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SPINAL CORD INJURY RESEARCH EVIDENCE
Professional

Walking Following Spinal Cord Injury

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Key Points

- People with SCI may have no sensation or movement in their legs, while some maintain the ability to move their legs, feel pain, and some are able to walk. Though the rehabilitation of lower extremity walking may not be possible (e.g., in someone with complete tetraplegia), some forms of exercise and rehabilitation for lower limbs can be used to maintain muscle health as well as minimize other complications, such as osteoporosis, spasticity, pain, or wounds.

- Generally speaking, those with lower levels of injuries and incomplete SCI (i.e., the spinal cord is not completely severed) will be more likely to walk post-SCI. There has been some research on predicting who will or will not be able to walk after SCI, looking at factors like age, injury level and severity, and voluntary movement or strength in certain muscle groups. Hicks et al. (2017) (https://www.ambulation.ca/) states that walking ability can be predicted with relatively high accuracy with 3 variables: age, L3 motor score at admission, and S1 light touch sensory score at admission.

- Rehabilitation strategies for enhancing lower limb function after SCI typically have focused on range of motion (ROM) and stretching, building strength, attempting functional tasks, and pairing electrical stimulation (ES) to strengthen or help activate functioning musculature. Standing and overground ambulation training are also important components of conventional rehabilitation, either with or without bracing or assistive devices.

- In the last several years, we have seen increasing emphasis on providing task-specific training of functional movements, such as walking, with the help of body weight support treadmills (BWST). We have also seen technological applications for assisting walking rehabilitation, such as robotic devices or exoskeletons, virtual reality, and different neuromodulation strategies.

Overground Training

- Overground gait training (OGT) has been the predominant approach for regaining walking function, until recent years when the emphasis shifted to other forms of locomotor training (LT).
- Overground walking training (OWT) does not require expensive devices, and it more closely resembles conditions in daily life compared to walking on a treadmill.
- Walking training that is progressively challenging, over different surfaces, and includes motor skills training (MST), as well as strength/weight-bearing training and range of motion (ROM) stretching may result in long-lasting benefits in people with incomplete and complete SCI.

Body-Weight Supported Treadmill Training (BWSTT)

- Body-weight supported treadmill training (BWSTT) is a rehabilitation technique that uses a system of harness/straps connected to an overhead suspension system, supporting a portion of the person's weight as they walk on a motorized treadmill.
- For people in the acute/subacute phase of SCI (i.e., less than 12 months post-SCI), body-weight supported treadmill training (BWSTT) may be as effective on walking ability as overground mobility training of similar intensity.
- Body weight-support training can improve gait outcomes in patients with chronic and incomplete SCI, but there is no clear evidence that one specific strategy is superior to another (i.e., overground, treadmill training, robotic-assisted treadmill training, exoskeleton-assisted walking [EAW]; with/without functional electrical stimulation [FES]).
- Longer durations of BWSTT sessions are encouraged, if possible, to move beyond strength and stability to provide improvements in functional walking (i.e., walking at home or in the community).

Orthoses/Braces

- Ankle-foot-orthosis (AFO) can enhance walking function in patients with incomplete SCI who have drop-foot.
- Knee-ankle-foot orthosis (KAFO) can enable slow walking with elbow crutches or a walker in people with motor complete and low thoracic lesions, but usually not at speeds sufficient for community ambulation.

Wearable Powered Exoskeletons (WPEs)

- A wearable exoskeleton can enable safe walking training and improvements in strength outcomes in most patients with SCI.
- There are several limitations to exoskeleton use as a rehabilitation therapy tool such as device safety, set-up requirements, high cost, and limited accessibility and availability for gait rehabilitation.
- There is insufficient evidence regarding whether wearable exoskeleton-assisted training provides better walking function compared with other approaches to walking training in patients with SCI.
- There is little consensus with regards to training regimens and which exoskeleton models to use.

