NeuroRehabilitation 33 (2013) 77–84
DOI:10.3233/NRE-130930
IOS Press

Evidence of end-effector based gait machines in gait rehabilitation after CNS lesion

S. Hesse[a,*], N. Schattat[a], J. Mehrholz[b] and C. Werner[a]
[a]*Medical Park Berlin Humboldtmühle, Charité University Medicine Berlin, Berlin, Germany*
[b]*Klinik Bavaria, Kreischa, Germany*

Abstract.
BACKGROUND: A task-specific repetitive approach in gait rehabilitation after CNS lesion is well accepted nowadays. To ease the therapists' and patients' physical effort, the past two decades have seen the introduction of gait machines to intensify the amount of gait practice. Two principles have emerged, an exoskeleton- and an endeffector-based approach. Both systems share the harness and the body weight support. With the end-effector-based devices, the patients' feet are positioned on two foot plates, whose movements simulate stance and swing phase.
OBJECTIVE: This article provides an overview on the end-effector based machine's effectiveness regarding the restoration of gait.
METHODS: For the electromechanical gait trainer GT I, a meta analysis identified nine controlled trials (RCT) in stroke subjects ($n = 568$) and were analyzed to detect differences between end-effector-based locomotion + physiotherapy and physiotherapy alone.
RESULTS: Patients practising with the machine effected in a superior gait ability (210 out of 319 patients, 65.8% vs. 96 out of 249 patients, 38.6%, respectively, $Z = 2.29$, $p = 0.020$), due to a larger training intensity. Only single RCTs have been reported for other devices and etiologies.
CONCLUSION: The introduction of end-effector based gait machines has opened a new succesful chapter in gait rehabilitation after CNS lesion.

Keywords: Gait rehabilitation, robotics, physiotherapy, locomotion, stroke

1. Introduction

Restoration and improvement of gait are a major issue in neurorehabilitation. Stroke patients are the largest group, stroke affects 180 per 100.000 inhabitants in the industrialized world, annually (Kolominsky et al., 2001). Three months after the stroke, 20% of the surviving patients remain wheelchair-bound, and in 60% gait velocity and endurance are impaired (Wade et al., 1987). Among the ambulatory patients, the self-selected speed helps to distinguish three functional classes, a gait speed < 0.4 m/s classifies a patient who is ambulatory at home, a gait speed ranging from 0.4 to 0.8 m/s a limited community ambulator, and a gait speed > 0.8 m/s an unlimited community ambulator (Perry, 1992). To pass safely a cross-walk in Berlin, a gait speed of at least 0.9 m/s is required (Hesse et al., 2009). Regarding climbing up and down stairs, an Italian study reported that only 5% out of 437 stroke patients relearned climbing up and down a flight independently following an in-patient rehabilitation (Paolucci et al., 2008).

The currently mostly favoured treatment concept is a task-specific repetitive approach (Carr & Shepard, 1987), expressed by the slogan: "who wants to relearn walking, has to walk" (Hesse et al., 1994). Two decades ago, neurophysiological treatment concepts

*Address for correspondence: Prof. Dr. med. Stefan Hesse, Medical Park Berlin Humboldtmühle, An der Mühle 2-9, 13507 Berlin, Germany. Tel.: +49 30 300 240 9312; Fax: +49 30 300 240 9319; E-mail: s.hesse@medicalpark.de.

with tone-inhibiting and gait preparatory manoeuvres were prevailing; gait itself was practiced very little (Hesse et al., 1995). Treadmill training with partial body weight support was a first step towards a more intensive gait practice (Hesse et al., 1994). A harness compensated for postural deficiencies, part of the body weight was relieved according to the paresis of the affected weight-bearing muscles, and the motor-driven treadmill enforced locomotion. In case of non-ambulatory patients, two therapists had to place the paretic limb and had to assist with shifting weight. Controlled studies, however, failed to show any superior effect of treadmill training as compared to floor walking in non-ambulatory stroke patients with respect to gait restoration (Moseley et al., 2003; Franceschini et al., 2009; Duncan et al., 2011). Ambulatory stroke subjects profited from an aerobic treadmill training, the belt velocity and the inclination were increased in a stepwise manner to reach a preset target heart rate (Eich et al., 2004; Macko et al., 2005).

