Robot-assisted gait training for stroke patients: current state of art and perspectives

Giovanni Morone, Stefano Paolucci, Andrea Cherubini, Domenico de Angelis, Vincenzo Venturiero, Paola Coiro, Marco Iosa

Robot-assisted gait training for stroke patients: current state of art and perspectives

Morone G, Paolucci S, Cherubini A, De Angelis D, Venturiero V, Coiro P, Iosa M

Abstract

In this review, we give a brief outline of robot-mediated gait training for stroke patients, as an important field emerging in rehabilitation. Technological innovations are allowing rehabilitation to move towards more integrated processes, with improved efficiency and less long-term impairments. In particular, robot-mediated neurorehabilitation is a rapidly advancing field, which uses robotic systems, often coupled with virtual reality haptic interfaces and emerging theories in neuroscience, to define new methods for treating neurological injuries such as stroke, spinal cord injury, and traumatic brain injury. The use of robots in gait training can enhance rehabilitation, following neuroscientific principles that justify the use of the robot. The field of robot-mediated neurorehabilitation brings challenges to both bioengineering and clinical practice. This paper reviews the state of art (including commercially available systems) and perspectives of robotics in post-stroke rehabilitation for walking recovery. A critical revision, including the problems at stake regarding robotic clinical use will also be presented.

INTRODUCTION

Stroke is a leading cause of movement disability in the U.S. and Europe [1]. The World Health Organization (WHO) estimates that in Europe stroke events will increase by 30% between 2000 and 2025 [2]. The proportion of patients achieving independence in self-care by one year after a stroke ranges from around 60% to 83% [3] and between 10% and 15% of survivors resident in a clinical institution during one year. Concerning mobility recovery, a 2008 study showed that about 50% of patients with stroke leave the rehabilitation hospital on a wheelchair, less than 15% are able to walk indoor without aids, less than 10% are outdoor, and less than 5% are able to climb stairs [4]. Post stroke rehabilitation demand will increase in the next future, leading to stronger pressure on healthcare budgets. For example, in the USA, the estimated direct and indirect cost of stroke in 2010 was $73.7 billion, and the mean lifetime cost of ischemic stroke was estimated at $140.048 [5]. For ethical reasons, in adjunction to the above reported economical reasons, an increase of rehabilitation efficacy is mandatory. New technologies, early discharge after intensive training, home rehabilitation are among the innovations proposed for achieving this. The current literature suggests that rehabilitative interventions are more effective if they ensure early, intensive, task-specific and multisensory stimulation, with both bottom-up and top-down integration, favoring brain plasticity [REF revisione belda lois?, Masiero et al Expert Review]. In fact, there is growing evidence that the motor system is plastic following stroke and that motor training can aid, particularly in the first 3 months [9]. Neuroplasticity can lead to recovery mechanisms and functional adaptation resulting from global changes in neuronal organization. It is associated with changes in excitatory/inhibitory balance and the spatial extent and activation of cortical maps and structural remodeling [10].

The present review aims at exploiting, following user-centered principles, the clinical efficacy of the robotic devices and their role in the next generation of rehabilitation protocols.

What can a robot add to a walking neurorehabilitation program?
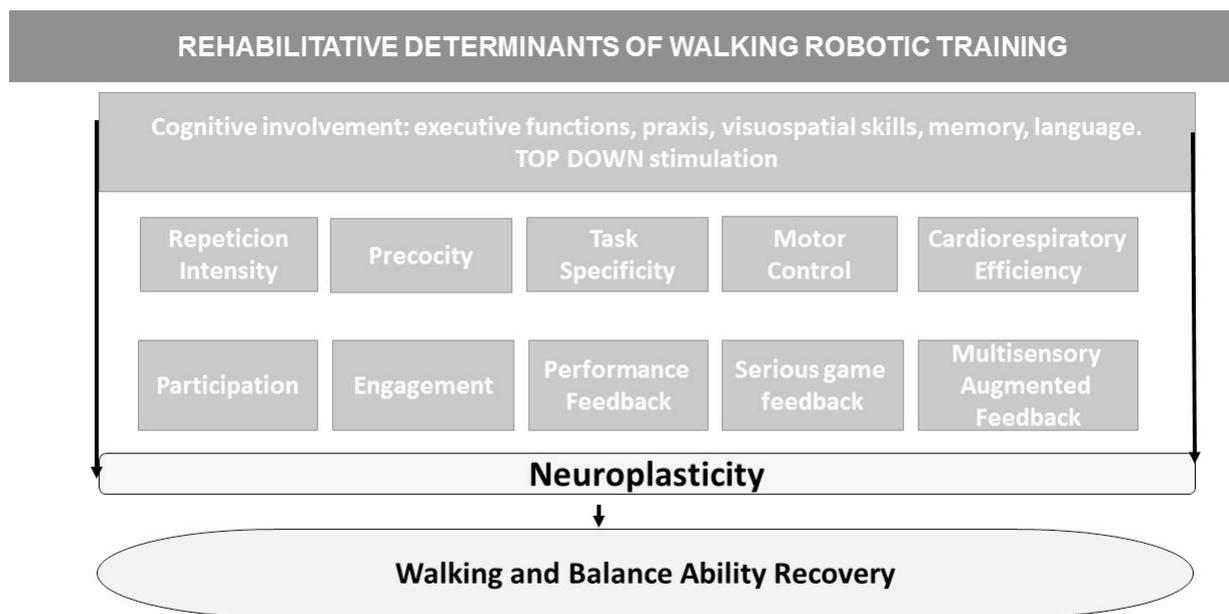
One of the main goals for stroke patients is the return to independency in walking. In the light of the recent developments in rehabilitation technology, it is necessary to understand what role a robot has in optimizing walk recovery.

New findings in neuroscience and translational researches from animal models showed that neurorehabilitation requires the following: increasing the therapy dosage and intensity [11], high repetitiveness [12], task-oriented exercises [13] and combination of top-down and bottom-up approaches (e.g., non-invasive brain stimulation with robot therapy as in [14 krakauer].

