formation affects presentation of impairments and function. Advances and applications in bioengineering provide robotic tools for quantification that discriminate the patterns and shed light on mechanisms of injury and recovery, $[1-3]$ $[1-3]$. Although developmental sequences are orderly with known age ranges in typical children, those with developmental disabilities have considerable variability. Sequencing of developmental postures, for example a priority for children, does not naturally apply to the adult. Cerebral palsy is the most common motor disability of childhood, [\[4\]](#page-17-2). Abnormal muscle tone is one of the important features that influence movement and function in the child with CP. Objective measurement of tone, strength, and limitations of movement are body structure and function parameters or domains that are enhanced with robotics, [\[5](#page-17-3)]. Known variability among children with cerebral palsy make cohort comparison and control groups difficult for research. However, the GMFCS, which is now in standard use makes it possible to create more homogeneity, [\[6\]](#page-17-4). Another example of the moving target conundrum of childhood, or in particular cerebral palsy, is that the motor type and clinical presentation has changed and will continue to change as successful neonatal treatment occurs. Kernicterus is now rare but was once a common cause for cerebral palsy. As the field of neonatology advances the care of the neonate is modified, which creates different patterns of recovery from injury with the goal of reducing perinatal morbidity. Currently, babies born as young as 22-weeks gestation survive with new clinical presentations, [\[7](#page-17-5)]. In all countries there are important ethical issues surrounding the study of children. Typically, ethical review boards have additional protections for minors and scrutiny of research with vulnerable populations. Working with children though is made simpler now with IRB or ethical review board templates for assents, verbal and written and parent consents written at different age levels.

2 Robotics for Lower Limb Rehabilitation: Effects Beyond the Intervention

One of the main goals of neuromotor rehabilitation is recovery of the locomotion ability as it allows the patients to improve their independence and quality of life. Traditionally, physical therapy has played a critical role in lower limb rehabilitation. Treadmill training, usually with a partial support of body weight (Body Weight Support Treadmill Training or BWSTT), is also gaining importance as the therapy is provided in a controlled and safe way, [\[8](#page-17-6)]. Generally, training protocols include a gradual increase of difficulty level by decreasing the amount of body weight support provided, or by increasing the treadmill speed or the time spent walking.

A review of the effect of treadmill training on CP population by Willoughby et al. (2009) showed augmented speed of over-ground walking measured during a 10 m walking test (10 mWT) and improvements in gross motor skills (evaluated by means of Gross Motor Function Measure—GMFM). Moreover, walking endurance (measured with the 6 min walking test—6MWT) obtained some mild increase only in the more impaired group of subjects (with Gross Motor Function Classification System—GMFCS III or VI) [\[9](#page-17-7)]. The review by Damiano et al. (2009) confirmed the results highlighting that many studies noted positive, yet small, effects with a significant increase in self-selected gait speed after BWSTT.

Nevertheless, insufficient evidence is found for CP patients exercised with treadmill training, [\[10](#page-17-8)], and some drawbacks that can be highlighted include that the trunk and the lower limbs are difficult to control during exercise; thus BWSTT demands high physical effort especially for severely impaired subjects, [\[11\]](#page-17-9). In addition, treadmill training is conducted on artificial walking surface and neuromuscular feedback and sensation are different compared with over-ground walking, [\[8\]](#page-17-6).

In this framework robotics is emerging as a leading technology for motor rehabilitation of subjects with neurological impairments and, in particular, for recovery of walking. In fact, Robot-Assisted Gait Training (RAGT) has some possible promising advantages with respect to traditional training or BWSTT including the fact that it is intensive, controlled, repetitive, and provided with goal-oriented tasks that are known to be related to the cortical organization and motor learning process, [\[12](#page-17-10)]. These are particularly important for the pediatric population that could obtain better results thanks to their greater neuroplasticity. Moreover, it can be performed in a safe manner and allows hand-free operation by therapists, which in traditional therapy has a high physical burden. Finally, robotic rehabilitation is often delivered in conjunction with virtual reality (VR) resulting in cognitive engaging tasks that stimulate the subject's active participation, [\[13](#page-17-11)].

2.1 Clinical Results

Interesting results were obtained with RAGT on 999 stroke adult subjects, [\[14](#page-17-12)] and on SCI, [\[15](#page-17-13)], assessing significant improvement after RAGT, and also with respect to traditional treatment and BWSTT. Only a few studies assessed the positive effect of robot-assisted lower limb training on the pediatric population, [\[16\]](#page-17-14).

Till date, few robotic devices are available for the pediatric population and, among them, two are primarily used: Lokomat (Hocoma AG, Switzerland) and Gait trainer GT I (RehaStim, Germany), [\[16](#page-17-14)]. These robots follow two different training principles: the first principle provides training with a driven orthosis that guides the lower limb in a sequence of gait cycles on a treadmill. The second uses the end-effector paradigm: the lower extremities are fixed on two moving plates that are moved in a sequence similar to the gait cycle. During the training, both provide the body weight support allowing the fruition of training for subjects with different levels of impairment.

Some positive results on the CP population are reported in the literature. Borggraefe et al. (2010) showed positive effects with 12 sessions of training with Lokomat and described improvements in standing and walking ability (dimensions D and E of the GMFM, respectively) in 20 children with bilateral CP, which were maintained after a period of 6 months, [\[17](#page-17-15), [18\]](#page-18-0). The authors also reported a dosedependence efficacy of the intervention as the improvements of the task specifically trained (walking) measured in dimension E of GMFM are positively correlated with higher distance and time walked. Lokomat has also been used by Meyer-Heim et al. (2009), who obtained some significant improvements in terms of 10 m walking test (10 mWT) and dimension D of GMFM-66 after 12–20 sessions of training 22 CP children, [\[12](#page-17-10)].

Two randomized controlled trials studied the difference between robot-based therapy and conventional therapy with Lokomat (20 sessions), [\[19\]](#page-18-1) and Gait Trainer (10 sessions over 2 weeks), [\[11](#page-17-9)]. Druzbiki et al. (2013), [\[19](#page-18-1)] recruited 52 CP subjects that underwent 20 sessions of 45 min each with either Lokomat or traditional

physiotherapy ($N = 26$ each). They observed only few improvements (not statistically significant) in spatiotemporal parameters and kinematics of gait analysis both in the study group and in the control group. Differently, Smania et al. (2011), [\[11\]](#page-17-9) analyzed the results of 18 diplegic and tetraplegic CP trained with 10 sessions of 40 min each. Nine children of the study group underwent 30 min of RAGT with Gait Trainer $+10$ min of traditional training while nine of the control group had 40 min of traditional training. Results assessed significant improvements in terms of 10 mWT and 6 min walking test (6MWT) only in the study group, while no groups gained significant improvement in an index of activities of daily living (Functional Independence Measure for Children—WeeFIM). The controversial results of these studies suggest that the RAGT therapy seems to be ineffective in modifying motor strategy consolidated in chronic disorders like cerebral palsy, thus the gait analysis cannot highlight modification in the kinematics pattern. However, improving muscular strength or reduction of energy expenditure could intervene in obtaining the overall effect of augment speed or endurance during walking observed in other studies, [\[11,](#page-17-9) [18](#page-18-0)] sustainably. The results remain uncertain, thus they should be regarded as preliminary with further studies necessary in RAGT in the CP population.

2.2 Rehabilitative Factors

2.2.1 Subject-Specific Responsiveness to RAGT

Recently, some evidence on pediatric treadmill training suggests a possible heterogeneity in the response to task-specific therapies in children, [\[20\]](#page-18-2). In particular, some studies assessed possible different outcomes following training for subjects with different impairment levels at baseline [\[9](#page-17-7), [18,](#page-18-0) [20\]](#page-18-2).

Borggraefe et al. (2010) observed that patients with moderate to severe cerebral palsy achieved less improvements after the robotic training compared to mildly affected patients. Schroeder et al. (2014) suggest that gross motor function at baseline can be considered as an independent determinant of improvement in GMFM-66 total score and GMFM-E score, meaning that patients with higher motor abilities at baseline improved more during RAGT than patients with lower gross motor abilities at baseline, [\[20](#page-18-2)]. These results are in line with findings by Hanna et al. (2008), who observed that CP patients with GMFCS levels of I and II exhibit a higher potential to gain motor function over time compared to severely affected patients using developmental curves of GMFM-66, [\[21](#page-18-3)].