The major limitation of treadmill training and conventional physiotherapy in wheelchair-bound subjects was the physical assistance required to assist gait, thereby limiting the intensity of gait practice due to effort and budget constrains.

Gait machines helped to relieve the therapists' physical effort, Colombo et al. introduced the exoskeleton-based Lokomat, and Hesse et al. the end-effector-based Gait Trainer GT I (GT I) both in the late nineties of the last century (Hesse, Sarkodie-Gyan, & Uhlenbrock, 1999; Colombo et al., 2000). The two devices shared the harness and the body weight support, with the Lokomat the patient wore an exoskeleton with drives flexing the hip and knee during the swing phase, the ankle was passively guided, the treadmill provided the stance phase. With the GT I the patients' feet were positioned on two foot plates; which simulated stance and swing phase. Cables attached to the patients' harness controlled the vertical and horizontal movements of the centre of gravity. Mehrholz & Pohl conducted an indirect comparison between the two approaches. They included 18 trials involving 885 patients. They found significantly higher rates of independent walking in end-effector compared with exoskelton-based training ($p = 0.03$). They suggested that the type of electromechanical-assisted device might positively influence the outcome of gait rehabilitation after stroke (Mehrholz & Pohl, 2013).

Other gait machines followed the end-effector approach in combination with harness support and body weight relief. The Haptic Walker, Berlin, Germany is a robot with fully programmable foot plates in 3 dimensions (step, length and height, and ankle rotation), enabling not only simulated walking on the floor but also climbing stairs up and down (Schmidt et al., 2003). The commercial successor was the gait robot G-EO, Bolzano, Italy, which also included an actuated weight relief system (Hesse, Waldner, & Tomelleri, 2010). The Lokohelp, Weil am Rhein, Germany, combined a treadmill and an add-on option, to be mounted on the treadmill, moving both feet in a gait like fashion (Freivogel et al., 2009), and the Gaitmaster, Japan, was designed as a footpad-type locomotion interface (Tanaka et al., 2012).

The following article will present an overview of controlled clinical studies on the use of end-effector gait machines in stroke, CP and M. Parkinson patients. A meta-analysis on studies in stroke subjects treated with the electromechanical GT I is included. It is the most common end-effector based device, for the other end-effector devices only open studies or preliminary data are available. For patients with other etiologies, only open studies have been reported so far.

2. Methods of the literature search and search terms used

We searched the Cochrane Stroke Group Trials Register, CENTRAL, MEDLINE, EMBASE, CINAHL, AMED, SPORTDiscus, PEDro, COMPENDEX

and INSPEC. Our search strategy used for MEDLINE and modifications for other databases is reported and published elsewhere (Mehrholz & Pohl, 2012).

In addition, we hand-searched relevant conference proceedings, searched trials and research registers, checked reference lists in an effort to identify further published, unpublished and ongoing trials. Our final search was completed on December 2012.

We included studies as follows: (i) randomized controlled trials that evaluated end-effector based gait machines in gait rehabilitation after CNS lesion; (ii) studies of automated end-effector based gait machines used in combination with functional electrical stimulation applied to the legs during gait training or transcranial direct current stimulation during gait training; (iii) outcome measure walking ability.

3. Meta-analysis

We identified 2521 studies and excluded obviously irrelevant trials. We obtained the full text for the remain-

ing studies. Based on our inclusion criteria (types of studies, participants, outcome measures) we ranked these studies as relevant or irrelevant. We excluded all trials ranked initially as irrelevant, but included all other trials at this stage. We excluded all trials of specific treatment components, such as electrical stimulation as stand-alone treatment, treadmill training and continuous passive motion treatment. We resolved any disagreements through discussion between the review authors. Afterwards we extracted trial and outcome data from the selected trials and pooled data for every subpopulation such as stroke, Parkinson's disease and CP children. For all statistical comparisons we used the current version of the Cochrane Review Manager software, RevMan 5. We analysed binary outcomes with an odds ratio (OR) random-effects-model with 95% confidence intervals (CI) or calculated risk differences (RD) instead of ORs as appropriate using the methods described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins J, Green S. Cochrane handbook for systematic reviews of interventions, version 5.1.0. The Cochrane Collaboration 2011; available from www.cochrane-handbook.org.).