As aforementioned, the best time for boosting plasticity-dependent recovery is within 3 months from the stroke event. On the other hand, animal models have shown that an increased therapy within 5 days from the stroke can enlarge brain damage and favor spasticity [14 krakauer].

Robotic systems are well suited to produce intensive, task-oriented motor training for moving the patient's limbs under the supervision/help of a therapist, as part of an integrated set of rehabilitation tools that would include other new devices [seven capital devices] as well as simpler and more traditional ones [15]. In this context, robots would enhance conventional post-stroke rehabilitation via intense and task oriented training.

Robotic rehabilitation versus or together with Physiotherapy?

A recently updated Cochrane revision of 17 trials, including 837 participants, showed that robotic gait training combined with physiotherapy might improve recovery of independent walking in post-stroke patients. This review also highlighted that determining the frequency, duration, and timing (after stroke) for the robotic gait training to be the most effective, is still an open problem. Assessing the benefit duration also requires further research.[33]

The use of robots should not replace the neurorehabilitation therapy performed by a physiotherapist. Robots, as all technological devices, must be considered as a tool in the hands of the physiotherapist and never rehabilitative "per se". [editorial Morone] In fact, the robot can alleviate all labor-intensive phases of physical rehabilitation, hence allow the physiotherapist to focus on functional rehabilitation during individual training, and to supervise several patients at the same time during robot-assisted therapy sessions. With this approach, the expertise and time of physiotherapists is optimized, increasing at the same time the rehabilitation program efficacy and the efficiency [17].

With respect to conventional therapy alone, the addition of robotic intervention brings another important advantage: it allows an on-line and off-line instrumented, quantitative (hence, objective) evaluation of several parameters related to patient performance. These include: range of motion, velocity, smoothness of movements, amount of forces, etc.

Thus, robotic systems may be used not only to produce simple and repetitive stereotyped movement patterns, as in the case of most of the existing devices, but also to generate a more complex, controlled multisensory stimulation of the patient. This includes, but is not limited to, the assessment of the patient's performance with a biofeedback or with a report. The impact of rehabilitation technology could be improved by making the nervous system experience "real" activity-related sensorimotor input during upper limb training [9]. This would produce a level of interaction and stimulation that is higher than that experienced during usual hand-over-hand therapy.

The three laws of neurorobots for walking recovery

A recent review, inspired by Isaac Asimov's famous three laws of robotics and based on the most recent studies in neurorobotics, proposed 3 similar laws valid for neurorehabilitation robots. The objective is to propose guidelines for designing and using such robots [Iosa et al. The 3 laws of neurorobotics]. These laws were driven by the ethical need for safe and effective robots, by the redefinition of their role as therapist helpers, and by the need for clear and transparent human-machine interfaces. The three laws are:

1) a neurorobot shall not injure a patient or let him/her come to harm;

2) a neurorobot must obey the therapist's orders, except if such orders is in conflict with the First Law;

3) a neurorobot must adapt its behaviour to the patients' abilities in a transparent way, except if this is in conflict with the First or Second law.

Although the first law may seem obvious, in [Iosa et al. The 3 laws of neurorobotics] the term "harm" has been redefined to include all possible damage for patients, including time wasted on an ineffective, unefficient or even detrimental robot. In fact, many robots are commercialized without proving their quality. Hence, this law implies that robot usage should be at least as safe and effective as other treatments, implying that it should have a higher benefit-to-risk ratio than human administered treatments.

The second law recalls that neurorobots are in the first place tools in the hands of therapists, just as medical robots for surgeons. Robots should "disobey" clinicians' orders only if their sensors highlight that a potential risk for the patient can be provoked by that order. This highlights the importance of sensors, which is at the base of the adaptability and autonomy of any robotic system.

This last aspect is reinforced in the third law, that claims the importance of artificial intelligence as a support for human intelligence, with real-time adaptation to the continuously monitored and measured patient's ability.

Theoretical and practical robotic support to gait rehabilitation

A common feature of gait training robots is the possibility to support (partially or totally) the body weight and the movement of patients.

Body weight support seems to be the condition sine qua non for facilitating gait recovery with robotic devices [REF Iosa 2011]. Other desired features of rehabilitation robots are: their ability to provide therapy for long periods, in a consistent and precise manner, without causing fatigue; their adaptability to perform in different functional modes and with various automated functions [16]. To restore gait, in fact, clinicians prefer a task-specific repetitive approach [27] and in recent years better outcomes have been achieved with higher intensities of walking practice programs [28,29].

Another role of robotic devices is to facilitate the administration, to non-ambulatory patients, of intensive and highly repetitive training of complex gait cycles, something a single therapist cannot easily do alone.

With respect to treadmill training with partial body weight support, yet another advantage of these robotic devices may be the reduced effort for therapists: they no longer need to set the paretic limbs or assist trunk movements [32].

A secondary but important aspect related to body weight support and to robotic rehabilitation in general is the possibility of favoring the restoration of an adequate level of cardiorespiratory efficiency. Despite this aspect is rarely taken into account in evaluating robotic efficiency, De Lussu et al 2014 [REF JNER De Lussu et al 2014] have shown that robotic gait training reduces energy-consumption and cardiorespiratory load. In fact, for severely impaired neurological patients, robotic walk training allows an early verticalization without the risk of increasing spasticity on antigravitational muscles, hence avoiding deconditioning that would worsen cardiologic comorbidities. This is a very important feature, if one considers that over 85% of stroke patients suffer from cardiovascular comorbidities [REF De lussu].

Energy consumption and cardiorespiratory load during walking with robot-assistance seems to depend not only body-weight support, but also on factors such as : robot type, walking speed, and amount of effort. These parameters could be adjusted in robotic rehabilitation to make it more or less energy-consuming and stressful for the cardiorespiratory system. [*Disabil Rehabil Assist Technol. 2016 Oct 20:1-15. The immediate effects of robot-assistance on energy consumption and cardiorespiratory load during walking compared to walking without robot-assistance: a systematic review.Lefeber N1,2,3, Swinnen E1,2,3, Kerckhofs E1,2,3.*]

Ghost in the shell: the neglected role of psychological aspects in robotic rehabilitation

The patients' engagement and participation in exercises is considered as a key factor to increase rehabilitation performances and therefore boost plasticity [REF]. During robotic assisted therapy, this can be achieved via extrinsic feedback of serious game scenarios, where the known scores assess the patients' performance [19]. The acceptance of robotic technology by patients and physiotherapists may be an issue per se, although there is no evidence of this for the devices developed to date.