Neuromodulation

Neuroplasticity refers to the capacity of the nervous system to modify its structural and functional organization, adjusting itself to changing demands and environment;

neuromodulation can be defined as the induction of neuroplastic changes via local application of electrical, magnetic, acoustic, optic, tactile, or pharmacological stimuli. The SCIRE YouTube channel demonstrates neuromodulation a number of ways, including chemically (intrathecal baclofen), via electrical stimuli (FES and epidural stimulation), and magnetic fields (transcranial magnetic stimulation [TMS]).

Neuromodulation can be applied to three main areas of the body: the brain, the spinal cord, and the peripheral nerves, through invasive and/or non-invasive approaches.

In recent years, the combination of walking or strength training with neuromodulation of the brain or the spinal cord has been investigated as a means to enhance the excitability of motor circuits and to increase training efficacy, promoting motor recovery.

- Functional Electrical Stimulation (FES) - electrical stimulation is applied to peripheral muscles and the nerves located outside the spinal cord and brain. This stimulation causes the muscles to contract and can assist with purposeful or functional movement in weak or paralyzed muscles. FES is delivered using a variety of handheld or specialized commercial electrical therapy machines connected to electrodes that are placed on the skin's surface.
- Studies in SCI typically show that FES paired with exercise or walking training leads to better improvements in walking or strength than the exercise alone. This is often because a muscle is activated by the stimulation that normally cannot be voluntarily activated by the person with SCI.
- Of greater interest are the carryover effects found after FES training. Several investigators have reported that improvements in walking have (e.g., overground walking speed and distance, step length) been present even when the stimulator was turned off, suggesting that neuroplastic changes have taken place in response to regular use of FES and walking training.
- Other types of transcutaneous stimulation, like repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), or transcutaneous spinal current stimulation (tSCS), attempt to stimulate the brain and the spinal cord non-invasively (i.e., from outside of the body). Pairing this kind of electrical stimulation with exercise has been studied much less than FES, though some evidence exists that tSCS is useful for improving standing training and walking in people with SCI.
- There are also implantable types of stimulation that attempt to replace the electricity directly in the spinal cord. Epidural spinal cord stimulation has been completed successfully and had some effects on recipients and their walking abilities. This procedure, however, has yet to be approved in many countries including Canada and the USA.

Biofeedback and Virtual Reality

- Biofeedback is a process where instruments measure physiological activity and 'feed back' information to the user, as in electromyography, mirror therapy, or force sensors.

- Virtual Reality (VR) is a technology in which users interact in a computer-generated environment, allowing the practice of rehabilitation exercises in a safe and controlled manner; it can be low-tech and semi-immersive (e.g., video game consoles with cameras) or high-tech and fully immersive (e.g., VR goggles, VR caves).
- Because people with SCI lack sensation/sensory input below their level of injury, biofeedback and VR can compensate and provide visual feedback on body position, cue stepping and standing, enhance movement practice, as well as increasing adherence to home-based rehabilitation or telerehabilitation.
- Several studies have been conducted including people with chronic SCI, who performed standing and walking programs coupled with virtual reality (VR) or biofeedback with promising results that VR/biofeedback enhances walking more than walking training alone.

Table of Contents

1 Executive Summary

What Lower Limb and Walking problems occur after Spinal Cord Injury?

- Loss of function in the lower limbs due to SCI can extend from complete paralysis to varying levels of voluntary muscle activation. The research on rehabilitation of lower limb function after SCI has generally focused on the recovery of walking.
- Even when functional ambulation may not be possible (e.g., in complete tetraplegia), lower limb interventions can be targeted to maintain muscle health as well as reduce other complications, such as decreased cardiovascular health, osteoporosis, or wounds. Minimizing the risk of these complications would ease health costs related to the treatment of these sequelae and also could promote participation in society and/or the workforce.

What are the chances of recovering the ability to walk after Spinal Cord Injury?

