MECHANICAL GAIT TRAINING IN NEUROLOGICAL DISORDERS: A REVIEW OF EVIDENCES

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ABSTRACT

Robotic technologies are becoming more prevalent for treating neurological conditions in clinical settings. We conducted a literature search of original articles to identify all studies that examined the use of robotic devices for restoring walking function in adults with neurological disorders. A search was conducted in MEDLINE, Cochrane Library, Physiotherapy Evidence Database, Google Scholar, CINAHL and EBSCO host from 2005 to 2014. Keywords used were gait, locomotor training, multiple sclerosis, neurological disorders, rehabilitation, robotics, spinal cord injury, stroke, traumatic brain injury and walking. This review analyzed 27 articles that examined the effects of locomotor training with robotic assistance in patients following stroke, spinal cord injury (SCI), multiple sclerosis (MS), traumatic brain injury (TBI), and Parkinson disease (PD). This review supports that locomotor training with robotic assistance is beneficial for improving walking function in individuals following a stroke and SCI. Gait speed and endurance were not found to be significantly different among patients with motor incomplete SCI after a variety of locomotor training approaches. Limited evidence demonstrates that locomotor training with robotic assistance is beneficial in populations of patients with MS, TBI, or PD. We discuss clinical implications and decision making in the area of gait rehabilitation for neurological dysfunction.


INTRODUCTION

The most common Neurological causes of immobility in the adult population include stroke, spinal cord injury (SCI), traumatic brain injury (TBI), and progressive neurological diseases such as multiple sclerosis (MS) or Parkinson disease (PD). Neurological injuries and diseases often result in physical impairments that interfere with a person’s ability to walk. Improving walking function is often a key component of the rehabilitation program for a person diagnosed with a neurological impairment. Traditionally, physical therapists retrain walking function in people with mobility

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deficits by providing support for standing and walking (for example, through use of orthoses). Although compensation-based strategies using orthoses may facilitate walking, such strategies may limit the recovery of walking ability as experienced prior to the injury or neurological disease.

Research on locomotor training through the use of partial body weight support (BWS) and manual assistance first began with spinalized cats in the 1980s [1-5] and then progressed to human subjects [6-9]. This technique is based on a normal physiological gait pattern, with attention to the ideal kinematic and temporal aspects of gait [7]. The therapeutic goals of this approach are built on entirely different principles than conventional gait training and seek to achieve restoration and recovery of walking through the inherent capacities of the spinal and supraspinal locomotor centers [10].

To replicate a normal gait pattern during manually facilitated locomotor training, two or three therapists are needed to control or assist with trunk and limb kinematics. Locomotor training with manual assistance can be physically taxing on therapists when faster training speeds, which have demonstrated improved gait kinematics and muscle activation patterns [11] are used.

The success of treadmill training with BWS in restoring or improving overground locomotion has been documented in individuals following SCI [12-15], stroke [16-20], MS [21], PD [22-24], and TBI [25]. Despite these promising reports, the use of this specific therapeutic intervention in most rehabilitation settings is limited because of the strenuous and exhausting nature of manual training for the therapist. Due to the significant resources required for clinical deployment of manual-assistance treadmill training with BWS and to improve the delivery of BWS in the clinical setting, sophisticated automated electromechanical devices have been developed. The purpose of this review is to assess the effectiveness of mechanical gait training in neurological conditions such as stroke, spinal cord injury, TBI, MS & PD.

METHODS

Independent search was carried out by authors using a well-defined search strategy in following databases; MEDLINE, Cochrane Library, Physiotherapy Evidence Database, Google Scholar, CINAHL and EBSCO host published from 2005 to 2014 using the key terms gait, locomotor training, multiple sclerosis, neurological disorders, rehabilitation, robotics, spinal cord injury, stroke, traumatic brain injury and walking. The Boolean operator AND was used to link terms describing diagnosis with terms describing intervention. To avoid search bias, the testers performed independent searches and then disagreements were solved by consensus at various stages of the study.