4. Stroke patients/GT I

Pohl et al. conducted the largest study (DEGAS, Deutsche Gangtrainerstudie). Four German centres included 155 non-ambulatory subacute, first-time stroke patients, and allocated them to two groups (Pohl et al., 2007). A lacking cardiovascular fitness, an activated lower limb joint arthrosis, and severe lower limb spasticity excluded the patients from participation in the study.

The experimental group A practised on the GT I (Fig. 1) 20 minutes net time every workday for four weeks, a therapy session including donning and doffing lasted 30 min. In addition, A-patients received 30 min of individual physiotherapy every workday; the content of the physiotherapy sessions was the restoration of gait including stair climbing. The control group B received 60 min of individual physiotherapy every workday for four weeks; the content of these sessions again was the restoration of gait including stair climbing. Primary variables were gait ability (Functional Ambulation Category, 0–5;) (Holden et al., 1984), and the Barthel Index (0–100) (Mahoney & Barthel, 1965), which were blindly assessed at study onset, end, and six months later for follow-up. Responders of the therapy had to become ambulatory (Functional Ambulation Category 4 or 5) or reach a Barthel Index (BI, 0–100) of > or = 75. The intention-to-treat analysis revealed that a significantly greater number of patients ($p < 0.0001$) in group A walked independently without a person helping, it means that 41 out of 77 versus 17 out of 78 patients in group B became a responder after the 4 week treatment period. Also, significantly more group A patients had reached a Barthel Index > or = 75 : 44 of 77 versus 21 of 78. At six-month follow-up, the superior gait ability in group A persisted (54 of 77 versus 28 of 78), while the Barthel Index responder rate did not differ.

Fig. 1. A left hemiparetic non-ambulatory patient practicing gait repetitively on the Gait Trainer GT I.

A meta analysis, undertaken according to Cochrane guidelines and following the checklist in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Higgins & Green, 2008), identified nine GT I studies in stroke subjects. Table 1 presents an overview of the studies (Dias et al., 2007; Geroin et al., 2011; Morone et al., 2011; Peurala et al., 2005; Peurala et al., 2009; Pohl et al., 2007; Rumiantsateva et al., 2010; Tong et al., 2006; Werner et al., 2002). (Table 1).

The primary outcome was defined as the ability to walk independently by the end of the study. The ability to walk was measured with the Functional Ambulation Category (FAC). A FAC score of 4 or 5 indicated independent walking over a 15-m surface irrespective of aids used (such as a cane) and were defined as "event". An "event" therefore represented the ability to walk independently. A FAC score of less than 4 indicates

Table 1
Table list with overview of studies included

Endeffector studies (reference)	Device	Number of subjects	Mean age (years)	Time since stroke	Severity	Outcome variable(s) for walking	Treament duration	Additional therapy
Dias et al., 2007	Gait Trainer	40	69	47 months	34 Barthel Index points	FAC, 10 metre walking test and gait cycle parameters, Time up and Go test, 6 minutes walking distance test, Step test	4 weeks	–
Geroin et al., 2011	Gait Trainer	30	63	26 months	80 points on the European Stroke Scale	10-metre walk test, Six-minute walk test	2 weeks	Transcranial galvanic stimulation in one treatment group #
Morone et al., 2011	Gait Trainer	48	61	20 days	60 Barthel Index points	FAC	12 weeks	–
Peurala et al., 2005	Gait Trainer	45	52	3 years	Scandi-navian Stroke Scale 42 points	10-metre walk test, Six-minute walk test, FAC	3 weeks	–
Peurala et al., 2009	Gait Trainer	56	68	8 days	unclear	FAC, 10-metre walk test, Six-minute walk test	3 weeks	electrical stimulation #
Pohl et al., 2007	Gait Trainer	155	63	4 weeks	37 Barthel Index points	FAC, walking velocity, walking endurance	4 weeks	–
Rumiantseva et al., 2010	Gait Trainer	110	64	unknown	unable to walk at study onset	Ability to walk, FAC	3 weeks	Experimental group received 30 minutes of additional gait training with the Gait Trainer I every working day
Tong et al., 2006	Gait Trainer	54	68	3 weeks	51 Barthel Index points	FAC, 5-metre walking speed	4 weeks	electrical stimulation #
Werner et al., 2002	Gait Trainer	30	60	7 weeks	38 Barthel Index points	FAC, fast walking speed over 10 metres	2 weeks	–