- Most patients classified with an AIS A (complete motor and sensory) spinal cord injury have lower likelihood of walking independently in the community compared to the other AIS grading levels (Scivoletto et al. 2014). People first classified as AIS A who regain some community walking function usually have lower levels of injuries (T12-L3) and change classification (i.e., improve) over the course of rehabilitation (Scivoletto et al. 2014).
- Overall ambulation recovery for people with AIS B injuries (motor complete, sensory incomplete) is approximately 33% (Scivoletto et al. 2014).
- People with AIS C and AIS D injuries generally have a good prognosis for regaining some ambulation or standing function (Scivoletto et al. 2014). This will depend on the level of injury, as well as pain and spasticity issues that may limit mobility.
- There has been some research done on predicting who will or will not be able to walk after SCI, looking at factors like age, injury level and severity, and voluntary movement or strength in certain muscle groups. Hicks et al. (2017) (https://www.ambulation.ca/) state that walking ability can be predicted with relatively high accuracy with 3 variables: age, L3 motor score at admission, and S1 light touch sensory score at admission. Generally speaking, those with lower levels of injuries or incomplete SCI (i.e., the spinal cord is not completely severed) will be more likely to walk post-SCI.

What management options are there for lower limb and walking following Spinal Cord Injury?

Overground Training

- Overground training is most feasible in individuals with higher function (i.e., motor incomplete SCI). Overground training provides an important mode of exercise for improving walking function, and likely other physical and mental functions (e.g., muscle strength, bone health, cardiovascular function, depression symptoms) shown to be positively affected by exercise in the general population. Different overground training approaches (e.g., progressively challenging locomotor training [LT] over variable surfaces, motor skills training [MST], and intradural/intramedullary surgical intervention combined with long-term weight-bearing LT) may result in long-lasting benefits in patients with SCI (Lotter et al. 2020; Brazg et al. 2017; Amatachaya et al. 2021; Evans & Field-Fote 2024; Liu et al. 2021; Oh & Park 2013).
- Mobility improvements of overground and treadmill-based training are comparable in patients with SCI (Senthilvelkumar et al. 2015). One RCT showed that high-intensity (70%-85% HR_{max}) LT provides significantly greater improvements in selected walking variables (peak treadmill speed and fastest-possible speeds) compared to low-intensity (50%-65% HR_{max}) LT in participants with chronic and motor incomplete SCI (Brazg et al. 2017).

Body-Weight Supported Treadmill Training (BWSTT)

- There is evidence from multiple RCTs and pre-post-studies that body weight-support gait training can improve walking outcomes in people with acute or chronic SCI, but most body weight-support strategies (overground, treadmill [body-weight supported treadmill training, BWSTT], with functional electrical stimulation [FES], with the hybrid assistive limb [HAL] exoskeleton) are equally effective at improving walking function (walking speed, walking distance and/or walking ability) and/or lower extremity muscle strength (Alcobendas-Maestro et al. 2012; Yildirim et al. 2019; Sadeghi et al. 2015; Dobkin et al. 2006; Hornby et al. 2005a; Çinar et al. 2020; Field-Fote & Roach 2011; Alexeeva et al. 2011; Piira et al. 2019a; Piira et al. 2019b).
- There is one RCT which showed that intensive sessions (walking time per session > 50 min) of Lokomat-assisted BWSTT for 8 weeks could provide more improvement in functional walking than non-intensive sessions (walking time per session < 25 min) in patients with acute SCI; so, longer durations of BWSTT sessions are encouraged when possible (Wirz et al. 2017).

Orthoses/Braces

- Many people with SCI use orthoses/braces to improve lower limb stability or deal with problems like drop-foot, even though there is limited research supporting their use.
- It has been suggested that orthoses or braces are best for people with complete SCI at T9 or below or incomplete SCI at any level, with good postural control and good level of fitness (Franceschini et al. 1997; Thoumie et al. 1995; Hong et al. 1990).
- Two studies examined the immediate effects of an ankle-foot orthosis (AFO) after randomizing different brace conditions (Kim et al. 2004; Arazpour et al. 2013). Positive effects consisted of increased gait speed, step length, cadence and improved performance on the 6MWT. It is generally recognized in the field that effects from an AFO are attained immediately, although it is likely that practice over a few sessions may improve a participant's confidence, learning and function. It is also possible that people with orthoses, or those using walkers, elbow crutches, or other assistive aids, may not achieve walking speeds that are safe for community ambulation (Senthilvelkumar et al. 2023).