The full text of all relevant studies were obtained, studies that examined locomotor training with a robotic device with the goal of improving walking ability were included. Additionally, several articles examining the kinesiological and metabolic aspects of locomotor training with robotics were included to further understand the potential of this method of locomotor training. Studies with adult participants (mean age of 18 years and older) with a neurological diagnosis were included, regardless of the duration of illness (acute or chronic) or level of initial walking ability. Studies using hybrid strategies such as overground gait training or functional electrical stimulation (FES) were also included.

Studies included reported measurable outcomes for walking ability such as the following: (1) walking speed either free cadence or fast walking (10-meter walk test [10MWT], 5-meter walk test [5MWT], 25-foot walk test [25FWT]); (2) walking endurance, defined as the capacity to cover a distance in a defined time (6-minute walk test [6MWT], 2-minute walk test [2MWT]); (3) timed measures of functional mobility, such as the Timed “Up and Go” Test (TUG); and (4) level of independence in walking, measured by the Functional Independence Measure (FIM), Walking Index for Spinal Cord Injury (WISCI or WISCI II), Functional Ambulatory Capacity (FAC), or Expanded Disability Status Scale (EDSS).

RESULTS

A total of 27 articles on the effects of locomotor training with robotic assistance and partial BWS in patients with a variety of neurological
diagnoses including stroke, SCI, MS, and TBI were reviewed. No literature was found regarding the effects of locomotor training with robotic assistance on patients with PD. All studies included in this review examined the effect of locomotor training on walking function with one of the following robotic-assisted devices: Lokomat (Hoc-oma; Zurich, Switzerland) [26], Electromechanical Gait Trainer (referred to here as “Gait Trainer” (Reha-Stim; Berlin, Germany) [27], Auto Ambulator, Geo System (28),

**Studies Using Locomotor Training with Robotic Assistance and BWS in Stroke:** Sixteen eligible trials were identified that examined persons with stroke six of which were excluded. Trials were excluded if their primary outcomes were not related to gait or, as in one of the study, the data were previously presented or were a subset of a larger study. Six trials were analyzed and met our inclusion criteria [29-34].

These 6 studies included a total of 389 subjects. All studies used Gait Trainer, Geo System & Lokomat [26]. For the intervention studies, treatment intensity included 20 to 30 minutes daily, 3 to 5 times a week. Most studies chose a duration of 4 to 6 weeks, for a total number of sessions ranging from 12 [29] to 48 [32]. One of the study used the intervention periods were only 2 weeks. However, the investigator repeated the intervention two additional times for a total duration of 6 weeks. Gait training time did not differ between the control and experimental groups in any of these studies.

Most studies investigated improvement in walking function as the primary outcome and used the FAC or comparable scales to assess independent walking [33]. Furthermore, most studies also included outcomes of walking function, such as gait speed (meters/second), gait endurance (2MWT or 6MWT), or functional mobility. Secondary measures included ability to perform activities of daily living (ADLs) and measures of motor function, balance, and spasticity.

**Gait Outcomes in Stroke Studies:** Five studies [30-34] measured recovery of independence by use of the FAC. A significantly greater number of subjects who trained with the Lokomat, Gait Trainer, or LokoHelp than control patients who received conventional gait training reached a FAC score of >3 as reported in three of the six studies [31-33]. Of these three studies, three used the Gait Trainer and one used the Lokomat. No studies demonstrated a significantly improved FAC with conventional physical therapy or treadmill training with BWS and manual assistance versus treadmill training with BWS and robotic assistance.

Six studies [29-34] measured changes in walking speed at study end using the 10MWT, the 5MWT, or an instrumented walkway. Two studies demonstrated a significant improvement in overground gait speed in the group that used the Gait Trainer [31,33] compared with control participants who received conventional therapy. In contrast, one of the study [29] reported significantly greater gains in the group that received locomotor training with BWS and manual assistance or conventional gait training compared with Lokomat training. Careful examination reveals that distinct differences exist in these studies. Patients recruited for the studies that demonstrated an improvement in gait speed with robotic training were in the acute to subacute phase, ranging from 2.5 to 14 weeks poststroke[24,33], while the patients in the two studies who improved their gait speed with BWS treadmill training with manual assistance (200 to 292 weeks poststroke)[29]. Furthermore, Hornby et al.[29] and recruited patients who were able to walk over ground independently for at least 5 meters in contrast to the other two studies [31,33] that recruited subjects who were unable to walk without assistance.