Nevertheless, not all patients, especially the elderly, accept to be treated with a robot, and [Bragoni et al.] has shown that anxiety may reduce the efficacy of robotic walking training .

In the future, the cultural gap between technology providers, rehabilitation professionals, and end users should be filled thanks to: 1) dissemination of technological knowledge, 2) diffusion of increasingly user-friendly and safer technology.

Machines for walking rehabilitation

A complete review of all the machines developed worldwide is very difficult to realize, also because of the number of prototypes tested within the scientific community.

Firstly, it is necessary to clarify the difference between a robot and other electromechanical devices. The Robot Institute of America defines 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" [REF 9 di Seven capital devices]. Hence, in contrast with the popular – and erroneous - perception (which includes, e.g., kitchen aids), a robot is by definition capable of mobility, with various levels of autonomy.

Based on this definition, an incomplete list of commercial robot walk trainers includes: Gait Trainer (RehaStim, Berlin), Geo (RehaStim, Berlin), Lokomat (Hocoma, Switzerland); Tibion Bionic Leg (Tibion Bionic Technologies, USA), eLEGS (UC Berkeley/Ekso Bionics, USA), ReWalk (Argo Medical Technologies, Israel), REX (Rex Bionics, New Zealand). Another list may include single or multiple prototypes such as: Lopes, Lopes 2 (developed at the University of Twente, The Netherlands), Knexo (for single leg rehabilitation training, Vrije Univeristy Brussel, Belgium), Alex (for single leg rehabilitation training, University of Delaware, USA), Mindwalker (assistive exoskeleton for spinal cord injured patients, Delft University), VanderBilt Exoskeleton (VanderBilt University, USA), Hercule (CEA-LIST/R3BD, France).

These devices can be classified according to the motion they apply to the patient's body. For instance, "Exoskeletons" move all joints, whereas "End-effector robots" move only the feet, or if they move patients, "static" vs. "dynamic" devices [Iosa et al. 2012 Seven Capital Devices].

Exoskeletons are outfitted with programmable drives or passive elements, which move the limb joints during training. For example, during robotic walk training, ankles, knees and hips can be controlled during the gait phases.

On end-effector robots, the patient's extremities (feet) are placed on a support (foot-plate), that imposes specific trajectories, simulating the stance and swing phases during gait training.

Among static devices, id est devices designed for performing motion in place, and not around the environment, the most common ones are the Lokomat, a robotic exoskeleton, the Gait Trainer and GEO, both electromechanical end-effectors.

Lokomat [58] is a robotic gait orthosis combined with a harness-supported body weight system, used in combination with a treadmill. The main difference with treadmill training is that the patient's legs are guided according to a pre-programmed gait pattern.

Gait Trainer is based on a double crank and rocker gear system. In contrast with treadmills, it consists of two foot-plates positioned on two bars, two rockers and two cranks, which provide the propulsion. The foot-plates symmetrically generate the stance and swing phases [30]. Again, the main difference with treadmill training is that gait training is automated and supported by an electromechanical solution. GEO System (Reha Technology AG; Olten, Switzerland; eo comes from Latin for "I walk") is based on the end-effector principle and was designed to minimize the therapeutic effort needed for relearning walking and stair climbing. The trajectories of the foot-plates and the vertical and horizontal movements of the centre of mass are fully programmable. The device is an evolution of the HapticWalker, a research prototype with limited clinical applicability because of its dimensions [62].

In recent years, extensive research efforts have been dedicated to dynamic exoskeletons for neurorehabilitation, as well as military applications (e.g., to augment the soldiers' walking functions). Robotic hip-knee-ankle-foot exoskeletal orthoses have become commercially available and may post-stroke patients to stand and walk again. These devices also have applications beyond mobility, e.g., exercise, amelioration of secondary complications related to lack of ambulation, and promotion of neuroplasticity. Wearable exoskeletons are recently developed technologies that allow walking on a hard flat surface (chen g et al 2013 review lower extremity robot). The device incorporates the actuator that moves the patients' leg during the gait cycle, through a pre-programmed and near normal gait cycle. [wereable robot Molteni EJPRM 2017] Preliminary results showed the possibility of performing individual walking training on patients with subacute and chronic stroke. [wereable robot Molteni EJPRM 2017].

Almost all functional exoskeletons rely on additional support aids to assure balance. Healthy users would perform the proper foot placement and other actions to assure balance stability. Instead, impaired people, would need additional means like crutches.

From efficacy for all to all for efficacy

Most studies on walking neurorehabilitation robots focus on their effectiveness, giving controversial results. For instance, [71] showed that patients who receive robot-assisted gait training in combination with physiotherapy gain independent walking more easily than patients trained without these devices. However, clinical trials suggest that manual therapy may still be more effective than robotic gait training both in subacute and in chronic phases [72,73]. The reason may be a reduction in voluntary postural control during robot-assisted gait training, due to the pelvis and trunk restraint coupled with the passive swing assistance provided by the robotic system employed in the studies [72].

In the complex scenario of gait recovery robots, it is fundamental to understand the clinical meaning of each design feature, such as body weight support (a "*conditio sine qua non*"), especially for training non ambulatory patients in an intensive and safe manner [80].

Both end-effectors and exoskeleton robotic devices, have their own strengths and weaknesses. It is therefore important to consider the rationale of the two types of devices and the related benefits or disadvantages of each.

In particular, end-effector walking devices allow the patient to extend his/her knee with more freedom. Also, the task of maintaining balance may be more demanding (since the required degree of balance depends on the harness setup and on whether or not the patient is holding the hand rails). An advantage of exoskeletons is that gait cycles can be controlled more easily. We are not aware of any studies directly comparing different electromechanical devices for gait rehabilitation in patients with a cerebral damage, with exception of a single case report [81].