However, a different trend was highlighted in a review for BWSTT: greater benefits were gained by children with more severe functional involvement (GMFCS III and IV), [\[9\]](#page-17-7).

This inconsistency might be related to the heterogeneity of the studies analyzed (the first two related to the use of RAGT and the third one to BWSTT) and the use of different outcome measures to analyze data. It should be noticed that even if children with severe walking impairment (GMFCS IV) may be expected to obtain

only reduced changes in functional abilities after training, they may obtain other potential benefits that can have an enormous impact on the children's health and well-being, [\[9](#page-17-7)].

Schroeder et al. (2014) provided a wider evaluation of the patient-specific responsiveness to RAGT, [\[20](#page-18-2)], considering also other factors that could influence the recovery (age, gender, etiology, and add-on botulinum toxin therapy). In their study they recruited 83 children (aged between 4 and 18 years) with various developmental disorders (bilateral spastic CP, unilateral CP, ataxic CP, hereditary spastic paraparesis, and genetic syndrome). The patients underwent 12 sessions of training within 3 weeks with Lokomat and were evaluated before and after the training by means of GMFM, obtaining some improvements in GMFM-66 and GMFM-E. The correlation between the results obtained and the other factors considered revealed that age seems to have an inverse effect on the improvement of standing abilities (GMFM-D), while no correlation was found between GMFM, gender, etiology, or previous intervention with botulinum toxin treatment.

2.2.2 Effects of Enhanced Active Contribution on Clinical Outcomes

Active participation of the subjects involved in training is recognized as one of the more important determinants of positive outcome, [\[22\]](#page-18-4).

Some research groups investigate it analyzing the muscular activity during robotassisted locomotion. Two studies assessed that the EMG activity of quadriceps and hamstrings is reduced with robot-assisted training with respect to therapist-assisted treadmill training [\[23,](#page-18-5) [24](#page-18-6)], but this difference is reduced if during RAGT subjects were vocally encouraged to maximize their effort, [\[24\]](#page-18-6). Schuler et al. (2013) observed that muscular activity follows a more physiological activation timing with respect to training on treadmill without orthosis, [\[25](#page-18-7)]. The reduced active contribution during robot-assisted training could be one of the responsible facts for the controversial results described in the literature, as it is recognized as a principle factor in eliciting performance improvements, [\[22](#page-18-4)].

Virtual reality has been suggested as an effective means to encourage subjects' motivation and active participation during training, especially in the pediatric population. Evaluation of EMG patterns on nine children with motor impairment and eight healthy subjects showed that there is an increased EMG activity during tasks with virtual realities than during normal walking conditions for both groups, [\[26](#page-18-8)]. These results are confirmed by two other studies, [\[25,](#page-18-7) [27\]](#page-18-9) that, robot assisted treadmill training showed that the EMG activity of the hip muscles in the swing phase is significantly correlated with the presence of virtual reality, together with the encouragement provided by physiotherapists.

To conclude, RAGT seems to be a promising strategy to provide rehabilitation treatment in children affected by cerebral palsy and its effectiveness may be enhanced in the presence of active participation, promoted by therapists and/or virtual reality.

Definitive conclusions about RAGT cost-effectiveness cannot be drawn. Crucial elements to be considered for future studies include the small sample size, especially

on the pediatric population, the absence of a randomized control trial design, and the lack of instrumental evaluations. There is no clear evidence of benefits of the robot-assisted training in cerebral palsy, also with respect to traditional training. Explanation for this might be due to different methods and protocols during intervention/group of patients studied as there are no well-established protocols shared by clinics to provide training. Moreover, it should be considered that there are only few effective assessment methods able to identify possible variation after training in a quantitative and not operator-dependent fashion. Changes to body structure and function (e.g., muscle tone, energy expenditure, muscle strength, bone density) are not often considered although they could be critical to provide a comprehensive evaluation of the training. Finally, some studies suggest that the effects of training are patient-dependent and a lot should still be done to identify specific factors that allow for prediction of the training efficacy and that could provide important indications to clinicians to customize the rehabilitation treatment.

3 Biofeedback as Rehabilitation Tool Using Physiological Sensors

Biofeedback, for use in treatment of children with cerebral palsy, can be defined as the use of sensory feedback through which objective performance observation related to a specific motor task is presented to provide the child with immediate, consistent feedback of performance, [\[28](#page-18-10)]. The aim of providing patients with biofeedback during exercise is twofold. First of all, to improve the effectiveness of the rehabilitation treatment, both by allowing patients to adjust their movements according to the feedback of performance and by providing an incentive to exercise. In the second instance, recording the physiological parameters to be fed back to the patient provides quantitative monitoring and documentation of patient progress during treatment. The latter feature is particularly important when the rehabilitation treatment is extensive and prolonged, which is typically the case with patients with CP.

3.1 Underlying Mechanisms

The neurological mechanisms underlying biofeedback training are still not completely clear. One of the primary problems for children with abnormal movement may be inefficient sensory information. Harris postulated that biofeedback devices that provide augmented or exteroceptive sensory information can be used by children with cerebral palsy to better calibrate the proprioceptive information they receive and, therefore, help them to achieve improved motor control, [\[29\]](#page-18-11). Biofeedback may enhance neuralplasticity by involving auxiliary sensory inputs, thus making it an appropriate tool for neurorehabilitation.

3.2 Biofeedback Modalities

Modalities of biofeedback are diverse and the appropriate sensors to use in a biofeedback system depend on the motor control mechanism, the training task, and the therapeutic goal. Clinicians may use sensors that detect such parameters as brain waves, muscle activity, reaction forces, joint angles, or positions. In neurofeedback training, surface sensors are placed on selected areas of the scalp to record EEG activity, thus teaching participants to control the frequency content of the EEG signal and gaining self-regulation of brain functions, [\[30](#page-18-12)]. For EMG training, surface EMG electrodes are attached to the skin over the muscle(s) being targeted. The goal of the EMG-based biofeedback is generally to provide subjects with enhanced information about their muscle activity to improve basic motor control skills, coordinated recruitment of synergistic muscles, or functional use of an impaired muscle during daily activities, [\[31](#page-18-13)]. Force platform biofeedback systems are used to measure the ground reaction forces generated by a body standing or moving on them. These systems are usually employed in protocols aimed at enhancing stance symmetry, steadiness, and dynamic stability, [\[32\]](#page-18-14). Inertial measurement units (IMUs) are systems typically based on accelerometers and gyroscopes that have been used to examine and quantify human movement, [\[33\]](#page-18-15). Because of their small and unobtrusive dimension, they have been used in several biofeedback protocols during static and dynamic balance training, [\[34,](#page-18-16) [35\]](#page-18-17).

Since biofeedback therapy always involves a monitoring instrument capable of providing accurate physiological information, new and innovative sensor technology is particularly important in order to provide participants with a significant, accurate, and low-latency clue, thus improving the training outcome.

3.3 Early Studies

Starting from the 1970s, scientific studies investigated the effects of biofeedback therapy on the treatment of motor deficits in cerebral palsy. In an early work, Wooldridge and Russell, [\[36](#page-18-18)] tested a mercury-switch device to provide 12 cerebral palsied children with auditory and visual information regarding the spatial position of the head. It was concluded that the head position trainer was effective in the development of head control and position awareness in children with cerebral palsy. Postural control was also investigated in another early study, [\[37](#page-18-19)], where a pressure switch that activated a videocassette recorder was placed in the seat insert of five children with spastic diplegia or quadriplegia with inadequate trunk control. Based on the amount of time they exerted pressure against the switch, the study showed that children improved their sitting posture by voluntarily extending their trunk. In one pioneer study, Nash et al. [\[38](#page-18-20)] used the gain of the tonic stretch reflex of the gastrocnemius muscle derived from the level of EMG activity while the child's joint was rotated by the operator, to control video games. The protocol was tested on three spastic diplegic children with

normal intelligence and aimed at facilitating the control of the reflex sensitivity, thus reducing spasticity. They reported that the range of voluntary joint rotation increased significantly, but that only one subject had a significant reduction in spasticity. They also highlighted that the protocol made the training interesting and enjoyable for all the children.