Four trials [29-32] measured walking endurance (6MWT or 2MWT) at study end. Pohl et al reported that the use of the Gait Trainer for 20 minutes, 5 times a week significantly increased the 6MWT for individuals who presented with hemiparesis [31]. However, in contrast, Hornby et al.[29] reported that participants who received BWS treadmill training with manual assistance or conventional gait training 30 to 45 minutes, 3 times a week experienced significantly greater gains in walking distance than those trained on the Lokomat. One study compared the Lokomat with BWS treadmill train-ing and conventional gait train-ing [32] but was unable to demonstrate any differences between groups.
for 6MWT or 2MWT. As noted previously, a more impaired participant population at an earlier time poststroke[31] versus a participant population that is already ambulating and at an extended duration poststroke[29] may possibly explain the differences observed in this study. Another confounding factor is the differences observed in training schedule. Pohl et al[31] used a more intense training schedule, 5 days a week compared with 3 days a week in Hornby et al[29].

Secondary Outcomes in Stroke Studies:
Secondary outcomes that were collected in many of the studies included the following: (1) balance as measured by the Berg Balance Scale (BBS) or postural sway tests; (2) spasticity as measured by the Modified Ashworth Scale (MAS); (3) measures of disability/ADL as measured by the Barthel Index (BI), FIM, or Frenchay Activities Index (FAI); (4) assessment of motor function as measured by the Motoricity Index (MI), Fugl Meyer, or Motor Assessment Scale; and (5) bodily mobility as measured by the Rivermead Mobility Index (RMI). Although not direct measures of gait, these are components that may affect an individual’s ability to walk. Two studies included the BBS [29,33], spasticity was assessed with the MAS in three studies [30-34]. Eight studies examined measures of disability/ADL with the BI [30,31,33], FIM [32,33], or FAI [29]. Although two studies reported a significant increase in the BI following training [30,33], no significant differences were found between the groups that received robotic gait training and conventional gait training. Only one study reported that subjects who received locomotor training on the Gait Trainer improved significantly on the BI [30].

Motor function was assessed with the MI [30,31,33]. Although two studies reported a significant improvement in motor function from baseline to post training [30,33], no differences were noted between the experimental or control groups. Pohl et al. was the only group to report that sub-jects who received locomotor training with the Gait Trainer had significantly improved MI scores [31]. One study specifically measured the RMI as an index of bodily mobility [31]. The RMI was developed from the Rivermead Motor Assessment Gross Function subscale testing functional abilities such as gait, balance, and transfers [35]. One of the study reported a significant improvement in the RMI following locomotor training; however, only one study has reported a significant difference between the groups that received robotic training [31].