Interestingly, these two robotic solutions train patients in two different ways in terms of constriction/freedom of patients' ability. For this reason, they should not be seen as alternative, but complementary: each one represents the best option for a specific kind of patient impairment.

It is important to understand how different robotic approaches will respond to different rehabilitation problems and patients (Fig.2), and to all users (patients, therapist, clinicians) needs in general. As affirmed recently by Cochrane [33], it is imperative to define the characteristics of patients that may benefit the most from robotic therapy.

Most studies aim at answering the question: "are robotic devices effective for all kind of post-stroke patients?". However, [Morone 2012] has highlighted the need for changing this question into: "for whom are robotic devices the most effective?". The goal should not be to test the efficacy for all patients, but to dispose of all the possibilities for improving efficacy. For instance, the least affected patients would rather benefit from device-free

conventional overground training, to avoid artificial interventions that may alter recovery of their physiological patterns [Morone 2012].

A key point for the diffusion and correct use of new technologies is to know for which patients and which rehabilitation phase each type of technology is more beneficial. Following this principle, Morone and co-workers found that patients with more severe motor legs impairments are those who benefit the most from robotic-assisted therapy in combination with conventional therapy [82,83]. This finding likely results from the augmented intensity of robotic therapy, as compared to conventional therapy (especially for the most impaired patients). Conversely, patients with a greater voluntary motor function in the affected limb can perform intensive training also during conventional therapy. Neurorehabilitators may prefer less constrained and more variable exercises in these patients. This idea has been confirmed by results showing that in already ambulant patients, over ground walk training is more effective for improving balance and preventing falls [84]. Patients may benefit from machines providing external support, until they recover the capacity of walking over ground, unsupported. Robots can favour this recovery allowing a progressive decrease of external support matching the patients' level of gait dependency [83]. Thus, the question needs to be changed from "Are robotic devices effective for rehabilitation?" to "Who may benefit the most from robotic rehabilitation"?
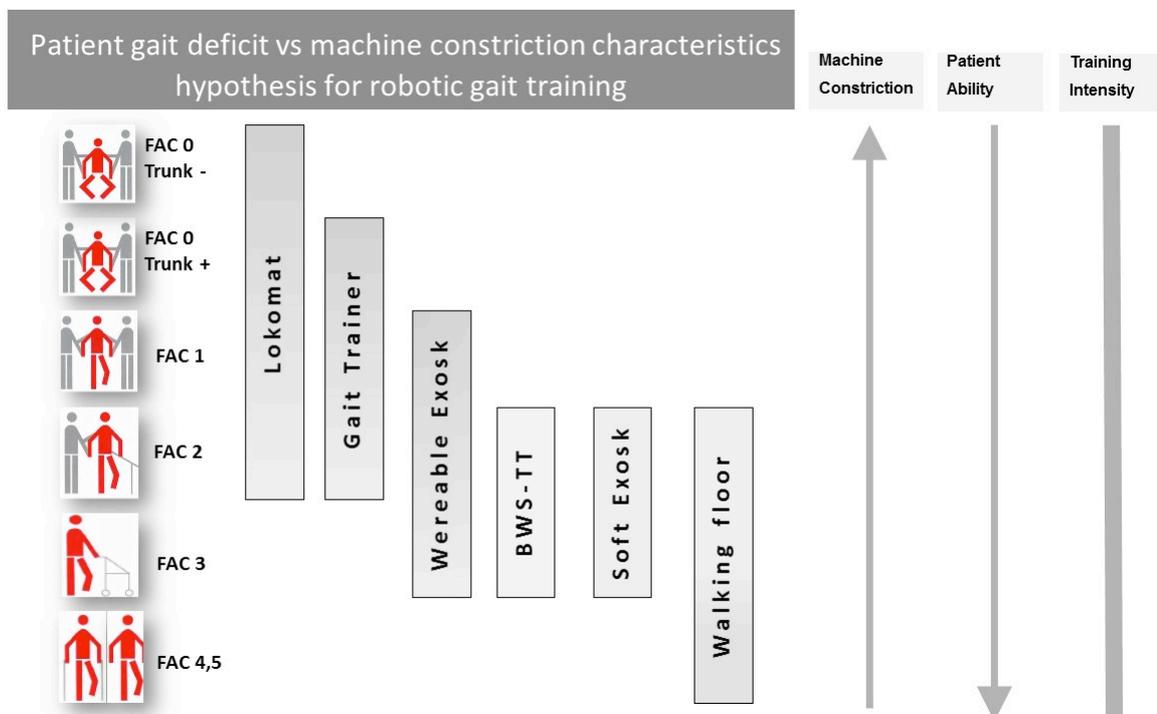

Figure. Theoretical schema combining patient's level of ability with best possible solution in terms of motor constriction.

Current perspective and open problems

According to the present literature, it is not yet clear how different rehabilitation approaches contribute to restorative processes of the central nervous systems after stroke.

Combining different technologies should be a promising approach, where each one facilitates the other. This is the case of vibrational therapy coupled to robotic use [REF] or of non invasive stimulation (tDCS and TMS) associated with robotic walking training [REF]. In particular, non-invasive brain stimulation (transcranial direct current stimulation) associated with robots provided limited results [89,90], unless the parameters were properly tuned according to the candidate patients [91].

At this step, the role of the clinical researcher becomes to investigate if the available robot is effective or not. This corresponds to changing the research question from "is the robotic technology effective?" to "which patients is this technology effective for?" as suggested by Morone et al. [83,97]. This new paradigm will increase robotic effectiveness and diffusion within the rehabilitation team.

Some other points should be considered. Despite most studies claim that robots would increase rehabilitation intensity, repetition of tasks alone is not sufficient to guide neural plasticity *(Plautz et al; 2000)*. Furthermore, most robots replicate physiological patterns, not always achievable by patients. The approach is analogous to training football players with many matches, without focusing on specific aspects, to be improved separately. Actually, robots seem to partially emulate PhT skills, and in general provide constant assistance, without taking into account the patients' ability *(Sanguineti et al; 2009).* Instead, they should be tools in the hands of therapists for improving their skills (as claimed in the three laws of neurorobots [Iosa et al. 2016]).