3.4 State of the Art

Early approaches have several limitations that prevent long-term use in children. In the first place, the types of cues used to convey the information to the subject were relatively simple, usually employing analog, digital, or binary values. A common form of performance information employed response-contingency systems, in which a desirable event such as the operation of a television set occurs as long as the required activity occurs, [\[28](#page-18-10), [36\]](#page-18-18). Such feedback requires attention and can be distracting to the child and to other children nearby, preventing its use, for instance, during school. To have a significant effect on brain plasticity, it seems desirable to have the child training for several hours a day during daily activities. To address this limitation, Bloom and colleagues, [\[39\]](#page-18-21) developed a wearable device that provided the subject with a mechanical tactile stimulation. The device was based on a mechanical vibrating stimulator attached to the skin, which provided the patient with a vibration proportional to the activity of the most impaired muscle and it was tested on 11 cerebral palsy children during daily activity. Results, based on parental questionnaires and Goal Attainment Scale assessments, showed significant clinical improvements in all the children who completed the study.

Another limitation of early studies is the reduced information available to the patient, typically limited to one or two channels so as not to overwhelm him during movement execution. Therefore, an effective task-oriented biofeedback system requires synergistic feedback of multiple channels that characterize the task performance without overwhelming a patient's perception and cognitive ability. Bolek et al. [\[40\]](#page-18-22) developed multiple-site performance-contingent feedback to treat motor dysfunction in two patients with cerebral palsy. Specifically, they conveyed information from four muscles of the lower limb to train postural stability while sitting. Right and left gluteusmedius were targeted to remain above threshold, while the right and left gluteus maximus were required to be below threshold. When this constellation of muscle groups was on target, a reward was activated. Failure to maintain any muscle at the therapeutic threshold terminated the reward. The aim of this approach was to internalize the correct muscle pattern recruitment rather than individual muscle activity. Improvement, expressed in percent of time the threshold was met, was reported for both the participants.

One more shortcoming of earlier biofeedback approaches was that the information presented often took the form of lines or bars on a computer screen or simple beeps. These were neither intuitive nor attention grabbing. Motivation and attention are two key factors for biofeedback training. The success of therapies aimed at inducing

neuroplasticity is strictly related to the amount of time spent on active training. As a result, the training task should be attractive and motivating to keep the subject attentive for several repetitions of the task. This feature is particularly important when working with children who get tired and distracted easily, [\[38\]](#page-18-20). Multimediabased technology uses computerized graphics and animation, together with sound and haptic stimulation, to immerse the subject in a constructed virtual reality (VR), [\[41\]](#page-19-0); thus it can be exploited to design biofeedback cues with the required features. Novel VR-based biofeedback systems have the potential to promote sustained attention, self-confidence, and motivation of participants during the repetitive task therapy. Therefore, there is widespread interest in using VR in rehabilitation of children with cerebral palsy, to address upper extremity, [\[42,](#page-19-1) [43\]](#page-19-2) and lower extremity motor functions, [\[44](#page-19-3)]. Yoo and colleagues, [\[43\]](#page-19-2) investigated the effectiveness of a combined EMG biofeedback and VR intervention system to improve muscle imbalance between triceps and biceps during reaching movements in three children with spastic cerebral palsy. Results reported an improvement in the muscle imbalance ratio between triceps and biceps compared to a traditional EMG-based biofeedback training. Another case report, [\[45\]](#page-19-4) investigated the effects of VR therapy on cortical reorganization and associated motor function in an 8-year-old children with hemiparetic cerebral palsy. After VR therapy, the altered activations disappeared and the contralateral primary sensorimotor cortex was activated. This neuroplastic change was associated with enhanced functional motor skills, which were not possible before the intervention.

An important feature of these novel systems is that virtual applications that are Internet-deliverable pave the way for possible home-based rehabilitation, which has the potential to reduce the costs associated with long periods of hospitalization or traveling long distances, [\[46](#page-19-5)]. Interactive technologies also provide children with movement disorders with the chance to be involved without being judged because of their disability [\[47](#page-19-6)]. In this framework, Golomb and colleagues, [\[48](#page-19-7)] carried out a 3-month proof-of-concept pilot study on three adolescents with severe hemiplegic cerebral palsy, where they tested a VR video-game telerehabilitation system using a sensing glove fitted to the plegic hand, [\[49](#page-19-8)]. Based on several outcome measures, such as occupational therapy assessments, fingers' range of motion (ROM), dualenergy x-ray absorptiometry (DXA), and peripheral quantitative computed tomography (pQCT) of the plegic forearm bone health, functional magnetic resonance imaging (fMRI) of hand grip task, the study reported improved hand function and forearm bone health for patients who practiced regularly. To address the need for technologies that facilitate children's acquisition of play experiences, another group tested the effectiveness of an affordable home-based musical play system (the movementto-music system (MTM)) on children with severe physical disabilities, who are typically limited to play and create music, [\[50](#page-19-9)]. The results, based on parental interviews, showed that the MTM technology had the potential to improve children's body functions and enhance their participation in family activities. Another study developed a low-cost VR therapy system based on commercially-available game consoles (Sony PlayStation 2 equipped with an EyeToy video camera) to elicit practice of targeted neuromotor movements in five children with hemiplegia. The evaluation, based on

the Quality of Upper Extremity Skills Test and on caregivers and parents questionnaires, showed that the system successfully elicited targeted neuromotor movements of the hemiplegic limb, [\[51](#page-19-10)].

The use of biofeedback techniques looks well suited for rehabilitation of children with cerebral palsy as a natural part of their daily activities. Findings indeed report a positive effect in motor rehabilitation, with improvements in motor control, spatial orientation skills, mobility, and an increase in motivation to practice even for children with severe grades of disabilities. However, even if at present studies report a general positive effect, there is scarcity of evidence of a strong beneficial effect, especially when it comes to VR studies. Indeed, studies that address the use of VR for rehabilitation of children with cerebral palsy are few, and the level of evidence is primarily limited to experimental and pilot studies with small samples. The large variation in outcome measures makes it hard to compare and integrate the results. In some studies, the assessment is based on qualitative interview, while there may be the need for more sensitive outcome measures that have the capacity to capture small motor changes. To conclude, the results show that the use of biofeedback and VR-based biofeedback in rehabilitation of children with cerebral palsy is a highly promising area in which further research is encouraged. In particular, further efforts to develop sensitive outcome measures and a common vocabulary within this research field is needed.

4 Noninvasive Brain Stimulation for Cerebral Palsy Rehabilitation

Noninvasive brain stimulation is growing as a very active research line because of its possibilities to enhance cognition, motor performance, rehabilitation after brain damage, and treatment of different psychopathologies. Basically, brain activity can be modulated by manipulation of neuron resting potential, rendering cells more prone to be activated if depolarized or reducing the probability of firing if hyperpolarized. Both effects, activation and inhibition, are reached by passing through the scalp a magnetic pulse or a weak electrical current, [\[52\]](#page-19-11). Transcranial Magnetic Stimulation (TMS) is based in a stimulator device that generates high intensity electrical pulses into a coil, superimposed above the scalp, to induce magnetic fields that easily pass the skull and modify actual electrical currents inducing activation or inhibition of cells. If the magnetic pulse is strong enough firing of neurons can also be induced. There are two main types of magnetic stimulation: single pulse (TMS) and repetitive transcranial magnetic stimulation (rTMS), [\[53\]](#page-19-12). Transcranial Direct Current Stimulation (tDCS) is based in an electrical device, battery powered, that delivers continuous current to a pair of electrodes situated above the scalp. The device contains specific software for programming the experimental setup and for maintaining a constant current intensity in function of variation on skull impedance. Electrodes are positioned to direct current flow between them, in such a way that tissue under anode is expected to become depolarized while brain tissue under cathode is said to be hyperpolarized. Electrical

intensity is weak enough, between 0 and 2 mA, to ensure that no neuronal firing is triggered, [\[53\]](#page-19-12).