Studies using Locomotor Training with Robotic Assistance and BWS in SCI: Eight SCI studies were recognized for possible inclusion in this review, of which four were excluded because primary outcomes were not related to gait or were strictly related to reflex activity. Four trials were analyzed and deemed appropriate as they met all aspects of our inclusion criteria [35-38]. The four studies included a total of 114 subjects. All studies used Lokomat & Gait trainer, treatment intensity ranged from 20 to 45 minutes a day and frequency varied from 2 to 5 times a week. Most studies had duration of 8 to 12 weeks, 50 to 60 sessions. Two of the studies reported on outcomes in which subjects initially participated in locomotor training with robotic assistance but were transitioned to treadmill training with BWS and manual assistance once a level of independence with overground walking had been reached [35,36]. One study compared outcomes between four types of locomotor training with BWS in persons with chronic injuries (>1 year) [37]. The four BWS conditions were treadmill training with manual assistance, treadmill training with electrical stimulation, over ground training with electrical stimulation, and tread-mill training with robotic assistance. Gait training time did not differ between the four conditions in either of the included RCT studies. These studies included a mean age range of 24 to 63 years. The majority of studies included subjects who were motor incomplete, American Spinal Injury Association impairment scale (ASIA) classification C or D. Large variability was found in the subjects’ baseline walking ability. Two studies involved subjects with lumbar level injuries [37,38], while all the other studies included subjects with thoracic and cervical injuries only. The majority of studies investigating improvement in overground walking function included outcomes of timed walking tests using gait speed (meters/second...
or centimeters/second) and/or gait endurance (6MWT). Some studies were stratified by lower-limb motor score, while others were stratified by initial walking speed [38]. Changes in stride length, step length, and step length ratio were reported to evaluate the effects of robotic treadmill training on gait quality [37]. Changes in physical assistance, assistive devices, and lower-limb orthotics were captured using the WISCI [38]. One study demonstrated the use of a prediction model in determining which types of patients may benefit most from treadmill training using robotic technology [36].

Gait Outcomes in SCI Studies: One study in this review [37] provided a direct comparison of the four BWS intervention groups previously mentioned: treadmill training with manual assistance, treadmill training with electrical stimulation, over ground training with electrical stimulation, and treadmill training with robotic assistance. Overall, these results yielded no significant differences in gait speed or distance covered in a timed test between the four intervention groups. Qualitative analysis showed an increase in step length in all groups except the robotic group, but the robotic group demonstrated the greatest improvement in step symmetry. Nooinjen et al focused on temporal distance measures of gait using the GAITRite system (CIR Systems Inc; Peekskill, New York), but no significant between-group differences could be detected between the outcomes based on group allocation. The GAITRite system is a portable walkway used in clinical settings to obtain objective data regarding gait parameters. The GAITRite system measures the temporal and spatial parameters of gait. As the patient or subject walks across the walkway, the system captures data with respect to each footstep and calculates these aspects of gait using 18,432 sensors. The authors did report, however, an interaction effect showing less improvement in step and stride length in the robotic group compared with the other three intervention groups; the treadmill training with electrical stimulation group showed a significantly larger gain compared with subjects in the treadmill training with robotic assistance group in step length of the stronger leg and in stride length of the weaker limb. These authors hypothesized that these results could be due to the use of the robot in a state of high impedance control rather than varied to low impedance control because subjects were able to support and control more of their own movements. Low impedance forces allow the subject to have more flexibility to influence the pre-defined walking pattern and activate his or her muscles in order to assist with an appropriate walking pattern. High impedance forces provide more guidance to the pattern and require less muscular input from the participant, possibly creating a more passive activity.

Gait speed was a primary outcome in four studies [35-38] and gait distance was a primary outcome in one study [38]. Physical assistance, orthosis use and the need for assistive devices was captured with the WISCI in several studies. These investigators reported improvements in gait speed and distance in all three subjects but reported improvements in gait speed and distance as well as decreased time required to complete the TUG after 8 weeks of locomotor training with robotic assistance [38].

A prediction model for determining overground walking speed after locomotor training was presented by Winchester et al [39]. They completed a retrospective review and statistical modeling of 30 subjects with incomplete SCI who had previously undergone 36 sessions of progressive locomotor training beginning with robotic-assisted and transitioning to manual-assisted training. In a stepwise regression analysis, these authors identified four clinical variables that were statistically significant in predicting overground gait speed following locomotor training in this population: voluntary bowel/bladder control, functional spasticity score, overground walking speed before locomotor training, and time post-onset.
Studies Using Locomotor Training with Robotic Assistance and BWS in MS: Only two studies, have reported on the effects of using locomotor training with robotic assistance in treating gait dysfunction in persons with MS [40,41]. Both studies met the previously discussed inclusion criteria and included a total sample size of 48. The Lokomat was the intervention used in both of these studies. Lo and Triche completed a randomized crossover design, testing two protocols of treadmill training using BWS [40]. Thirteen subjects were initially stratified by their baseline EDSS score of <5 or >5 and then randomly assigned to one of the following two groups: (1) 3 weeks of treadmill training with manual assistance followed by a 6-week washout period and another 3 weeks of treadmill training with robotic assistance or (2) 3 weeks of treadmill training with robotic assistance followed by a 6-week washout period and another 3 weeks of treadmill training with manual assistance.