This leads to the need for active on-board control algorithms combined with functional motor learning tasks, to improve participation, required assistance and error augmentation, *(Krishnan et al; 2013; Wang et al 2009)*

Finally, most of the robots commercialized nowadays are based on the "a priori" idea that walking is an automatic subcortical ability. However, this aspect was recently re-considered:

- from a biomechanical point of view, by reviewing the role of the trunk from a passive (Perry; 1990) to an active actor (Iosa et al. Development and decline of upright gait stability),
- from a neurological point of view, in which the conventional bottom-up approach has been integrated in a Top down approach *(Belda-Lois M; et al 2011; Iosa et al; 2014)*,
- from a neuromechanic point of view, in which structures and functions are strictly connected around specific harmonic points of equilibrium that maximize the efficiency of walking [Iosa et al. 2016 Anthropometry and Golden Ratio; Dzelaidini 2014; Serrao et al. submitted].

Financial disclosure

The authors have no relevant affiliation or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject, matter, or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

References

1. Rosamond W, Flegal K, Furie K *et al.* Heart disease and stroke statistics-2007 update: A report from the American heart association statistics committee and stroke statistics subcommittee. *Circulation*. 115(5), 69–17 (2007).

2. World Health Organization, World health statistics. Epidemiology and Burden of Disease, WHO Geneva (EBD/GPE). http://www.who.int/healthinfo/statistics/bod_cerebrovasculardiseasestroke.pdf accessed 13 february 2017

3. Appelros P, Nydevik I, Viitanen M. Poor outcome after first-ever stroke: predictors for death, dependency, and recurrent stroke within the first year. Stroke. 2003 Jan;34(1):122-6.

4. Paolucci S, Bragoni M, Coiro P, 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. *Cerebrovasc Dis.*26(1),16-22 (2008).

5. Lloyd-Jones D, Adams RJ, Brown TM, *et al.* Writing Group Members; American Heart Association Statistics Committee and Stroke Statis-tics Subcommittee. Heart disease and stroke statistics— 2010 update: a report from the American Heart Associa-tion. *Circulation.*121(7), 46–215 (2010).

6. Masiero S and Carraro E. Upper limb movements and cerebral plasticity in post-stroke rehabilitation. *Aging Clin Exp Res*. 20(1), 103-108 (2008).

7. Wolpert DM, Diedrichsen J, Flanagan JR. Principles of sensorimotor learning. *Nature Rev. Neurosci.* 12(12), 739–751 (2011).

8. Huber D, Gutnisky DA, Peron S, *et al.* Multiple dynamic representations in the motor cortex during sensorimotor learning. *Nature*. 484(7395), 473–478, (2012).

9. Nudo RJ. Postinfarct cortical plasticity and behavioral recovery. *Stroke*, 38(2), 840-845, (2007).

10. Oulad Ben Taib N, Manto M, Laute MA, Brotchi J. The cerebellum modulates rodent cortical motor output after ripetitive somatosensory stimulation. *Neurosurgery*. 56(4): 811-20, (2005).

11. Nelles G. Cortical reorganization – effects of intensive therapy. *Restor Neurol Neurosci*. 22(3-5), 239–244, (2004).

12. Butefisch C, Hummelsheim H, Denzler P, Mauritz KH. Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. *J Neurol Sci*. 130(1), 59–68, (1995).

13. Bayona NA, Bitensky J, Salter K, Teasell R. The role of task-specific training in rehabilitation therapies. *Top Stroke Rehabil*. 12(3): 58–65 (2005).

14. Krakauer JW, Carmichael ST, Corbett D, Wittenberg GF. Getting neurorehabilitation right: what can be learned from animal models? *Neurorehabil Neural Repair*, 26(8):923-31 (2012).

15. Johnson MJ, Feng X, Johnson LM, Winters JM. Potential of a suite of robot/computer-assisted motivating systems for personalized, home-based, stroke rehabilitation. *J Neuroeng Rehabil*. 4:6, (2007).

16. Dobkin BH. Strategies for stroke rehabilitation. *Lancet Neurol*; 3(9): 528–36 (2004).

17. Kahn LE, Lum PS, Rymer WZ, Reinkensmeyer DJ. Robot-assisted movement training for the stroke-impaired arm: Does it matter what the robot does? *J Rehabil Res Dev*. 43(5),619-630, (2006).

18. Wagner TH, Lo AC, Peduzzi P, *et al.* An economic analysis of robot-assisted therapy for long-term upper-limb impairment after stroke. *Stroke.* 42(9):2630-2, (2011).

19. Van Vliet PM, Wulf G. Extrinsic feedback for motor learning after stroke: What is the evidence? *Disability and Rehabilitation*, 28(13-14), 831–840, (2006).

20. Prange GB, Jannink MJ, Groothuis-Oudshoorn CG, Hermens HJ, Ijzerman MJ: Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke. *J Rehabil Res Dev*, 43(2):171-184 (2006).

21. Sanchez RJ, Liu J, Rao S,et al. Automating arm movement training following severe stroke: functional exercises with quantitative feedback in a gravity-reduced environment. *IEEE Trans Neural Syst Rehabil* Eng 14(3):378-389 (2006).

22. Wisneski KJ, Johnson MJ. Quantifying kinematics of purposeful movements to real, imagined, or absent functional objects: implications for modelling trajectories for robot-assisted ADL tasks. *J Neuroeng Rehabil.* 23;4:7(2007).

23. Edmans JA, Gladman JR, Walker M, Sunderland A, Porter A, Fraser DS. Mixed reality environments in stroke rehabilitation: development as rehabilitation tools. *5th International Conference of Disability, Virtual Reality & Assoc Tech (ICDVRAT):* Oxford, UK (2004)

24. Timmermans AA, Seelen HA, Willmann RD, et al. Arm and hand skills: training preferences after stroke. *Disabil Rehabil.* 31(16),1344-52, (2009).

25. Levack WM, Taylor K, Siegert RJ, Dean SG, McPherson KM, Weatherall M. Is goal planning in rehabilitation effective? A systematic review. *Clin Rehabil,* 20(9):739-755, (2006).