Both techniques are being actively investigated for, directly or indirectly, enhancing neurorehabilitation. Thus, different reports show better performance on learning tasks (motor, sensory, or cognitive) of healthy participants as well of patients with brain damage (stroke, TBI, Alzheimer, Parkinson, epilepsy, amyotrophic lateral sclerosis, cerebral palsy, etc.), [\[52,](#page-19-11) [54\]](#page-19-13). Specifically the problem of spasticity has been targeted in various reports, mainly focused on stroke patients but also in cerebral palsy children. Two approaches can be indentified in the literature: direct modulation of spasticity by direct modulation of brain activity or modulation of typical motor training programs. Primary motor cortex, M1, sends out projections directly to the spinal cord, where it modulates spinal interneurons and reflex. Damage to M1 can result in spasticity because the absence, or reduction, of high-order motor commands imply the reduction of spinal inhibitory processes and a consequent overactivation of muscles. Thus, noninvasive M1 stimulation should increase spinal inhibition and spasticity. Working with this hypothesis has shown temporal reductions in upper or lower limb spasticity in stroke patients by stimulation itself but also by combination with physiotherapy or other functional motor tasks [\[55](#page-19-14)[–57\]](#page-19-15). In 2007 Valle et al. [\[58](#page-19-16)], stimulated for 5 days the primary motor cortex of 17 CP children from 5 to 18 years old. 5 Hz stimulation, but not sham or 1 Hz, produced modest benefit in some, but not all, measures taken, namely upper limb joints range of motion. The more important information about these reports rely in safety data as no side effects were noted and no convulsions were generated in well-medicated patients diagnosed of epilepsy.

tDCS has been tested in the context of rehabilitation of CP children with the objective of improving functional training. Thus, Grecco et al. [\[59](#page-19-17)] compared 12 ambulant children with CP (GMFCSI-III) with 12 control children with the same characteristics. All of them were subjected to treadmill training; the experimental group was stimulated 5 days/week for 2 weeks with 20 daily minutes of 1 mA of anodal tDCS over the primary motor cortex, while control group was sham stimulated. Gait performance improvements were recorded for the experimental group both at the end of treatment and 1 month later. Cortical excitability, measured by TMS stimulation of motor cortex and motor evoked potentials, was also modulated by tDCS treatment, [\[60\]](#page-20-0). In a following paper the same group has shown that simultaneous tDCS M1 stimulation (1 mA) during 20 min of treadmill training resulted also in improvements of static balance and functional balance that lasted for 1 month, [\[60,](#page-20-0) [61\]](#page-20-1). Thus, tDCS also seems a promising technique for CP neurorehabilitation. In fact, just a single session of stimulation with the same parameters has shown improvements in oscillations during standing as well as gait velocity, [\[60](#page-20-0)]. In these experiments it is supposed that anodal stimulation, by depolarizing underlying tissue, will help in motor activation and plasticity, and as a consequence improve treadmill motor training. But anodal M1 1 mA stimulation has also been shown to reduce spasticity in children with CP; a reduction of spasticity would, for sure, improve motor learning. Thus it is important to discern the exact mechanism for this beneficial effect over treadmill motor learning.

Nevertheless, safety issues about both techniques are not convened for the pediatric population. Thus a plus of prudence is claimed by some authors: brain surface and physiology varied between children and adults together with skull and meningeal volume. It is important, then, to perform safety studies and, probably, basic research using animal models to ensure that actual stimulation parameters and, perhaps more important, a chronic stimulation schedule is safe for a developing brain, [\[62](#page-20-2), [63\]](#page-20-3).

5 Potential Effectiveness of Devices Designed for Stroke in Cerebral Palsy

5.1 Introduction

Stroke is the leading cause for adult disability in the US, [\[64](#page-20-4)], and accordingly, much of the novel technology-based rehabilitation research has been focused on treating adults with stroke. However, approximately 500,000 children and adults are also living with motor impairments caused by cerebral palsy, yet relatively little research has been done on how to best address current impairments and prevent further deterioration of movement abilities. Even with all the dedicated therapy research, there are no current widely accepted comprehensive clinical therapies that completely address impairments of the arm and hand for any condition. Inability to fully use either or both hands can have a major effect on performing both basic daily tasks and meaningful vocational activities. Providing therapy for the upper-extremity after stroke is especially challenging because of highly varied combinations of impairments such as spasticity, [\[65](#page-20-5)], weakness, movement inefficiency [\[66,](#page-20-6) [67](#page-20-7)], joint discoordination, [\[68\]](#page-20-8), limited ranges of motion, increased trunk compensation, [\[69\]](#page-20-9), and reduced movement speed, [\[70](#page-20-10)]. Because each stroke survivor has a unique array and severity of impairments, as well as potentially confounding neurological and mobility conditions caused by the stroke or other pre-morbid conditions, prescribing one therapy to adequately address movement behaviors throughout the recovery period is difficult. Many of the motor impairments and confounding factors are similarly seen in people with cerebral palsy, and this section will explore different types of upperextremity therapies from theoretical, clinical, and technological angles and discuss how each therapy might translate to the treatment of children and adults with cerebral palsy. Therapies discussed include assistive robotics, virtual reality and feedbackbased rehabilitation, constraint-induced movement therapy, vibration therapy, and functional electrical stimulation.

5.2 Assistive Robotic Therapy

One of the most popular ways to use robotic therapy is as a physically assistive device. This involves a robotic device that interfaces directly with the affected limb(s) and either assists the movement or moves the passive limb without any action from the user. Robotic devices such as these can be used as a stationary device that the person interacts with or as an ambulatory, wearable exoskeleton, or a combination of both types [\[71](#page-20-11)[–74\]](#page-20-12). Assistive wearable robotic devices have been created to address issues of the hand, arm, and gait. Many of these robots also use a computer screen to provide some feedback to the user and create incentive for use. The Hand Mentor (KMI) is a commercially available repetitive task robot that passively moves or actively assists the hand in a way to practice wrist flexion/extension movements, [\[75](#page-20-13)[–77\]](#page-20-14). This product has a small computer screen associated with the exercise so the user can play a game with the movements of the hand. The same company has also created the Foot Mentor, which uses similar principles to train ankle range of motion. The MIT Manus is another hand and arm robot where the user grasps a cylinder and the user's forearm is strapped onto the robot. The user can perform active anti-gravity movements, or if needed, be assisted by the robot, while they are playing a rehabilitation game, [\[78](#page-20-15)]. While assistive robotics can be extremely useful in augmenting a therapist's ability to help patients produce repetitive movements with a high frequency, they have also tended to focus on the technology, rather than on the specific clinical benefit. Many robots are designed to move the limb completely independently, which greatly limits the patient's opportunity to engage in active motor learning. The robots may also fail to adapt to the patient's specific movement impairments or to change the assistance based on improvements in movement or function. Because repetitive movements can become tedious even with assistive robots, robotic protocols often include visual feedback or games to incentivize the user to practice more often and for longer time periods. The feedback can also help the patient improve the movement in conjunction with the intervention of the robot.

The field of rehabilitation robotics has grown substantially during the past 15 years. Studies of upper limb robot-assisted therapy for adults with moderate to severe hemiparesis after stroke have shown significant gains compared with usual care in isolated control, coordination, and strength in the paretic arm. Researchers have recently extended their focus to children with neurologically based movement disorders arising from cerebral palsy and acquired brain injury or stroke. Section [2](#page-2-0) has described the state of the art of robotic devices for gait pediatric rehabilitation. Some devices as InnoSmart (from Made for Movement) and Lokomat are examples of robotic systems that offer a specific version for children.

There are currently a limited number of robotic systems targeting the upper extremity that have been applied to children with CP, [\[79](#page-21-0)]. These devices propose goal-directed tasks and reaching movement to rehabilitate the hand and arm function. The InMotion2, also called shoulder-elbow robot, is an end-effector robot, a commercial version of MIT-MANUS (Interactive Motion Technologies), [\[80](#page-21-1)], which is capable of continuously adapting to and challenging each patient's ability. This device aims to improve the range of motion, coordination, strength, movement speed, and smoothness. 117 subjects with stroke were trained with InMotion2, and during the training patients were able to execute shoulder and elbow joint movements with significantly greater independence. At the end of the experiment, subjects were better able to draw circles, [\[81\]](#page-21-2). In most cases, studies conducted with patients with stroke

have encouraged new experiments with people with CP. This is the case of an experiment where 12 children aged 5–12 with cerebral palsy and upper-limb hemiplegia received robotic therapy twice a week for 8 weeks. The children showed significant improvement in the total Quality of Upper Extremity Skills Test (QUEST) and Fugl-Meyer Assessment Scores, [\[80](#page-21-1)]. Following the distal approach, Interactive Motion Technologies has developed the MIT-Manus InMotion3. This robotic handle works with flexion and extension, as well as pronation and supination of the affected wrist. The results are similar to with InMotion2, but in this case, InMotion3 can operate both as a standalone device and as an InMotion2 module. There are no studies using InMotion3 by children with CP.