FAC = Functional Ambulation Categories; RMA = Rivermead Motor Assessment Scale.
# In two studies (Peurala et al., 2005; Tong et al., 2006). additional functional electrical stimulation of leg muscles during gait training was applied in one of the treatment groups. Since functional electrical stimulation was done as an adjunct during electromechanical-assisted gait training and the results of these experimental groups did not differ significantly, we combined the results of both experimental groups in one (collapsed) group and compared this with the results of the control group. In one study (Geroin et al., 2010). additional transcranial direct current stimulation was applied in one treatment group. Since this stimulation was done as an adjunct during electromechanical-assisted gait training and the results of these experimental groups did not differ significantly, we combined the results of both experimental groups in one (collapsed) group and compared this with the results of the control group.

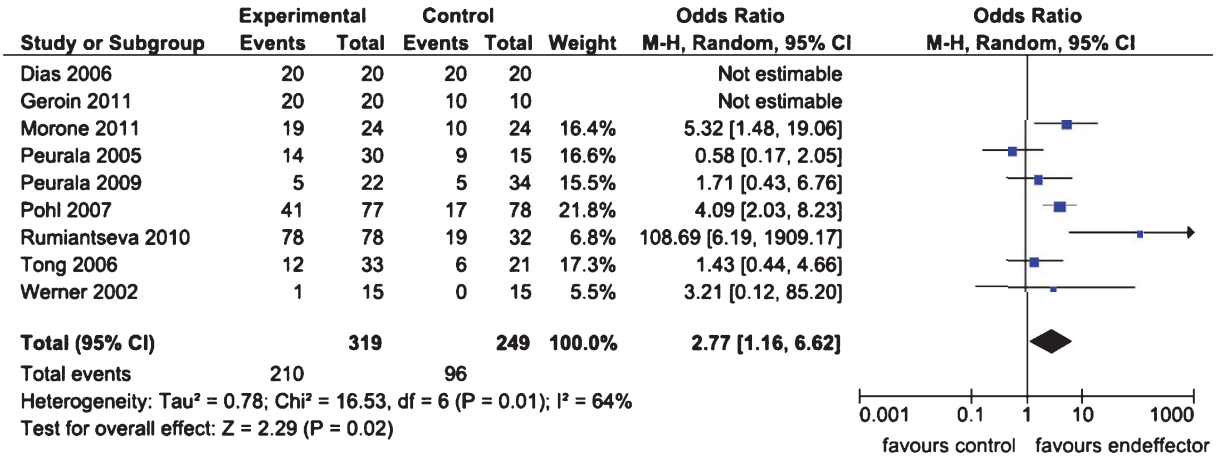

Fig. 2. The Forest plot of a meta-analysis on 9 studies evaluating the GT I in stroke gait rehabilitation as compared to conventional physiotherapy. Please note, that the odds ratio is in favour of the experimental group.

dependency in walking (supervision or assistance, or both, must be given in performing walking) and was defined as a "non-event". A "non-event" therefore represented the inability to walk independently. If FAC scores were not reported in the included studies we used alternative indicators of independent walking, such as: a score of 3 on the ambulation item of the Barthel Index (BI); or a score of 6 or 7 for the walking item of the Functional Independence Measure (FIM) (Granger, 1984); or a "yes" response to the item "walking inside, with an aid if necessary (but with no standby help)" or "yes" to "walking on uneven ground" in the Rivermead Mobility Index (RMI) (Collen et al., 1991). We contacted all study investigators and requested information regarding walking ability status at study onset and study end.

The review authors independently read the titles and abstracts of the identified references and eliminated obviously irrelevant studies and independently ranked these studies as relevant, irrelevant or possibly relevant. The authors independently extracted trial and outcome data from the selected trials. We analyzed the binary outcomes with an odds ratio (OR) random effects model with 95% confidence intervals (CI) using the methods described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2008).

Nine studies with a total of 568 patients used the GT I device in the experimental group (Table 1). Its use in gait rehabilitation for patients after stroke increased the chance to walk independently (OR 2.77, 95% CI 1.16 to 6.62, $p = 0.02$; random effects model, level of heterogeneity $I^2 = 64\%$). However, one study investigated patients who were already independent in walking at study onset, (Dias et al., 2007). Some studies investigated a mix of independent and dependent walkers without stratification of ambulatory status. (Peurala et al., 2005; Peurala et al., 2009). In the total population 78 patients of 568 patients (14%) were independent walkers at study onset.