26. Krebs HI. Robot-Mediated Movement Therapy: a Tool for Training and Evaluation. *European Symposium Technical Aids for Rehabilitation TAR 2007*; (2007).

27. French B, Thomas L, Leathley M, et al. Does repetitive task training improve functional activity after stroke? A Cochrane systematic review and meta-analysis. *J Rehabil Med.* 42(1), 9-14, (2010).

28. Wevers L, van de Port I, Vermue M, Mead G, Kwakkel G. Effects of task-oriented circuit class training on walking competency after stroke: a systematic review. *Stroke.* 40(7): 2450-9, (2009).

29. Van de Port IG, Wood-Dauphinee S, Lindeman E, Kwakkel G. Effects of exercise training programs on walking competency after stroke: a systematic review. *Am J Phys Med Rehabil.* 86(11):935-51(2007).

30. Schmidt H, Werner C, Bernhardt R, Hesse S, Krüger J. Gait rehabilitation machines based on programmable footplates. *J Neuroeng Rehabil.* 9;4:2, (2007).

31. Riener R, Lünenburger L, Jezernik S, Anderschitz M, Colombo G, Dietz V. Patient-cooperative strategies for robot-aided treadmill training: first experimental results. IEEE *Trans Neural Syst Rehabil Eng.* 13(3):380-94, (2005).

32. Hesse S, Mehrholz J, Werner C. Robot-assisted upper and lower limb rehabilitation after stroke: walking and arm/hand function. *Dtsch Arztebl Int.* 2;105(18):330-6 (2008).

33. Mehrholz J, Werner C, Kugler J, Pohl M. Electromechanical-assisted training for walking after stroke. *Cochrane Database Syst Rev.*;4: CD006185. (2007)

34. Dobkin BH, Duncan PW. Should body weight-supported treadmill training and robotic-assistive steppers for locomotor training trot back to the starting gate? *Neurorehabil Neural Repair.* May;26(4):308-17, (2012).

35. Masiero S, Carraro E, Ferraro C, Gallina P, Rossi A, Rosati G. Upper limb rehabilitation robotics after stroke: a perspective from the University of Padua, Italy. *J Rehabil Med.* 41(12):981-5 (2009).

36. Mehrholz J, Hädrich A, Platz T, Kugler J, Pohl M. Electromechanical and robot-assisted arm training for improving generic activities of daily living, arm function, and arm muscle strength after stroke. *Cochrane Database Syst Rev.* 13;6:CD006876 (2012).

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

38. Reinkensmeyer D, Mahoney R, Rymer WZ, Burgar C. Robotic devices for movement therapy after stroke: current status and challenges to clinical acceptance. *Top Stroke Rehabil,* 8(4):40-53, (2002).

39. Dipietro L, Ferraro M, Palazzolo JJ, et al. Customized interactive robotic treatment for stroke: EMG-triggered therapy. *IEEE Trans Neural Syst Rehabil Eng*, 13(3):325-334, (2005).

40. Stein J, Krebs HI, Frontera WR, Fasoli SE, Hughes R, Hogan N. Comparison of two techniques of robot-aided upper limb exercise training after stroke. Am *J Phys Med Rehabil*, 83(9):720-728, (2004).

41. Volpe BT, Krebs HI, Hogan N, Edelstein L, Diels C, Aisen ML. A novel approach to stroke rehabilitation: robot-aided sensorimotor stimulation. *Neurology,* 54(10):1938-1944,(2000).

42. Lum PS, Burgar CG, Loos M Van der, Shor PC, Majmundar M, Yap R. MIME robotic device for upper-limb neurorehabilitation in subacute stroke subjects: A follow-up study. *J Rehabil Res Dev,* 43(5):631-642, (2006).

43. Hesse S, Schulte-Tigges G, Konrad M, Bardeleben A, Werner C. Robot-assisted arm trainer for the passive and active practice of bilateral forearm and wrist movements in hemiparetic subjects. *Arch Phys Med Rehabil,* 84(6):915-920 (2003).

44. Hesse S, Werner C, Pohl M, Rueckriem S, Mehrholz J, Lingnau ML. Computerized arm training improves the motor control of the severely affected arm after stroke: a single-blinded randomized trial in two centers. *Stroke*, 36(9):1960-1966, (2005).

45. Coote S, Murphy B, Harwin W, Stokes E. The effect of the GENTLE/s robot-mediated therapy system on arm function after stroke. *Clin Rehabil*. 22(5):395-405, (2008).

46. Loureiro R, Amirabdollahian F, Topping M, Driessen B, Harwin W. Upper Limb Robot Mediated Stroke Therapy – GENTLE/s Approach. *Autonomous Robots*, 15:35-51, (2003).

47. Amirabdollahian F, Loureiro R, Gradwell E, Collin C, Harwin W, Johnson G. Multivariate analysis of the Fugl-Meyer outcome measures assessing the effectiveness of GENTLE/S robotmediated stroke therapy. *J Neuroengineering Rehabil,* 4:4, (2007).

48. Guidali M, Duschau-Wicke A, Broggi S, Klamroth-Marganska V, Nef T, Riener R. A robotic system to train activities of daily living in a virtual environment. *Med Biol Eng Comput.* 49(10):1213-23, (2011).

49. Kahn LE, Lum PS, Rymer WZ, Reinkensmeyer DJ. Robot-assisted movement training for the stroke-impaired arm: Does it matter what the robot does? *J Rehabil Res Dev,* 43(5):619-630, (2006).

50. Fazekas G, Horvath M, Toth A. A novel robot training system designed to supplement upper limb physiotherapy of patients with spastic hemiparesis. *Int J Rehabil Res.* 29(3):251-4, (2006).

51. Masiero S, Celia A, Rosati G, Armani M. Robotic-assisted rehabilitation of the upper limb after acute stroke. *Arch Phys Med Rehabil*, 88(2):142-149, (2007).

52. Masiero S, Armani M, Rosati G. Upper-limb robot-assisted therapy in rehabilitation of acute stroke patients: focused review and results of new randomized controlled trial. *J Rehabil Res Dev.;*48(4):355-66, (2011).