5.3 Constraint-Induced Movement Therapy

Constraint-induced movement therapy (CIMT), [\[82\]](#page-21-3) was a method pioneered to encourage use of the affected arm. The patient puts a restrictive glove or mitt on their less affected hand and therefore is forced to use the more affected hand for activities of daily living (ADLs). As the person is restrained from using the less affected hand and arm, they must adapt to using the more affected arm in everyday real-world scenarios, which creates more natural practice than controlled therapy tasks. Constraint-induced movement therapy has been shown to increase movement and function of the affected arm, but studies have linked the higher amount of use to increased compensatory strategies and not to the recovery of pre-morbid movement patterns, [\[83\]](#page-21-4). Other studies have also shown that practice without a focus on improving movement quality may increase function, but will have an adverse effect of increasing compensation or inefficient movements, [\[84](#page-21-5)]. Another disadvantage of CIMT is that rendering one hand unusable severely restricts the performance of bimanual tasks that are crucial to many ADLs. The therapy may also not be ideal for people suffering from bilateral impairments, as they do not have a good arm to be constrained and may need to practice using both hands.

5.4 Feedback Systems

Feedback-based rehabilitation systems collect bio-data from sensors placed on the body and transform the data into usable feedback to allow the patient to alter their performance in some way. Sensors can collect muscle signals (EMG), kinematic data (motion capture or joint angle sensors), force, galvanic skin response, or brain signals (EEG) among others. The purpose of such systems is to encourage or correct certain patterns detected through the sensors. An EMG biofeedback system, [\[85\]](#page-21-6) uses electrodes placed on the upper arm, whose signal control is a computer cursor. The cursor is used to play a game and can only be controlled correctly through the

reduced use of abnormal muscle synergies. This can help retrain correct muscle activation patterns, although transference to significant increase in daily use or function. Another group, [\[86\]](#page-21-7) has used combined EMG and kinematic signals to provide visual feedback on elbow extension, however, this system has not yet been used in active retraining movement patterns. Kinematic-based feedback can also be used to provide people with stroke useful information on their speed, trajectory efficiency, targeting accuracy, joint angles, and compensation, [\[87\]](#page-21-8), but it is currently very difficult to provide high-level feedback on hand function as the movements are complex and difficult to measure. Feedback systems are also generally associated with complex and long setups to apply the sensors correctly and reducing the sensor set for an easier setup may result in lost important data. These systems are also not yet at the point of training functional, complex tasks. More research needs to be done on the best ways to provide multisensory integrated information about key movement features in a way that is intuitive and useful to the patient. Section of this chapter describes different studies using biofeedback for cerebral palsy.

5.5 Functional Electrical Stimulation and Vibration Therapy

Functional electrical stimulation (FES) uses electrodes to electrically stimulate weak or paralyzed muscles after stroke. FES has been used to reduce shoulder subluxation and reduce pain in the shoulder, which may potentially increase the use of that joint, [\[88\]](#page-21-9). However, repetitive task training has been shown to significantly increase active use of the hand when compared to FES therapy, [\[89](#page-21-10)]. However, the FES intervention may have been involved reducing spasticity in the hand flexors. This indicates that FES may be most beneficial in combination with other types of therapy as a way to reduce unwanted EMG signals or to enhance voluntary EMG signals during other types of occupational or physical therapy. The complexity of the FES setup as well as the inability to selectively activate smaller or more internal muscles could limit its overall usefulness in the clinic. Muscle vibration therapy is another way to reduce muscle tone and spasticity in the upper limb after stroke, [\[90\]](#page-21-11). Vibrations of the muscles are thought to increase corticospinal excitability as well as inhibitory neuronal activity in the antagonist muscle, [\[91\]](#page-21-12), which could explain the reduction in spasticity. However, reduction in unwanted muscle activity may not lead directly to increases in voluntary functional usage of the affected limb, but instead may be another way to augment more traditional therapies. Coupling tendon vibration with assistive movement may also augment sensory information related to movement, but the outcomes may be most significant in people with severe impairments, [\[92](#page-21-13)]. Additional work is still needed to determine if vibration therapy can be beneficially coupled with active relearning of complex movements. There are very limited numbers of studies of children with cerebral palsy. Ruck et al. [\[93](#page-21-14)] showed that 20 subjects receiving 9 min of side-alternating whole-body vibration in addition to physiotherapy increased the average walking speed in the 10 m test. Katusic et al. [\[94](#page-21-15)] evaluate the effect of sound wave vibration therapy on spasticity and motor function of children with CP. Eighty-nine children with CP participated in the study. The Asworth Scale and GMFM-88 were used as outcome measures, describing significant differences after 3 months' intervention.

6 Rehabilitation from a Parent's Perspective

Children with cerebral palsy and their parents are very eager to seek and improve physical function through the therapeutic use of robotics. To include the perspective of parents, the president and co-founder of the International Alliance for Pediatric Stroke was asked to contribute and conclude the chapter.

Rehabilitative therapy has been proven to improve the quality of life for children, but it only works if the child participates. It is difficult to keep a child engaged and motivated in an ongoing, consistent rehab program as the child gets older. School work, activities, family life, and playtime start becoming more and more important. Therapy becomes boring and a nuisance for the child. In addition, older children become accustomed to instant gratification through their use of social media, video games, and technology. Typical therapy does not provide this. Similarly, in school, children are rewarded for their hard work with good grades. However, telling a child that therapy will reward them in the future does not seem attainable in the present.

In order to keep children interested and get them to actively participate in rehab, we need to find a similar instant feedback or measurable goals scenario for children and teens. This is where innovative rehabilitation technology becomes a valuable resource. Technologies such as Biofeedback, Robotics, VR Therapy, and Transcranial Stimulation are excellent methods to provide the goal and instant feedback that would increase the child's participation. Additionally, it provides the use of technology which children thrive on. Typical therapies are not able to provide this type of feedback and stimulation that children are familiar with.

Accessing these types of technology and making them affordable to families will be the challenges however.We live in North Carolina, but a few years ago my daughter was able to try out the Intellistretch at Rehabilitation Institute of Chicago. She came home very excited about the prospect of using this on a regular basis because this was something that would keep her motivated. Unfortunately, the device was not available in our area.

Speaking from experience, I see these technologies not only as innovative and promising for children, but necessary to improve their quality of life. These types of rehabilitation therapies will be the key to keeping children motivated, enthused, and eager to stick with the programs because they will see the improvement. Therapy will be something they "want" to do, instead of something they "have" to do. Moving forward, we will need to find a way to make these technologies affordable and readily available for these children.

Acknowledgments The authors would like to thank the participation of Mary Kay Ballasiotes, President and Co-founder of the International Alliance for Pediatric Stroke. She is a mother of a 17 year-old daughter who has cerebral palsy as a result of a perinatal stroke. She has also worked with many families of other children with CP through nonprofit support and advocacy organizations that she founded. Her background has provided her with a perspective on real-life rehabilitation therapy successes and challenges for the pediatric population.