Wearable Powered Exoskeletons (WPE)

- Wearable powered exoskeletons (WPEs) are computer-guided systems using motorized orthoses that are donned by people with disabilities to assist with voluntary and involuntary movement (Rodriguez-Tapia et al. 2022; Jamwal et al. 2022).
- Newer generations of exoskeletons have been designed with increased mobility and portability (Yip et al. 2022). These devices, known as overground exoskeletons, are designed with portable systems that allow the user to ambulate freely indoors and outdoors, and have provided clinicians and patients with SCI a useful tool to increase overground walking capacity (Yip et al. 2022).
- There is evidence from multiple RCTs and other lower-quality studies that wearable exoskeleton-assisted gait training enables safe walking and provides improvements in gait and strength outcomes in patients with SCI at different levels of injury, AIS classification, or time since injury (Rodríguez-Fernández et al. 2022; Edwards et al. 2022; Xiang et al. 2021; Gil-Agudo et al. 2023; Tsai et al. 2024).
- There is insufficient evidence that wearable exoskeleton-assisted training provides better walking function, or energy expenditure outcomes compared with other approaches (such as robotic-assisted gait training [RAGT] with Lokomat or KAFOs) in patients with SCI (Rodríguez-Fernández et al. 2022; Edwards et al. 2022; Xiang et al. 2021; Gil-Agudo et al. 2023).

Neuromodulation

Neuroplasticity refers to the capacity of the nervous system to modify its structural and functional organization, adjusting itself to changing demands and environment; neuromodulation can be defined as the induction of neuroplastic changes via local application of electrical, magnetic, acoustic, optic, tactile, or pharmacological stimuli (De Ridder et al. 2016). The SCIRE YouTube channel demonstrates neuromodulation a number of ways, including chemically (intrathecal baclofen), via electrical stimuli (FES and epidural stimulation), and magnetic fields (transcranial magnetic stimulation [TMS]).

Neuromodulation can be applied to three main areas of the body: the brain, the spinal cord, and the peripheral nerves, through invasive and/or non-invasive approaches.

In recent years, the combination of walking or strength training with neuromodulation of the brain or the spinal cord has been investigated as a means to enhance the excitability of motor circuits and to increase training efficacy, promoting motor recovery (Hofer & Schwab 2019).

Functional Electrical Stimulation (FES) to Enhance Walking Function:

- Functional Electrical Stimulation (FES) - electrical stimulation is applied to peripheral muscles and the nerves located outside the spinal cord and brain. This stimulation causes the muscles to contract and can assist with purposeful or functional movement in weak or paralyzed muscles. FES is delivered using a variety of handheld or specialized commercial electrical therapy machines connected to electrodes that are placed on the skin's surface.
- Studies in SCI typically show that FES paired with exercise or walking training leads to better improvements in walking or strength than the exercise alone. This is often because a muscle is activated by the stimulation that normally cannot be voluntarily activated by the person with SCI.
- Of greater interest is carryover effects found after FES training. Several investigators have reported that improvements in walking have (e.g., overground walking speed and distance, step length) been present even when the stimulator was turned off, suggesting that neuroplastic changes have taken place in response to regular use of FES and walking training (Ladouceur & Barbeau 2000b; Wieler et al. 1999).

Transcranial Direct Current Stimulation (tDCS) and Repetitive Transcranial Magnetic Stimulation (rTMS):

- Other types of transcutaneous stimulation, like repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) attempt to stimulate the brain and the spinal cord non-invasively (i.e., from outside of the body).
- There are multiple RCTs showing that the concurrent application of transcranial direct current stimulation (tDCS) does not seem to further enhance the effects on walking and strength outcomes of MST (Evans et al. 2022; Evans & Field-Fote 2022), overground gait

training (OGT) (Klamruen et al. 2024), or BWSTT (Kumru et al. 2016b; Simis et al. 2021; Raithatha et al. 2016) in patients with motor-incomplete SCI.

- According to multiple RCTs, locomotor or exercise training combined with rTMS do not provide more benefits in walking function compared with exercise alone (Krogh et al. 2021; Kumru et al. 2016a; Nogueira et al. 2024).