53. Stein J, Narendran K, McBean J, Krebs K, Hughes R. Electromyography-controlled exoskeletal upper-limb-powered orthosis for exercise training after stroke. *Am J Phys Med Rehabil,* 86(4):255-261, (2007).

54. Johnson MJ, Feng X, Johnson LM, Winters JM. Potential of a suite of robot/computer-assisted motivating systems for personalized, home-based, stroke rehabilitation. *J Neuroeng Rehabil*, 4:6 (2007).

55. Johnson MJ, Ramachandran B, Paranjape RP, Kosasih JB. Feasibility study of TheraDrive: a low-cost game-based environment for the delivery of upper arm stroke therapy. *Conf Proc IEEE Eng Med Biol Soc*, 1:695-698, (2006).

56. Buschfort R, Brocke J, Heß A, Werner C, Waldner A, Hesse S. Arm studio to intensify upper limb rehabilitation after stroke: concept, acceptance, utilization and preliminary clinical results. *Journal of Rehabilitation Medicine.* 42(4), 310–314, (2010).

57. van Delden AL, Peper CL, Kwakkel G, Beek PJ. A systematic review of bilateral upper limb training devices for poststroke rehabilitation. *Stroke Res Treat.* Epub 2012 Nov 29, (2012).

58. Colombo G, Joerg M, Schreier R, Dietz V. Treadmill training of paraplegic patients using a robotic orthosis. *Journal of Rehabilitation Research and Development;*37(6):693–700, (2000).

59. Roy A, Forrester LW, Macko RF. Short-term ankle motor performance with ankle robotics training in chronic hemiparetic stroke. *J Rehabil Res Dev.* 48(4):417-29, (2011).

60. Banala S, Agrawal S, Scholz J. Active Leg Exoskeleton (ALEX) for gait rehabilitation of motor-impaired patients. *In 10th IEEE International Conference on Rehabilitation Robotics (ICORR), Noordwijk, The Netherlands*, 401–407, (2007).

61. Koopman B, van Asseldonk EH, van der Kooij H. Selective control of gait subtasks in robotic gait training: foot clearance support in stroke survivors with a powered exoskeleton. J Neuroeng Rehabil. 2013 Jan 21;10:3. doi: 10.1186/1743-0003-10-3.

62. Hesse S, Waldner A, Tomelleri C. Research Innovative gait robot for the repetitive practice of floor walking and stair climbing up and down in stroke patients. J *Neuroeng and Rehabil*, 7(30), 2010.

63. Bouri M, Stauffer Y, Schmitt C, Allemand Y, Gnemmi S, Clavel R, Metrailler R, Brodard R: The WalkTrainer. a robotic system for walking rehabilitation. *In Proceedings of the 2006 IEEE International Conference on Robotics and Biomimetics, Kunming, China*; (2006).

64. Peshkin M, Brown D, Santos-Munné J, Makhlin A, Lewis E, Colgate J, Patton J, Schwandt D. KineAssist: a robotic overground gait and balance training device. *In 9th IEEE International Conference on Rehabilitation Robotics (ICORR), Chicago, USA*;:241–246, (2005).

65. Kawamoto H, Sankai Y. Power Assist System HAL-3 for gait disorder person. In *Proceedings of the 8th International Conference on Computers Helping People with Special Needs (ICCHP), Linz, Austria,* (2002).

66. Reinkensmeyer D, Wynne J, Harkema S. A robotic tool for studying locomotor adaptation and rehabilitation. *In 24th Annual Conference and the Annual Fall Meeting of the Biomedical Engineering Society (EMBS/BMES), Houston, U.S.*;:2353–2354, (2002).

67. Aoyagi D, Ichinose W, Harkema S, Reinkensmeyer D, Bobrow J. An assistive robotic device that can synchronize to the pelvic motion during human gait training. *In 9th IEEE International Conference on Rehabilitation Robotics (ICORR), Chicago, U.S.* 565–568, (2005).

68. Lo AC, Guarino PD, Richards LG, *et al.* Robot-assisted therapy for long-term upper-limb impairment after stroke. *N Engl J Med.* 362(19):1772-83, (2010).

69. Hsieh YW, Wu CY, Liao WW, *et al.* Effects of treatment intensity in upper limb robot-assisted therapy for chronic stroke: a pilot randomized controlled trial. Neurorehabilitation and Neural Repair;25(6):503-11, (2011).

70. Burgar CG, Lum PS, Scremin AM, *et al.* Robot-assisted upper-limb therapy in acute rehabilitation setting following stroke: Department of Veterans Affairs multisite clinical trial. Journal of Rehabilitation Research and Development;48(4):445-58, (2011).

71. Mehrholz J, Pohl M. Electromechanical-assisted gait training after stroke: a systematic review comparing end-effector and exoskeleton devices. *J Rehabil Med.* 44(3):193-9, (2012).

72. Hornby TG, Campbell DD, Kahn JH, Demott T, Moore JL, Roth HR. Enhanced gait-related improvements after therapist- versus robotic-assisted locomotor training in subjects with chronic stroke: A randomized controlled study, *Stroke.* 39(6), 1786–1792, (2008).

73. Hidler J, Nichols D, Pelliccio M, et al. Multicenter randomized clinical trial evaluating the effectiveness of the Lokomat in subacute stroke. *Neurorehabilitation and Neural Repair.* 23(1), 5–13, (2009).

74. Oujamaa L, Relave I, Froger J, Mottet D, Pelissier JY. Rehabilitation of arm function after stroke. Literature review. *Ann Phys Rehabil Med.*52(3):269-93 (2009).

75. Cauraugh JH, Lodha N, Naik SK, Summers JJ. Bilateral movement training and stroke motor recovery progress: a structured review and meta-analysis. *Hum Mov Sci.* 29(5):853-70, (2010).

76. Tijs E, Matayas TA. Bilateral training does not facilitate performance of copying tasks in post-stroke hemiplegia. *Neurorehabil Neural Repair*;20(4), 473–83, (2006).