References

- 1. Hawe, R.L., Sukal-Moulton, T., Dewald, J.P.: The effect of injury timing on white matter changes in the corpus callosum following unilateral brain injury. NeuroImage Clin. **3**, 115– 122 (2013)
- 2. Sukal-Moulton, T., Krosschell, K.J., Gaebler-Spira, D.J., Dewald, J.P.: Motor impairment factors related to brain injury timing in early hemiparesis, part I: expression of upper-extremity weakness. Neurorehabil. Neural Repair. **28**(1), 13–23 (2014)
- 3. Sukal-Moulton, T., Krosschell, K.J., Gaebler-Spira, D.J., Dewald, J.P.: Motor impairments related to brain injury timing in early hemiparesis. Part II: abnormal upper extremity joint torque synergies. Neurorehabil. Neural Repair. **28**(1), 24–35 (2014)
- 4. Odding, E., Roebroeck, M.E., Stam, H.J.: The epidemiology of cerebral palsy: incidence, impairments and risk factors. Disabil. Rehabil. **28**(4), 183–191 (2006)
- 5. Wu, Y.N., Ren, Y., Hwang, M., Gaebler-Spira, D.J., Zhang, L.Q.: Efficacy of robotic rehabilitation of ankle impairments in children with cerebral palsy. Conf. Proc. IEEE Eng. Med. Biol. Soc. **1**, 4481–4484 (2010)
- 6. Palisano, R.J., Hanna, S.E., Rosenbaum, P.L., Russell, D.J., Walter, S.D., Wood, E.P., et al.: Validation of a model of gross motor function for children with cerebral palsy. Phys. Ther. **80**(10), 974–985 (2000)
- 7. Himmelmann, K., McManus, V., Hagberg, G., Uvebrant, P., Krageloh-Mann, I., Cans, C.: Dyskinetic cerebral palsy in Europe: trends in prevalence and severity. Arch. Dis. Child. **94**(12), 921–926 (2009)
- 8. Sheik-Nainar, M.A., Kaber, D.B.: The utility of a virtual reality locomotion interface for studying gait behavior. Hum. Factors: J. Hum. Factors Ergon. Soc. **49**(4), 696–709 (2007)
- 9. Willoughby, K.L., Dodd, K.J., Shields, N.: A systematic review of the effectiveness of treadmill training for children with cerebral palsy. Disabil. Rehabil. **31**(24), 1971–1979 (2009)
- 10. Damiano, D.L., DeJong, S.L.: A systematic review of the effectiveness of treadmill training and body weight support in pediatric rehabilitation. J. Neurol. Phys. Ther. **33**(1), 27 (2009)
- 11. Smania, N., Bonetti, P., Gandolfi, M., et al.: Improved gait after repetitive locomotor training in children with cerebral palsy. Am. J. Phys. Med. Rehabil. **90**(2) 137–149 (2001)
- 12. Meyer-Heim, A., Ammann-Reiffer, C., Schmartz, A.: Improvement of walking abilities after robotic-assisted locomotion training in children with cerebral palsy. Arch. Dis. Child. **94**(8), 615–620 (2009)
- 13. Holden, M.K.: Virtual environments for motor rehabilitation: review. Cyberpsychol. Behav. **8**(3) 187–211 (2005)
- 14. Mehrholz, J., Elsner, B., Werner, C., Kugler, J., Pohl, M.: Electromechanical-assisted training for walking after stroke updated evidence. Stroke **44**(10), e127–e128 (2013)
- 15. Hesse, S., Werner, C.: Connecting research to the needs of patients and clinicians. Brain Res. Bull. **78**(1), 26–34 (2009)
- 16. Fasoli, S.E., Ladenheim, B., Mast, J., Krebs, H.I.: New horizons for robot-assisted therapy in pediatrics. Am. J. Phys. Med. Rehabil. **91**(11) S280–S289 (2012)
- 17. Borggraefe, I., Schaefer, J.S., Klaiber, M., et al.: Robotic-assisted treadmill therapy improves walking and standing performance in children and adolescents with cerebral palsy. Eur. J. Paediatr. Neurol. **14**(6) 496–502 (2010)
- 18. Borggraefe, I., Kiwull, L., Schaefer, J.S., et al.: Sustainability of motor performance after robotic-assisted treadmill therapy in children: an open, non-randomized baseline-treatment study. Eur. J. Phys. Rehabil. Med. **46**(2), 125–131 (2010)
- 19. Druzbicki, M., Rusek, W., Snela, S., et al.: Functional effects of robotic-assisted locomotor treadmill therapy in children with cerebral palsy. J. Rehabil. Med. **45**(4) 358–363 (2013)
- 20. Schroeder, A.S., Von Kries, R., Riedel, C., et al.: Patient-specific determinants of responsiveness to robot-enhanced treadmill therapy in children and adolescents with cerebral palsy. Dev. Med. Child Neurol. **56**(12) 1172–1179 (2014)
- 21. Hanna, S.E., Bartlett, D.J., Rivard, L.M., Russell, D.J.: Reference curves for the Gross Motor Function Measure: percentiles for clinical description and tracking over time among children with cerebral palsy. Phys. Ther. **88**(5) 596–607 (2008)
- 22. Lotze, M., Braun, C., Birbaumer, N., Anders, S., Cohen, L.G.: Motor learning elicited by voluntary drive. Brain **126**(4) 866–872 (2003)
- 23. Hidler, J.M., Wall, A.E.: Alterations in muscle activation patterns during robotic-assisted walking. Clin. Biomech. **20**(2) 184–193 (2005)
- 24. Israel, J.F., Campbell, D.D., Kahn, J.H., Hornby, T.G.: Metabolic costs and muscle activity patterns during robotic-and therapist-assisted treadmill walking in individuals with incomplete spinal cord injury. Phys. Ther. **86**(11) 1466–1478 (2006)
- 25. Schuler, T.A., Müller, R., Van Hedel, H.J.A.: Leg surface electromyography patterns in children with neuro-orthopedic disorders walking on a treadmill unassisted and assisted by a robot with and without encouragement. J. Neuroeng. Rehabil. **10**(1), 78 (2013)
- 26. Schuler, T., Brütsch, K., Müller, R., et al.: Virtual realities as motivational tools for robotic assisted gait training in children: a surface electromyography study. NeuroRehabilitation **28**(4), 401–411 (2011)
- 27. Brütsch, K., Koenig, A., Zimmerli, L., et al.: Virtual reality for enhancement of robot-assisted gait training in children with neurological gait disorders. J. Rehabil. Med. **43**(6) 493–499 (2011)
- 28. Leiper, C.I., Miller, A., Lang, J., Herman, R.: Sensory feedback for head control in cerebral palsy. Phys. Ther. **61**, 512–518 (1981)
- 29. Harris, F.A.: Inapproprioception: a possible sensory basis for athetoid movements. Phys. Ther. **51**, 761–770 (1971)
- 30. Yucha, C., Montgomery, D.: Evidence-Based practice in biofeedback and neurofeedback. Assoc. Appl. Psychophysiol. Biofeedback Inc. (2008)
- 31. Middaugh, S.J.: Electromyographic feedback for evaluation and neuromuscular re-education in cerebral palsy. Biofeedback **35**(1), 27–32 (2007)
- 32. Nichols, D.S.: Balance retraining after stroke using force platform biofeedback. Phys. Ther. **77**, 553–558 (1997)
- 33. Kavanagh, J.J., Menz, H.B.: Accelerometry: a technique for quantifying movement patterns during walking. Gait Posture **28**, 1–15 (2008)