Spinal Cord Stimulation Combined With Locomotor Training (LT):

- Different neuromodulation approaches to stimulate the spinal cord have been used, including transcutaneous, which is a non-invasive method, and epidurally and laparoscopically, which are invasive methods requiring surgery.
- According to different RCTs and one prospective controlled trial, concurrent application of transcutaneous spinal current stimulation (tSCS) seems to enhance the effects on walking and strength outcomes of LT (BWSTT or overground) or sit-to-stand and standing training in patients with chronic SCI (Estes et al. 2021; Hawkins et al. 2022; Al'joboori et al. 2020).
- Several pre-post studies have been published generally showing that epidural spinal cord stimulation (ESCS) is a safe procedure, and combined with a subsequent LT has promising effects on the recovery and improvements in walking capacity, LEMS, and independence in ADLs in patients with chronic and complete or severe motor paralysis (Kathe et al. 2022; Rowald et al. 2022; Wagner et al. 2018). A few studies examining laparoscopic implantation of neuroprosthesis (LION) in the pelvic lumbosacral nerves (i.e., sciatic, pudendal, and femoral nerves) show that it is a safe surgical approach, and followed by an intensive rehabilitation protocol, it can provide long-term beneficial effects on walking ability in patients with chronic and complete SCI (Kasch et al. 2021; Lemos et al. 2023; Possover 2021).
- It should be noted that epidural spinal cord implantation has yet to be approved in many countries, including Canada and the USA. LION is approved only in certain circumstances and using only certain protocols for people with SCI.

Biofeedback and Virtual Reality

Biofeedback is a process where instruments measure physiological activity and 'feed back' information to the user, as in electromyography, mirror therapy, or force sensors.

Virtual Reality (VR) is a computer-based technology that allows users to interact in a computer-generated environment, allowing the practice of rehabilitation exercises in a safe and controlled environment; it can be low-tech and semi-immersive (e.g., video game consoles with cameras) or high-tech and fully immersive (e.g., VR goggles, VR caves).

Because people with SCI lack sensation/sensory input below their level of injury, biofeedback and VR can compensate and provide visual feedback on body position or cue stepping and

standing, to assist and enhance movement practice, as well as increasing adherence to rehabilitation and facilitating home-based or telerehabilitation.

- Several studies have been conducted including people with chronic SCI, who performed standing and walking programs coupled with virtual reality (VR) or biofeedback with promising results that VR/biofeedback enhances walking more than walking training alone (An & Park 2018, 2022; Donati et al. 2016; van Dijsseldonk et al. 2018; Villiger et al. 2017; Zwijgers et al. 2024; Amatachaya et al. 2023).

2 Introduction

Loss of function in the lower limbs due to SCI can extend from complete paralysis to varying levels of voluntary muscle activation and sensation. The research on rehabilitation of lower limb function after SCI has generally focused on the recovery of standing and walking. Even when functional walking may not be possible (e.g., in people with complete tetraplegia), lower limb interventions can be used to maintain muscle health as well as reduce other complications, such as decreased cardiovascular health, osteoporosis, spasticity, pain, or wounds.

Clinical prediction rules or tools for prognosticating independent walking after SCI have been developed according to different variables such as age or neurologic outcomes (Hicks et al. 2017; Hong et al. 2023; van Middendorp et al. 2011). The simplified clinical prediction rule of Hicks et al. (2017) (https://www.ambulation.ca/) is likely most recommended in patients with ASIA B or C at baseline, because those with complete injuries (AIS A) are highly unlikely to walk independently, and those with the least severe injuries (AIS D) are highly likely to walk independently post injury (Scivoletto & Di Donna 2009; Scivoletto et al. 2014).

Conventional rehabilitation strategies for enhancing lower limb function after SCI have focused on range of motion (ROM) and stretching, active exercises, electrical stimulation (ES) to strengthen functioning musculature, and functional training in daily mobility tasks. Standing and overground ambulation training are also important components of conventional rehabilitation using various bracing and assistive devices (O'Sullivan & Schmitz 1994; Somers 1992). In the last several years, we have seen increasing emphasis on providing task-specific training of functional movements, such as walking, with the help of body weight support treadmills (BWST). We have also seen exciting advances in technological applications for assisting gait rehabilitation strategies, such as robotic devices or exoskeletons (Hesse et al. 2004; Colombo et al. 2001; Moriarty et al. 2024), and different neuromodulation strategies (Hofer & Schwab 2019).