Beer et al[41] completed an RCT with 35 subjects, comparing 3 weeks of Lokomat training with conventional walking training in a group of stable MS patients [66]. Daily intensity was similar (30 to 40 minutes) in the two studies; however, training intensity varied. Lo and Triche[40] used a less intense training schedule of 2 times a week for a total of only 6 sessions compared with Beer et al[41], who used daily training 5 times a week for a total of 15 sessions.

Beer et al. reported an average time since disease onset of 15 years in both control and experimental groups [41], while Lo and Triche did not report this variable[40]. Beer et al required their subjects to have the ability to stand or walk within the last 3 months [41], while Lo and Triche required their subjects to be able to walk 25 ft without assistance at baseline [40].

Outcomes in MS: Significant improvements in overground gait velocity were reported by Beer et al in both control and experimental groups in response to both forms of locomotor training (robotic and conventional)[41]. After pooling all data, Lo and Triche also reported significant improvements in the 25FWT (31% improvement), 6MWT (38.5% improvement), double-limb support time, and EDSS after completing either training protocol [40]. No significant between-group differences were detected in either study between locomotor training with robotic assistance and conventional walking training or between treadmill training with manual assistance versus robotic assistance. Also, Lo and Triche found no significant differences due to treatment order effect between locomotor training with robotic- and man-ual-assisted approaches[40]. Beer et al reported that at 6-month follow up, all patients had returned to their base-line walking function [41]. On the contrary, Lo and Triche reported that subjects had maintained gains from the initial 3-week treatment intervention after the 6-week washout period[40], raising questions regarding long-term effects of these treatment interventions. Overall, both studies suggest efficacy for improving gait function.

Studies Using Locomotor Training with Robotic Assistance and BWS in TBI: An extensive search of the literature revealed only one refereed publication concerning the use of robotic devices for locomotor training in the TBI or polytrauma patient population[42]. This case study examined the effects of 20 sessions (30 minutes, 3 to 5 times a week) of locomotor training with the LokoHelp on gait function and impairment in two subjects with TBI. The two subjects (age 22 and 26 years) were 1 and 3 years post-TBI, respectively. No clinically significant changes were observed in FAC, RMI, BBS, or spasticity (MAS) following the 6-week intervention period. Both subjects remained non ambulatory according to the FAC assessment.

Studies Using Locomotor Training with Robotic Assistance and BWS in PD: Despite an extensive search of the literature, no studies have been reported regarding the use of robotic devices to improve locomotor function in individuals with PD.

DISCUSSION
The purpose of this review was to assess the efficacy of robotic locomotor training on improvement in overground walking for adults with neurological injury or disease. Overall, this review supports that locomotor training with robotic assistance is beneficial in improving locomotor function in individuals following a stroke and SCI. Evidence surrounding the use of locomotor training with robotic assistance in MS...
is limited; however, it appears that the potential effect on gait dysfunction from robotics is at least equal to that of other techniques in persons with MS that require assistance to walk. The evidence in TBI and PD is insufficient to suggest the use of locomotor training with robotic assistance is of benefit in these populations.

No conclusive evidence exists to suggest that manual or conventional locomotor training preferentially results in improved locomotor function. The cost of each form of locomotor training may also play a role in the clinical implementation of these interventions.