- 34. Crowell, H.P., Milner, C.E., Hamill, J., Davis, I.S.: Reducing impact loading during running with the use of real-time visual feedback. J. Orthop. Sports Phys. Ther. **40**, 206 (2010)
- 35. Giggins, O., Kelly, D., Caulfield, B.: Evaluating rehabilitation exercise performance using a single inertial measurement unit. In: 7th International Conference on Pervasive Computing Technologies for Healthcare (PervasiveHealth), pp. 49–56 (2013)
- 36. Wooldridge, C.P., Russell, G.: Head position training with the cerebral palsied child: an application of biofeedback techniques. Arch. Phys. Med. Rehabil. **57**, 407–414 (1976)
- 37. Bertoti, D.B., Gross, A.L.: Evaluation of biofeedback seat insert for improving active sitting posture in children with cerebral palsy. Phys. Ther. **68**(7), 1109–1113 (1988)
- 38. Nash, J., Neilson, P.D., ODwyer, N.J.: Reducing spasticity to control muscle contracture of children with cerebral palsy. Dev. Med. Child. Neurol. **31**(4), 471–480 (1989)
- 39. Bloom, R., Przekop, A., Sanger, T.D.: Prolonged electromyogram biofeedback improves upper extremity function in children with cerebral palsy. J. Child Neurol. (2010). doi[:10.1177/](http://dx.doi.org/10.1177/0883073810369704) [0883073810369704](http://dx.doi.org/10.1177/0883073810369704)
- 40. Bolek, J.E., Mansour, L., Sabet, A.: Enhancing proper sitting position using a new sEMG protocol, the Minimax procedure, with Boolean logic. Appl. Psychophys. Biofeedback **26**(1), 9–16 (2001)
- 41. Huang, H., Wolf, S.L., He, J.: Recent developments in biofeedback for neuromotor rehabilitation. JNER (2006). doi[:10.1186/1743-0003-3-11](http://dx.doi.org/10.1186/1743-0003-3-11)
- 42. Fluet, G.G., Qiu, Q., Kelly, D., et al.: Interfacing a haptic robotic system with complex virtual environments to treat impaired upper extremity motor function in children with cerebral palsy. Dev. Neurorehabil. (2010). doi[:10.3109/17518423.2010.501362](http://dx.doi.org/10.3109/17518423.2010.501362)
- 43. Yoo, J.W., Lee, D.R., Sim, Y.J., et al.: Effects of innovative virtual reality game and EMG biofeedback on neuromotor control in cerebral palsy. Biomed. Mater. Eng. (2014). doi[:10.](http://dx.doi.org/10.3233/BME-141188) [3233/BME-141188](http://dx.doi.org/10.3233/BME-141188)
- 44. Sukal-Moulton, T., Clancy, T., Zhang, L.Q., Gaebler-Spira, D.: Clinical application of a robotic ankle training program for cerebral palsy compared to the research laboratory application: does it translate to practice? Arch. Phys. Med. Rehabil. doi[:10.1016/j.apmr.2014.04.010](http://dx.doi.org/10.1016/j.apmr.2014.04.010)
- 45. You, S.H., Jang, S.H., Kim, Y.H., et al.: Case report Cortical reorganization induced by virtual reality therapy in a child with hemiparetic cerebral palsy. Dev. Med. Child. Neurol. **47**(9), 628–635 (2005)
- 46. Rizzo, A.A., Strickland, D., Bouchard, S.: The challenge of using virtual reality in telerehabilitation. Telemed. J. E-Health **10**, 18495 (2004)
- 47. Lupton, D., Seymour, W.: Technology, selfhood and physical disability. Soc. Sci. Med. **50**, 162–185 (2000)
- 48. Golomb, M.R., McDonald, B.C., Warden, S.J., et al.: In-home virtual reality videogame telerehabilitation in adolescents with hemiplegic cerebral palsy. Arch. Phys. Med. Rehabil. (2010). doi[:10.1016/j.apmr.2009.08.153](http://dx.doi.org/10.1016/j.apmr.2009.08.153)
- 49. Huber, M., Rabin, B., Docan, C., et al.: PlayStation 3-based tele-rehabilitation for children with hemiplegia. Virtual Rehabil. **2008**, 105–112 (2008)
- 50. Tam, C., Schwellnus, H., Eaton, C., et al.: Movement-to-music computer technology: a developmental play experience for children with severe physical disabilities. Occup. Ther. Int. **14**(2), 99–112 (2007)
- 51. Li, W., Lam-Damji, S., Chau, T., Fehlings, D.: The development of a home-based virtual reality therapy system to promote upper extremity movement for children with hemiplegic cerebral palsy. Technol. Disabil. **21**(3), 107–113 (2009)
- 52. Sandrini, M., Cohen, L.G.: Chapter 40—noninvasive brain stimulation in neurorehabilitatio. In: Lozano, A.M., Hallett, M. (eds.) Handbook of Clinical Neurology, pp. 499–524. Elsevier, a (2013). doi[:10.1016/B978-0-444-53497-2.00040-1](http://dx.doi.org/10.1016/B978-0-444-53497-2.00040-1)
- 53. Paulus, W., Peterchev, A.V., Ridding, M.: Chapter 27—transcranial electric and magnetic stimulation: technique and paradigms. In: Lozano, A.M., Hallet, M. (eds.) Handbook of Clinical Neurology, pp. 329–342. Elsevier (2013). doi[:10.1016/B978-0-444-53497-2.00027-9](http://dx.doi.org/10.1016/B978-0-444-53497-2.00027-9)
- 54. Kuo, M., Paulus, W., Nitsche, M.A.: Therapeutic effects of non-invasive brain stimulation with direct currents (tDCS) in neuropsychiatric diseases. NeuroImage **85**, Part 3, 948–960 (2014). doi[:10.1016/j.neuroimage.2013.05.117](http://dx.doi.org/10.1016/j.neuroimage.2013.05.117)
- 55. Butler, A.J., Shuster, M., O'Hara, E., Hurley, K., Middlebrooks, D., Guilkey, K.: A metaanalysis of the efficacy of anodal transcranial direct current stimulation for upper limb motor recovery in stroke survivors. J. Hand Ther.: Off. J. Am. Soc. Hand Ther. **26**(2), 162–170 (2013). doi[:10.1016/j.jht.2012.07.002](http://dx.doi.org/10.1016/j.jht.2012.07.002)
- 56. Gunduz, A., Kumru, H., Pascual-Leone, A.: Outcomes in spasticity after repetitive transcranial magnetic and transcranial direct current stimulations. Neural Regen. Res. **9**(7), 712–718 (2014). doi[:10.4103/1673-5374.131574](http://dx.doi.org/10.4103/1673-5374.131574)
- 57. Terreaux, L., Gross, R., Leboeuf, F., Desal, H., Hamel, O., Nguyen, J.P., Buffenoir, K.: Benefits of repetitive transcranial magnetic stimulation (rTMS) for spastic subjects: clinical, functional, and biomechanical parameters for lower limb and walking in five hemiparetic patients. The-ScientificWorldJournal **2014**, 350–389 (2014). doi[:10.1155/2014/389350](http://dx.doi.org/10.1155/2014/389350) [doi]
- 58. Valle, A.C., Dionisio, K., Pitskel, N.B., Pascual-Leone, A., Orsati, F., Ferreira, M.J., Fregni, F.: Low and high frequency repetitive transcranial magnetic stimulation for the treatment of spasticity. Dev. Med. Child. Neurol. **49**(7), 534–538 (2007). doi:DMCN534 [pii]
- 59. Collange Grecco, L.A., Duarte, N.A.C., Zanon, N., Galli, M., Fregni, F., Oliveira, C.S.: Effect of a single session of transcranial direct-current stimulation on balance and spatiotemporal gait