At the end of the study significantly more patients were walking independently when the GT I device was used compared with the control group without using any devices (210 of 319 patients, 65.8% vs. 96 of 249 patients, 38.6%, respectively, $Z = 2.29$, $p = 0.02$).

Neither functional electrical stimulation of selected lower limb muscles (Tong et al., 2006), nor transcranial direct current stimulation (Geroin et al., 2011), had an additional effect on robot-assisted gait training with the GT I in non-ambulatory stroke patients.

5. Stroke patients/other end-effector devices

The G-EO, enabling the repetitive practice of stair climbing up and down, was tested in a first preliminary controlled trial (Hesse et al., 2012). Thirty non-ambulatory subacute stroke patients (FAC 1 or 2) were assigned to two groups. During 60 min sessions every workday for four weeks, the experimental group received 30 min of robot training and 30 min of physiotherapy, and the control group received 60 min

of physiotherapy. The standardized robot training included both simulated floor walking and stair climbing. The primary variable was gait ability, assessed with the help of the Functional Ambulation Category, FAC, 0–5. Both groups were comparable at study onset, and functionally improved over time. The improvements were significantly larger in the experimental group. At the end of the intervention, seven experimental group patients and one control group patient had reached an FAC score of 5.

The end-effector-based Gaitmaster was evaluated in a preliminary study with 10 chronic stroke patients. Twelve 20 min sessions on the device were compared to usual care in a cross over design. Gait speed improved only significantly during the intervention phase (Tanaka et al., 2012).

6. CP children

Smania et al. conducted a first RCT, 18 ambulatory children with diplegic or tetraplegic cerebral palsy were randomly assigned to two groups (Smania et al., 2011). The experimental group received 30 min of GT I plus 10 min of passive joint mobilisation and stretching exercises. The control group received 40 min of conventional physiotherapy. Each subject underwent a total of 10 treatment sessions over a 2 week period. The experimental group showed significant post treatment improvement on the 10-m walk test, 6-min walk test, and hip kinematics, all of which were maintained at the 1-month follow-up. The small number of patients included limited the validity of the study.

7. M. Parkinson

Picelli et al. asked, whether robot-assisted gait training could have a positive influence on postural stability in M. Parkinson patients at Hoehn & Yahr stages 3–4 (Picelli et al., 2012, Hoehn & Yahr, 1967). The authors assigned 34 patients with M. Parkinson at Hoehn & Yahr stages 3–4 into two groups. The GT I group ($n = 17$) underwent locomotor training, while the physical therapy group ($n = 17$) underwent a conventional training programme. Each subject received twelve, 40-min treatment sessions, three days / week, for four consecutive weeks. Primary outcome was Berg Balance scale. At the end of the intervention, the GT I group scored significantly higher as compared to the control group: Berg: 43.44 ± 2.73 vs. 37.27 ± 5.68. The superior result persisted at the 1-month follow-up evaluation. The authors concluded that robot-assisted locomotor training on the GT I may improve postural stability in PD patients at Hoehn & Yahr stage 3–4. For the Lokomat, Carda et al. noted that robotic gait training with the Lokomat was not superior to treadmill training in Parkinson patients, Hoehn & Yahr stage < 3 (Carda et al., 2012).

8. Conclusion

The studies presented offered ample evidence that an end-effector based gait training was effective in restoring and improving gait in subacute and chronic stroke patients. Most of the studies had used the electromechanical gait trainer GT I, a meta-analysis identified nine RCTs on a total of 556 patients, the test for an overall effect for achieving independent walking was statically significant in favour of the GT I. The most likely explanation of the device's superior effect was a higher number of repetitions practised as compared to conventional physiotherapy, obviously outweighing the disadvantage, inherent to the concept, of a non-perfect simulation of the swing phase. Biomechanical analysis revealed that the patients tended to take advantage of the plate's support during the swing phase, loading it with approximately 10% – 15% of body weight during the swing phase. Obvious advantages of the GT I were an easy donning and doffing, and no risk of knee malalignment, thereby reducing the risk of lower limb muscle activation pattern perturbations, as reported for the Lokomat (Hidler, Wisman, & Neckel, 2008). Furthermore, one cannot exclude that the endeffector based GT I provided an enviroment that encouraged greater patient engagement, other open questions are the device's impact on gait dynamics and efficiency.