The use of robotic devices in gait rehabilitation for patients after stroke was found to significantly improve the independence of walking. Our conclusions are in agreement with the Cochrane review by Mehrholz et al [43], which provided evidence that the use of robotic-assisted gait training devices in combination with physical therapy improved recovery of independent walking ability for patients following stroke. All studies agreed that gait speed increased following locomotor training; however, two of the studies reported a preferential improvement in gait speed following robotic locomotor training [31,33]. In opposition, one study reported that conventional or therapist-assisted BWS training resulted in more improvements in gait speed [29].

No conclusive evidence exists that locomotor training with robotics is any different than conventional or therapist-assisted gait training in improving balance, lower-limb spasticity, ADL, or motor function. Preliminary evidence shows that locomotor training with robotic technology may improve mobility disability following a stroke as measured by the RMI.

In summarizing the studies that examined locomotor training with robotic assistance in SCI, this intervention appears to be beneficial in improving over ground gait speed and endurance in patients with acute, subacute, and chronic conditions of incomplete SCI. However, no statistically significant differences were seen in gait speed and endurance when patients with incomplete SCI were treated with either robotic-assisted, therapist-assisted, or overground training approaches. Evidence also suggests that those patients who walk at slower speeds (<0.1 m/s) before locomotor training may demonstrate more improvement from all forms of loco-motor training in terms of walking speed than those patients who ambulate at faster speeds (>0.1 m/s) prior to training.

Several studies also reported on the positive effects of walking function after using progression principles and/or combined locomotor training approaches that incorporated treadmill training with robotic assistance, treadmill training with manual assistance, and over-ground training [29,39]. This transition facilitated training progression from a more restrictive environment to a less restrictive environment for walking practice as the subject’s level of remediation improved and may be useful in the clinical setting.

Metabolic expenditure increases were reported in both robotic- and therapist-assisted locomotor training, but subjects need to be cued to provide maximum effort to reach similar levels of energy expenditure between the two conditions, indicating the continued need for skilled therapist involvement in either training approach.

The two studies evaluating locomotor training with robotic assistance in persons with MS were rated well in terms of methodological rigor. However, the small number of subjects and the lack of conclusive results when comparing the various forms of locomotor training limit generalizability and translation of these results into suggestions for shaping clinical decision making. The specific stage of the disease process and clinical presentation may be more indicative of when a program of locomotor training may be successful in individuals with MS [40,41].

Robotic devices are designed to provide a physiological gait pattern to complete repetitive walking training. This provides a very safe environment for patients with significant weakness to complete repetitive walking patterns without fear of falling. The consistency between steps is superior to that which can be provided during manual BWS, but this ability to control the kinematics may also limit the degrees of freedom in the various joint segments involved in over ground locomotion. This controlled patterning may limit an individual’s
ability to make error corrections and experience normal sensory feedback, potentially limiting the process of long-term motor learning and skill acquisition. On the other hand, it can be quite difficult for therapists to provide a safe and controlled environment for walking practice when manual assistance is required for individuals to initiate steps or support their body weight. Therefore, defining which locomotor training intervention is most effective may depend on evaluating each patient to determine which method is most appropriate given the patient’s functional status.

Backus and Tefertiller have developed a clinical decision-making algorithm for transitioning patients with postacute SCI through a robotic and manual locomotor training program. Locomotor training progression along a continuum is based on the clinical presentation of spasticity, trunk stability, and overground walking independence. Such algorithms may be helpful in guiding clinical decisions when multiple technologies and intervention options are available.

All treadmill systems, with or without robotics and BWS, provide unique sensory feedback for patients who are being trained (moving treadmill belt vs stable floor) and result in questions regarding the specificity of this repetitive practice for walking. Treadmill systems provide a repetitive pattern that may be important for neurological recovery of walking.

**CONCLUSION**

Many researchers have shown the efficacy of gait training with robotic assistance on improving walking function in variety of neurological diagnosis, but the process aimed at restoring walking function in individuals with neurological pathology are challenged by the complexity and variability inherent to these disorders. However, it remains unclear where these technologies fit in the continuum of care and their comparative effect to other forms of locomotor training. Further research involving larger trials is needed to address the above limitations and guide clinical decision making.

**Conflicts of interest:** None

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