variables in children with cerebral palsy: a randomized sham-controlled study. Braz. J. Phys. Ther. **18**(5), 419–427 (2014). doi[:10.1590/bjpt-rbf.2014.0053](http://dx.doi.org/10.1590/bjpt-rbf.2014.0053)

- 60. Collange Grecco, L.A., Carvalho Duarte, N.D.A., Mendonca, M.E., Cimolin, V., Galli, M., Fregni, F., Oliveira, C.S.: Transcranial direct current stimulation during treadmill training in children with cerebral palsy: a randomized controlled double-blind clinical trial. Res. Dev. Disabil. **35**(11), 2840–2848 (2014). doi[:10.1016/j.ridd.2014.07.030](http://dx.doi.org/10.1016/j.ridd.2014.07.030)
- 61. Carvalho, Duarte, N.D.A., Collange Grecco, L.A., Galli, M., Fregni, F, Oliveira, C.S.: Effect of transcranial direct-current stimulation combined with treadmill training on balance and functional performance in children with cerebral palsy: a double-blind randomized controlled trial. Plos One **9**(8), e105777 (2014). doi[:10.1371/journal.pone.0105777](http://dx.doi.org/10.1371/journal.pone.0105777)
- 62. Gillick, B.T., Kirton, A., Carmel, J.B., Minhas, P., Bikson, M.: Pediatric stroke and transcranial direct current stimulation: methods for rational individualized dose optimization. Front. Human Neurosci. **8**, 739 (2014). doi[:10.3389/fnhum.2014.00739](http://dx.doi.org/10.3389/fnhum.2014.00739)
- 63. Krishnan, C., Santos, L., Peterson, M.D., Ehinger, M.: Safety of noninvasive brain stimulation in children and adolescents. Brain Stimul. **8**(1), 76–87 (2015). doi[:10.1016/j.brs.2014.10.012](http://dx.doi.org/10.1016/j.brs.2014.10.012)
- 64. Mozaffarian, D., Benjamin, E.J., Go, A.S., Arnett, D.K., Blaha, M.J., Cushman, M., et al.: Heart disease and stroke statistics-2015 update: a report from the American Heart Association Circulation. **131**(4), e29–322 (2015)
- 65. Watkins, C.L., Leathley, M.J., Gregson, J.M., Moore, A.P., Smith, T.L., Sharma, A.K.: Prevalence of spasticity post stroke. Clin. Rehabil. **16**(5), 515–522 (2002)
- 66. Dipietro, L., Krebs, H.I., Fasoli, S.E., Volpe, B.T., Hogan, N.: Submovement changes characterize generalization of motor recovery after stroke. Cortex **45**(3), 318–324 (2009)
- 67. Michaelsen, S.M., Levin, M.F.: Short-term effects of practice with trunk restraint on reaching movements in patients with chronic stroke: a controlled trial Stroke. **35**(8), 1914–1919 (2004)
- 68. Levin, M.F.: Interjoint coordination during pointing movements is disrupted in spastic hemiparesis. Brain **119**(1), 281–294 (1996)
- 69. RobyBrami, A., Feydy, A., Combeaud, M., Biryukova, E., Bussel, B., Levin, M.: Motor compensation and recovery for reaching in stroke patients. Acta Neurol Scand. **107**(5), 36981 (2003)
- 70. Roby-Brami, A., Fuchs, S., Mokhtari, M., Bussel, B.: Reaching and grasping strategies in hemiparetic patients. Motor Control. **1**(72), 91 (1997)
- 71. Lo, A.C., Guarino, P.D., Richards, L.G., Haselkorn, J.K., Wittenberg, G.F., Federman, D.G., et al.: Robot-assisted therapy for long-term upper-limb impairment after stroke. N. Engl. J. Med. **362**(19), 1772–1783 (2010)
- 72. Takahashi, C., Der-Yeghiaian, L., Le, V., Cramer, S.: A robotic device for hand motor therapy after stroke. In: 9th International Conference on Rehabilitation Robotics, ICORR 2005. IEEE (2005)
- 73. Bovolenta, F., Goldoni, M., Clerici, P., Agosti, M., Franceschini, M.: Robot therapy for functional recovery of the upper limbs: a pilot study on patients after stroke. J. Rehabil. Med. **41**(12), 971–975 (2009)
- 74. Schabowsky, C.N., Godfrey, S.B., Holley, R.J., Lum, P.S.: Development and pilot testing of HEXORR: hand EXOskeleton rehabilitation robot. J. Neuroeng. Rehabil. **7**(1), 36 (2010)
- 75. Kutner, N.G., Zhang, R., Butler, A.J.,Wolf, S.L., Alberts, J.L.: Quality-of-life change associated with robotic-assisted therapy to improve hand motor function in patients with subacute stroke: a randomized clinical trial. Phys.Ther. **90**(4), 493–504 (2010)
- 76. Koeneman, E., Schultz, R., Wolf, S., Herring, D., Koeneman, J.: A pneumatic muscle hand therapy device. In: 26th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, IEMBS'04. IEEE (2004)
- 77. Sugar, T.G., He, J., Koeneman, E.J., Koeneman, J.B., Herman, R., Huang, H., et al.: Design and control of RUPERT: a device for robotic upper extremity repetitive therapy. IEEE Trans. Neural Syst. Rehabil. Eng. **15**(3), 336–346 (2007)
- 78. Krebs, H.I., Ferraro, M., Buerger, S.P., Newbery, M.J., Makiyama, A., Sandmann, M., et al.: Rehabilitation robotics: pilot trial of a spatial extension for MIT-Manus. J. Neuroeng. Rehabil. **1**(1), 5 (2004)
- 79. Smania, N., Bonetti, P., Gandolfi, M., Cosentino, A., Waldner, A., Hesse, S., Werner, C., Bisoffi, G., Geroin, C., Munari, D.: Improved gait after repetitive locomotor training in children with cerebral palsy. Am. J. Phys. Med. Rehabil. **90**(2), 137–149 (2011)
- 80. Frizera, A., Raya, R., Pons, J.L., Abellanas, A., Ceres, R.: The smart walkers as geriatric assistive device. In: 6th International Conference of the International Society for Gerontechnology (2008)
- 81. Fasoli, S.E., Fragala-Pinkham, M., Hughes, R., et al.: Upper limb robotic therapy for children with hemiplegia. Am. J. Phys. Med. Rehabil. **87**(11), 929–936 (2008)
- 82. Wolf, S.L., Winstein, C.J., Miller, J.P., Thompson, P.A., Taub, E., Uswatte, G., et al.: Retention of upper limb function in stroke survivors who have received constraint-induced movement therapy: the EXCITE randomised trial. Lancet Neurol. **7**(1), 33–40 (2008)
- 83. Krakauer, JW.: Arm function after stroke: from physiology to recovery. In: Seminars in Neurology. Thieme-Stratton Inc., New York, c1981 (2005)
- 84. Levin, M.F., Kleim, J.A., Wolf, S.L.: What do motor "recovery" and "compensation" mean in patients following stroke? Neurorehabil. Neural Repair **23**(4), 313–319 (2009)
- 85. Wright, Z.A., Rymer,W.Z., Slutzky, M.W.: Reducing abnormal muscle coactivation after stroke using a myoelectric-computer interface: a pilot study. Neurorehabil. Neural Repair **28**(5), 443– 451 (2013)
- 86. Song, R., Yu, K.: EMG and kinematic analysis of sensorimotor control for patients after stroke using cyclic voluntary movement with visual feedback. J. Neuroeng. Rehabil. **10**, 18 (2013)
- 87. Duff, M., Chen, Y., Cheng, L., Liu, S.M., Blake, P., Wolf, S.L., et al.: Adaptive mixed reality rehabilitation improves quality of reaching movements more than traditional reaching therapy following stroke. Neurorehabil. Neural Repair **27**(4), 306–315 (2013)
- 88. Faghri, P.D., Rodgers, M.M., Glaser, R.M., Bors, J.G., Ho, C., Akuthota, P.: The effects of functional electrical stimulation on shoulder subluxation, arm function recovery, and shoulder pain in hemiplegic stroke patients. Arch. Phys. Med. Rehabil. **75**(1), 73–79 (1994)
- 89. Hummelsheim, H., Maier-Loth, M.L., Eickhof, C.: The functional value of electrical muscle stimulation for the rehabilitation of the hand in stroke patients. Scand J. Rehabil. Med. **29**(1), 3–10 (1997)
- 90. Miyara, K., Matsumoto, S., Uema, T., Hirokawa, T., Noma, T., Shimodozono, M., et al.: Feasibility of using whole body vibration as a means for controlling spasticity in post-stroke patients: a pilot study. Complement. Ther. Clin. Pract. **20**(1), 70–73 (2014)
- 91. Binder, C., Kaya, A.E., Liepert, J.: Vibration prolongs the cortical silent period in an antagonistic muscle. Muscle Nerve. **39**(6), 776–780 (2009)
- 92. Cordo, P., Lutsep, H., Cordo, L., Wright, W.G., Cacciatore, T., Skoss, R.: Assisted movement with enhanced sensation (AMES): coupling motor and sensory to remediate motor deficits in chronic stroke patients. Neurorehabil. Neural Repair **23**(1), 67–77 (2009)
- 93. Ruck, J., Chabot, G., Rautch, F.: Vibration treatment in cerebral palsy: a randomized controlled pilot study. J. Musculoskelet. Neuronal Interact. **10**(1), 77–83 (2010)
- 94. Katusic, A., Alimovic, S., Mejaski-Bosnjak, V.: The effect of vibration therapy on spasticity and motor function in children with cerebral palsy: a randomized controlled trial. NeuroRehabilitation **32**(1), 1–8 (2013). doi[:10.3233/NRE-130817](http://dx.doi.org/10.3233/NRE-130817)
- 95. Sanger, T.D., Delgado, M.R., Gaebler-Spira, D., Hallett, M., Mink, J.W.: Classification and definition of disorders causing hypertonia in childhood. Pediatrics **111**(1), e89–97 (2003)
- 96. Rivera, D.R., Hartzema, A.G.: Pediatric exclusivity: evolving legislation and novel complexities within pediatric therapeutic development. Ann. Pharmacother. (2013)
- 97. Meyer-Heim, A., van Hedel, H.J.A.: Robot-assisted and computer-enhanced therapies for children with cerebral palsy: current state and clinical implementation. Semin. Pediatr. Neurol. **20**(2) 139–145 (2013)