The GT I studies in CP children and M. Parkinson patients as well as the first preliminary trials on the G-EO and the GaitMaster in stroke patients are promising but the small number of patients included does not warrant any definite conclusions.

Future research should focus more on efficiency aspects of the approach. A studio, combining gait machines for the non-ambulatory and a treadmill with partial body weight support for the ambulatory patients in a group setting, may be a cost-effective option. Furthermore, the potentially additional effect of virtual reality, stair climbing-option and sophisticated man-machine interactions via integrated force sensors need to be evaluated. Last but not least, head-to-head

comparisons between end-effector and exoskeleton solutions are highly mandatory. There is also a need to assess possible responders and non-responders to each device relative to acutity and impairments. For instance, Benito-Penalava et al. reported a similar effectiveness of the Lokomat and the GTI in 130 SCI patients studied (Benito-Penalva et al., 2012).

In summary, end-effector based gait machines have opened a new promising chapter in gait rehabilitation of non-ambulatory subjects; the scientific evidence in stroke subjects is strong.

Conflict of interest

Reha-Stim, Berlin, holds the national patents of the gait trainer GT I. The company is owned by Dr. Beate Brandl-Hesse, the spouse of the first author

References

Benito-Penalva, J., Edwards, D. J., Opisso, E., Cortes, M., Lopez-Blazquez, R., Murillo, N., Costa, U., Tormos, J.M., Vidal-Samoso, J., & Valls-Sole, J. (2012). European Multicentre Study about Human Spinal Cord Injury Study Group, Medina J. Gait training in human spinal cord injury using electromechanical systems: Effect of device type and patient characteristics. *Archives of Physical Medicine and Rehabilitation*, *93*, 404-412.

Carda, S., Invernizzi, M., Baricich, A., Comi, C., Croquelois, A., & Cisari, C. R. (2012). Robotic gait training is not superior to conventional treadmill training in parkinson disease: A single-blind randomized controlled trial. *Neurorehabilitation and Neural Repair*, *26*, 1027-34.

Carr, J. H., & Shepherd, R. B. (1987). *A motor relearing programme*. London: William Heinemann; pp. 1-25.

Collen, F. M., Wade, D. T., Robb, G. F., & Bradshaw, C. M. (1991). The Rivermead Mobility Index: A further development of the Rivermead Motor Assessment. *International Disability Studies*, *13*, 14-19.

Colombo, G., Joerg, M., Schreier, R., & Dietz, V. (2000). Treadmill training of paraplegic patients using a robotic orthosis. *Journal of Rehabilitation Research and Development*, *37*, 313-319.

Dias, D., Laíns, J., Pereira, A., Nunes, R., Caldas, J., Amaral, C., Pires, S., Costa, A., Alves, P., Moreira, M., Garrido, N., & Loureiro, L. (2007). Can we improve gait skills in chronic hemiplegics? A randomised control trial with gait trainer. *Europa Medicophysica*, *43*, 499-504.

Duncan, P. W., Sullivan, K. J., Behrman, A. L., Azen, S. P., Wu, S. S., Nadeau, S. E., Dobkin, B. H., Rose, D. K., Tilson, J. K., Cen, S., Hayden, S. K., & LEAPS Investigative Team. (2011). Body-weight-supported treadmill rehabilitation after stroke. *New England Journal of Medicine*, *26*, 2026-2036.

Eich, H. J., Mach, H., Werner, C., & Hesse, S. (2004). Aerobic traedmill plus Bobath walking training improves walking in subacute stroke: A randomized controlled trial. *Clinical Rehabilitation*, *18*, 640-651.

Franceschini, M., Carda, S., Agosti, M., Antenucci, R., Malgrati, D., & Cisari, C., Gruppo Italiano Studio Allevio Carico, Ictus, (2009). Walking after stroke: what does treadmill training with body weight support add to overground gait training in patients early after stroke?: A single-blind, randomized, controlled trial. *Stroke*, *40*, 3079-3085.