In the following sections, we review evidence for the efficacy of these rehabilitation interventions on walking ability following SCI. As will be evident from the review, injury level, severity, chronicity, as well as institutional resources, must all be considered to help guide the clinical decision-making process and expected outcomes.

3 Systematic Reviews with Meta-Analysis

Numerous systematic reviews with meta-analysis have examined various interventions that affect the walking function of people with SCI. Interventions examined include gait retraining strategies (such as body-weight supported treadmill training [BWSTT], body-weight supported overground training [BWSOGT], robotic-assisted gait training [RAGT], or orthoses), biofeedback (including virtual reality), neuromodulation, and physiotherapy or mixed protocols. These systematic reviews are outlined in this section and classified according to the interventions assessed; however, for a better understanding, the conclusions and recommendations related to these findings are incorporated in the specific sections later in the chapter that summarize the respective treatments.

3.1 Systematic Reviews With Meta-Analysis Assessing Gait Retraining Strategies

Table 1. Systematic Reviews With Meta-Analysis Assessing Gait Retraining Strategies (BWSTT, BWSOGT, RAGT, or Orthoses)

Author Year Country Date included in the review Number of articles Level of Evidence Type of Study AMSTAR Score	**Method Databases Outcome measures**	**Conclusions**
Arroyo-Fernández et al. 2024 Spain Reviewed published articles up to December 2023 N = 15 (673 participants) and 14 included in the meta-analysis **Level of evidence:** Risk of bias assessed based on recommendations by the Cochrane organization using Review Manager **Type of study:** RCT **AMSTAR:** 9	**Methods:** The present systematic review and meta-analysis of RCTs aimed to summarize the evidence about the effects of body-weight supported gait training (robot-assisted body weight-supported gait training and manually-assisted body weight-supported gait training) in participants with motor-incomplete SCI versus control, with a particular focus on gait parameters and balance as primary outcomes, as well as other clinical outcomes such as quality of life as a secondary outcome. **Databases:** MEDLINE (via PubMed), Scopus, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and PEDro. **Outcome Measures:** Study outcomes—gait (functionality, endurance, and speed) and balance as primary outcomes, and quality of life as a secondary outcome.	1. Walking functionality: a. Overall, the effectiveness of body-weight supported gait training was not superior compared to control (n = 356, SMD = 1.25, CI 95%: −0.03 to 2.52) with a high level of heterogeneity (I^2 = 96%, p < 0.00001). b. In the analysis by subgroups to account for body-weight supported gait training, the results showed that robotic-assisted gait training (RAGT) improved walking functionality when compared to the control group (n = 257, SMD = 1.74, CI 95%: 1.09 to 2.39). However, heterogeneity was high (I^2 = 77%, p = 0.002) c. When an analysis based on the time since injury was performed, a beneficial effect was observed for body-weight supported gait training in chronic patients (n = 62, SMD = 1.82, CI 95%: 0.99 to 2.65) but not in sub-acute patients (n = 294, SMD = 0.76, CI 95%: −1.04 to 2.56). 2. Walking endurance: a. The pooled analysis did not show a superior effect of body-weight supported gait training compared to the control (n = 335, MD = 4.87 m; CI 95% = −14.40 to 24.14), with a high