77. Foley NC, Bhogal SK, Teasell RW, Bureau Y, Speechley MR. Estimates of quality and reliability with the physiotherapy evidence-based database scale to assess the methodology of randomized controlled trials of pharmacological and nonpharmacological interventions. *Phys Ther.* 86(6):817-824, (2006).

78. Liao WW, Wu CY, Hsieh YW, Lin KC, Chang WY. Effects of robot-assisted upper limb rehabilitation on daily function and real-world arm activity in patients with chronic stroke: a randomized controlled trial. *Clin Rehabil.* 26(2):111-20, (2012).

79. Yang CL, Lin KC, Chen HC, Wu CY, Chen CL. Pilot comparative study of unilateral and bilateral robot-assisted training on upper-extremity performance in patients with stroke. *Am J Occup Ther.* 66(2):198-206 (2012).

80. Iosa M, Morone G, Bragoni M, et al. Driving electromechanically assisted Gait Trainer for people with stroke. *J Rehabil Res Dev.* 48(2):135-46 (2011).

81. Regnaux JP, Saremi K, Marehbian J, Bussel B, Dobkin BH. An accelerometry-based comparison of 2 robotic assistive devices for treadmill training of gait. *Neurorehabil Neural Repair.* 22(4):348-54, (2008).

82. Morone G, Bragoni M, Iosa M, et al. Who may benefit from robotic-assisted gait training? A randomized clinical trial in patients with subacute stroke. *Neurorehabil Neural Repair.* 25(7):636-44, (2011).

83. Morone G, Iosa M, Bragoni M, 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.*43(4):1140-2, (2012).

84. Duncan PW, Sullivan KJ, Behrman AL, et al. LEAPS Investigative Team. Body-weight-supported treadmill rehabilitation after stroke. *N Engl J Med.* 26:2026 –2036, (2011).

85. Bragoni M, Broccoli M, Iosa M, *et al.* Influence of psychologic features on rehabilitation outcomes in patients with subacute stroke trained with robotic-aided walking therapy. *Am J Phys Med Rehabil.* Oct;92(10 Suppl 1):e16-25, (2013).

86. Belda-Lois JM, Mena-del Horno S, Bermejo-Bosch I, et al. Rehabilitation of gait after stroke: a review towards a top-down approach. *J Neuroeng Rehabil.* 13;8:66, (2011).

87. Buch E, Weber C, Cohen LG, et al. Think to move: a neuromagnetic brain-computer interface (BCI) system for chronic stroke. Stroke, 39(3):910-917, (2008).

88. Wagner J, Solis-Escalante T, Grieshofer P, Neuper C, Müller-Putz G, Scherer R. Level of participation in robotic-assisted treadmill walking modulates midline sensorimotor EEG rhythms in able-bodied subjects. *Neuroimage.* 63(3):1203-11,(2012).

89. Hesse S, Werner C, Schonhardt EM, Bardeleben A, Jenrich W, Kirker SG. Combined transcranial direct current stimulation and robot-assisted arm training in subacute stroke patients: a pilot study. *Restor Neurol Neurosci.*;25(1):9-15 (2007)

90. Edwards DJ, Krebs HI, Rykman A, *et al.* Raised corticomotor excitability of M1 forearm area following anodal tDCS is sustained during robotic wrist therapy in chronic stroke. *Restor Neurol Neurosci.*;27(3):199-207, (2009).

91. Ochi M, Saeki S, Oda T, Matsushima Y, Hachisuka K. Effects of anodal and cathodal transcranial direct current stimulation combined with robotic therapy on severely affected arms in chronic stroke patients. J Rehabil Med. 45(2):137-40, (2013).

92. Johnson MJ. Recent trends in robot-assisted therapy environments to improve real-life functional performance after stroke. J Neuroeng Rehabil. 18;3:29, (2006).

93. Krakauer JW, Carmichael ST, Corbett D, Wittenberg GF. Getting neurorehabilitation right: what can be learned from animal models? *Neurorehabil Neural Repair*.;26(8):923-31, (2012).

94. Nielsen R, Soerensen K, Simonsen D, Jensen W.Effect of Early and Late Rehabilitation Onset in a Chronic Rat Model of Ischemic Stroke-Assessment of Motor Cortex Signaling and Gait Functionality Over Time. *IEEE Trans Neural Syst Rehabil Eng.* Oct 7, (2013).

95. Mackay-Lyons M, McDonald A, Matheson J, Eskes G, Klus MA. Dual effects of body-weight supported treadmill training on cardiovascular fitness and walking ability early after stroke: a randomized controlled trial. *Neurorehabil Neural Repair*. Sep;27(7):644-53, (2013).

96. Husemann B, Müller F, Krewer C, Heller S, Koenig E. Effects of locomotion training with assistance of a robot-driven gait orthosis in hemiparetic patients after stroke: a randomized controlled pilot study. *Stroke*. 38(2), 349-54, (2007).

97. Iosa M, Morone G, Fusco A, et al. Seven capital devices for the future of stroke rehabilitation. *Stroke Res Treat.* Epub 2012 Dec 13, (2012).

98. Takahashi CD, Der-Yeghiaian L, Le V, Motiwala RR, Cramer SC. Robot-based hand motor therapy after stroke. *Brain.* 131(2):425-37, (2008).

99. Masiero S, Celia A, Armani M, Rosati G, Tavolato B, Ferraro C, Ortolani M. Robot-aided intensive training in post-stroke recovery. *Aging Clin Exp Res*. 18:261-65, 2006).

100. Masiero, S., Celia, A., Armani, M., Rosati, G. A novel robot device in rehabilitation of post-stroke hemiplegic upper limbs. *Aging Clin Exp Res*. 18: 531-35, (2006).

A review of lower extremity assistive robotic exoskeletons in rehabilitation therapy.
Chen G, Chan CK, Guo Z, Yu H.
Crit Rev Biomed Eng. 2013;41(4-5):343-63. Review.
PMID: 24941413
Similar articles
Select item 22850839
25.
The next generation of exoskeletons: lighter, cheaper devices are in the works.
Mertz L.
IEEE Pulse. 2012 Jul;3(4):56-61. doi: 10.1109/MPUL.2012.2196836.

Figure: legend