Freivogel, S., Schmalohr, D., & Mehrholz, J. (2009). Improved walking ability and reduced therapeutic stress with LokoHelp. *Journal of Rehabilitation Medicine*, *41*, 734-739.

Geroin, C., Picelli, A., Munari, D., Waldner, A., Tomelleri, C., & Smania, N. (2011). Combined transcranial direct current stimulation and robot-assisted gait training in patients with chronic stroke: A preliminary comparison. *Clinical Rehabilitation*, *25*, 537-548.

Granger, C. V. (1984). A conceptual model for functional assessment. In Functional asessment in rehabilitation medicine. Williams & Wilkins, Baltimore.

Hesse, S., Bertelt, C., Schaffrin, A., Malezic, M., & Mauritz, K. H. (1994). Restoration of gait in non-ambulatory hemiparetic patients by treadmill training with partial body weight support. *Archives of Physical Medicine and Rehabilitation*, *75*, 1087-1093.

Hesse, S., Bertelt, C., Jahnke, M. T., Schaffrin, A., Baake, P., Malezic, M., & Mauritz, K. H. (1995). Treadmill training with partial body weight support as compared to physiotherapy in non-ambulatory hemiparetic patients. *Stroke*, *26*, 976-981.

Hesse, S., Sarkodie-Gyan, T., & Uhlenbrock, D. (1999). Development of an advanced mechanised gait trainer, controlling movement of the centre of mass, for restoring gait in non-ambulatory subjects. *Biomedizinische Technik*, *7*, 194-201.

Hesse, S., Welz, A., Assmann, E., Quentin, B., & Waldner, A. (2009). Pedestrians in Berlin. Recommendations for street and subway transit. *Nervenarzt*, *80*, 953-958.

Hesse, S., Waldner, A., & Tomelleri, C. (2010). Innovative gait robot for the repetitive practice of floor walking and stair climbing up and down in stroke patients. *Journal of Neuroengineering and Rehabilitation*, *28*, 7-30.

Hesse, S., Tomelleri, C., Bardeleben, A., Werner, C., & Waldner, A. (2012). Robot-assisted practice of gait and stair climbing in non-ambulatory stroke patients. *Journal of Rehabilitation, Research and Development*, *49*, 613-622.

Hidler, J., Wisman, W., & Neckel, N. (2008). Kinematic trajectories while walking within the Lokomat robotic gait-orthosis. *Clinical Biomechanics*, *23*, 1251-1259.

Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: Onset, progression and mortality. *Neurology*, *17*, 427-442.

Holden, M. K., Gill, K. M., Magliozzi, M. R., Nathan, J., & Piehl-Baker, L. (1984). Clinical gait assessment in the neurologically impaired: Reliability and meaningfulness. *Physical Therapy*, *64*, 35-40.

Higgins, J. P. T., & Green, S. (2008). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0. The Cochrane Collaboration.

Kolominsky-Rabas, P. L., Weber, M., Gefeller, O., Neundoerfer, B., & Heuschmann, P. U. (2001). Epidemiology of ischemic stroke subtypes according to TOAST criteria: Incidence, recurrence, and long-term survival in ischemic stroke subtypes: A population-based study. *Stroke*, *32*, 2735-2740.

Macko, R. F., Ivey, F. M., Forrester, L. W., Hanley, D., Sorkin, J. D., Katzel, L. I., Silver, K. H., & Goldberg, A. P. (2005). Treadmill exercise rehabilitation improves ambulatory function and cardio-

vascular fitness in patients with chronic stroke: A randomized controlled trial. *Stroke*, *36*, 2206-2211.

Mahoney, F. I., & Barthel, D. W. (1965). Functional evaluation: The Barthel Index. *Maryland State Medical Journal*, *14*, 61-65.

Mehrholz, J., & Pohl, M. (2012). Electromechanical-assisted gait training after stroke: A systematic review comparing end-effector and exoscelton devices. *Journal of Rehabilitation Medicine*, *44*, 193-199.

Morone, G., Bragoni, M., Iosa, M., De Angelis, D., Venturiero, V., Coiro, P., Pratesi, L., & Paolucci, S. (2011). Who may benefit from robotic-assisted gait training? A randomized clinical trial in patients with subacute stroke. *Journal of Rehabilitation Research and Development*, *48*, 135-146.