		level of heterogeneity (I^2 = 81%, p < 0.0001). b. In the analysis by subgroups, RAGT interventions significantly improved walking endurance versus the control (n = 231, MD = 26.59 m, CI 95% = 22.87 to 30.31), with a low heterogeneity value. c. Finally, no significant differences were found globally depending on the time since injury of the participants. 3. Walking speed: a. Body-weight supported gait training did not show a superior effect to that of conventional physical therapy or no intervention (n = 453, SMD = 0.66, CI 95% = −0.20 to 1.51), with a high level of heterogeneity (I^2 = 94%, p < 0.0001). b. In the analysis by subgroups to account for the intervention, neither RAGT (n = 284, SMD = 0.38, CI 95% = −0.98 to 1.75) nor manually assisted body-weight supported gait training (n = 113, SMD = 1.87, CI 95% = −0.04 to 3.79) achieved superior results compared to the control, with high values of heterogeneity (I^2 = 96% and 92%, respectively). c. Finally, in terms of the time since injury, greater effectiveness of the body-weight supported gait training in subacute patients (n = 253, SMD = 2.52, CI 95%: 0.64 to 4.40) was observed.
Moriarty et al. 2024 USA Reviewed published articles up to December 2023 N = 11 **Level of evidence:** Rob2 and ROBINS criteria to	**Methods:** The study aims to characterize the potential improvements of mobility and function with the use of exoskeletons in patients with SCI. **Databases:** Embase, Cochrane, and PubMed. **Outcome Measures:** WISCI II, SCIM-III, 6MWT.	1. Eleven RCTs involving 552 total participants were included in the meta-analysis. 2. The results of the meta-analysis indicated statistically significant improvement in SCIM III [MD 5.14, 95 % CI = (4.47, 5.810), P < 0.00001], WISCII [MD 2.31, 95 % CI = (2.13, 2.49), P < 0.00001] and 6MWT [MD 37.04, 95 % CI = (32.35, 41.74), P < 0.00001] in patients with

determine relative risk of bias **Type of study:** RCT **AMSTAR:** 7		SCI as compared to conventional gait training therapy.
Huang et al. 2024 China Reviewed published articles up to December 2022 N = 19 were included in the systematic review and 13 (LEMS) and 7 (10MWT) were in the meta-analysis **Level of evidence:** Cochrane Systematic Review Manual 5.1.0 **Type of study:** RCTs **AMSTAR:** 8	**Methods:** The study aimed to were to evaluate the rehabilitation efficacy of body weight supported training for patients with SCI and to compare the effect differences among three body weight supported training methods (body-weight supported treadmill training [BWSTT], RAGT, and aquatic exercise). **Databases:** PubMed, Web of Science, Cochrane Library, Excerpta Medica, China National Knowledge Infrastructure, China Biology Medicine, China Science and Technology Journal, and Wan Fang databases **Outcome Measures:** LEMS, walking speed, and Modified Barthel Index.	1. The meta-analysis showed that body weight supported training could improve LEMS (SMD = 6.38, 95% CI = 3.96–8.80, P < 0.05), walking speed (SMD = 0.77, 95% CI = 0.52–1.02, P < 0.05), and modified Barthel Index scores (MD = 9.85, 95% CI = 8.39–11.30, P < 0.05). 2. The network meta-analysis showed no significant difference among the three BWST methods for improving lower extremity motor scores in patients with SCI. The best probability ranking of the body weight supported training methods for improving lower extremity motor scores in patients with SCI was RAGT (P = 0.60), followed by aquatic exercise (P = 0.21) and body weight supported training (P = 0.19).
Wan et al. 2024 China Reviewed published articles up to December 2022 N = 11 **Level of evidence:** The PEDro scale and Begg's test (for detecting publication bias) **Type of study:** RCTs **AMSTAR:** 8	**Methods:** The aim of this meta-analysis is to examine the effectiveness of RAGT in improving cardiopulmonary function and lower extremity strength among individuals with SCI. **Databases:** PubMed/Medline, Embase, Web of Science, PEDro, China National Knowledge Internet, China Science and Technology Journal Database, Wanfang Data. **Outcome Measures:** Cardiopulmonary function and lower extremity strength (LEMS).	1. LEMS: The pooled analysis (n = 408 patients) demonstrated significant effect of RAGT on LEMS increasing after treatment in individuals with SCI (SMD = 0.81; 95% CI = 0.14–1.48). a. In lower-limb robots, ten studies used Lokomat and only one used exoskeleton-assisted walking (EAW). The results of subgroup analysis favored Lokomat over controls for LEMS increasing (SMD = 0.88; 95% CI = 0.16–1.60). No significant effect was immediately detected on the effect of EAW versus control group on LEMS after treatment (SMD = 0.07; 95% CI = −0.85–0.99).