Moseley, A. M., Stark, A., Cameron, I. D., & Pollock, A. (2003). Treadmill training and body weight support for walking after stroke. *Cochrane Database of Systematic Reviews*, *3*, CD002840.

Paolucci, S., Bargoni, M., Coiro, P., DeAngelis, D., Fusco, F. R., Morelli, D., Venturiero, V., & Pratesi, L. (2008). Quantification of the probability of reaching mobility independence at discharge from a rehabilitation hospital in nonwalking early ischemic stroke patients: A mutlivariate study. *Cerebrovascular Diseases*, *26*, 16-22.

Perry, J. (1992). *Gait analysis Normal and pathological function*. Thorofare: Slack Inc.

Peurala, S. H., Tarkka, I. M., Pitkanen, K., & Sivenius, J. (2005). The effectiveness of body weight-supported gait training and floor walking in patients with chronic stroke. *Archives of Physical Medicine and Rehabilitation*, *86*, 1557-1564.

Peurala, S. H., Airaksinen, O., Huuskonen, P., Jäkälä, P., Juhakoski, M., Sandell, K., Tarkka, I. M., & Sivenius, J. (2009). Effects of intensive therapy using gait trainer or floor walking exercises early after stroke. *Journal of Rehabilitation Medicine*, *41*, 166-173.

Picelli, A., Melotti, C., Origano, F., Waldner, A., Gimigliano, R., & Smania, N. (2012). Does robotic gait training improve balance in Parkinson's disease? A randomized controlled trial. *Parkinsonism Related Disorders*, *18*, 990-993.

Pohl, M., Werner, C., Holzgraefe, M., Kroczek, G., Mehrholz, J., Wingendorf, I., Hölig, G., Koch, R., & Hesse, S. (2007). Repetitive locomotor training and physiotherapy improve walking and basic activities of daily living after stroke: A single-blind, randomised multi-centre trial (Deutsche Gangtrainerstudie, DEGAS). *Clinical Rehabilitation*, *1*, 17-27.

Rumiantseva, N. A., Staritsyn, A. N., Samsygina, O. M., Suvorov, A. Y., Ivanova, G. E., Kovrazhkina, E. A., & Skvorttsova, V. I. (2010). Robotic-assisted mechanotherapy as a part of complex-ontogenesis based rehabilitation program aimed to restore gait function in acute stroke patients. *Cerebrovascular Disease*, *29*, 248.

Smania, N., Bonetti, P., Gandolfi, M., Consentino, A., Waldner, A., Hesse, S., Werner, C., Bisoffi, G., Geroin, C., & Munari, D. (2011). Improved gait after repetitive locomotor training in children with cerebral palsy. *American Journal of Physical Medicine and Rehabilitation*, *90*, 137-149.

Schmidt, H., Sorowka, D., Hesse, S., & Bernhard, R. (2003). Development of a robotic simulator for gait rehabilitation. *Biomedizinische Technik*, *48*, 281-286.

Tanaka, N., Kanamori, T., Saitou, H., Yano, H., Okuno, J., & Yanagi, H. (2012). Improvements of muscle strength and gait ability among chronic post-stroke patients by gait training with a footpad-type locomotion interface. *Journal of Novel Physiotherpies*, ISSN, 2165-7025 JNP, an open access journal.

Tanaka, N., Saitou, H., Takao, T., Lizuka, N., Okuno, J., Yano, H., Tamaoka, A., & Yanagi, H. (2012). Effects of gait rehabilitation with a footpad-type locomotion interface in patients with chronic post-stroke hemiparesis: A pilot study. *Clinical Rehabilitation*, it 26, 686-695.

Tong, R. K., NG., M. F., & Li, L. S. (2006). Effectiveness of gait training using an electromechanical gait trainer, with and without functional electric stimulation, in subacute stroke: A randomized controlled trial. *Archives of Physical Medicine and Rehabilitation*, *87*, 1298-1304.

Wade, D. T., Wood, V. A., Heller, A., Maggs, J., & Hewer, R. L. (1987). Walking after stroke. *Scandinavian Journal of Rehabilitation Medicine*, *19*, 25-30.

Werner, C., Bardeleben, A., Mauritz, K. H., Kirker, S., & Hesse, S. (2002). Treadmill training with partial body weight support and physiotherapy in stroke patients: A preliminary comparison. *European Journal of Neurology*, *9*, 1-6.