		b. Eight studies performed RAGT sessions over 6 weeks where results showed significant effect (SMD = 1.07; 95% CI = 0.23–1.91). Three studies performed RAGT sessions for less than six weeks, with results showing no significant effect (SMD = 0.08; 95% CI = −0.51–0.68). c. Four, six, and one study, compared the effects of RAGT with overground gait training (OGT), conventional physical therapy, and aquatic therapy (AT) on LEMS, respectively. Subgroup analysis shows that RAGT was more effective in improving LEMS than conventional physical therapy (SMD = 1.21; 95% CI = 0.09– 2.33). However, it was not better than OGT and AT (SMD = 0.46; 95% CI = −0.43– 1.35) / (SMD = 0.04; 95% CI = −0.65–0.72). d. No significant effects were immediately detected for Paraplegia nor Tetraplegia effects versus the control group on LEMS after treatment (SMD = 1.37; 95% CI = −0.11–2.84) and (SMD = 0.52; 95% CI = −0.19–1.23).
Liu & Chen 2024 China Reviewed published articles up to April 2022 N = 11 **Level of evidence:** the Cochrane Collaboration's risk of bias (RoB) 1.0 evaluation **Type of study:** RCTs **AMSTAR:** 7	**Methods:** The study aimed to explore the effect of exoskeleton robotic training on the recovery of ambulation in patients with SCI. **Databases:** PubMed, Embase, and CENTRAL. **Outcome Measures:** LEMS, WISCI II, 6MWT, and 10MWT, among other non-walking related outcome measures.	1. Eleven RCTs involving 456 participants were included in the meta-analysis. 2. Seven studies reported LEMS, involving 293 participants. The analysis results [MD = 4.64, 95%CI = (3.58, 5.70), P<0.05] indicated that exoskeleton robotic training significantly improved LEMS in patients with SCI compared with conventional gait training, with a statistical difference. 3. Six studies discussed WISCI II, involving 366 participants. The analysis results [MD = 1.76, 95%CI = (−0.32, 3.85), P = 0.1] showed that exoskeleton robotic training had no significant effect on improving WISCI II in patients with SCI compared with conventional gait training.

		4. Six studies described the 10MWT, with 195 participants. The analysis results [MD = −0.03, 95%CI = (−0.18, 0.11), P = 0.68] showed no significant difference in improving the walking speed of patients with SCI between the exoskeleton robotic training and conventional gait training groups. 5. Seven studies reported the 6MWT indicator, involving 191 participants. According to the analysis results [MD = 18.43, 95%CI = (−14.69, 51.56), P=0.28], no significant difference was observed in improving walking endurance between exoskeleton robotic training and conventional gait training.
Rodriguez-Tapia et al. 2022 Belgium Reviewed published articles up to February 2022 N = 41 **Level of evidence:** The Downs and Black checklist (D&B) **Type of study:** 6 RCTs 23 cohort studies 12 cases series **AMSTAR:** 8	**Methods:** The primary objective of this systematic review was to study whether gait training using wearable powered exoskeleton (WPE) is feasible and safe after tetraplegia due to SCI. A secondary objective was to assess if walking ability improved after gait training using WPE and whether this treatment leads to additional health benefits regarding gastrointestinal, urological, or musculoskeletal systems. **Database:** Scopus, PubMed and Embase. **Outcome Measures:** Walking parameters and walking functional tests (e.g., walking speed, walking distance, walking time, 6MWT, 10MWT).	1. A total of 570 patients with SCI were included (n = 166 [29%] patients with tetraplegia). 2. Eight types of WPE used for gait training were identified. 3. Rehabilitation protocols presented considerable heterogeneity among included studies. In most programs, session duration was set between 60 and 90 min at a frequency of 2–3 sessions per week. In 73% of studies, the training protocol included OGT without body weight support (BWS) systems. 4. A total of 174 adverse events (AEs) were retrieved. a. Occurrence of AEs (both minor and major) was significantly higher (p = 0.001) in patients with paraplegia (n = 157, 90%) compared to patient with tetraplegia (n = 17, 10%). b. 32 cases of mechanical and/or software issue or a manipulation error were reported, without any consequences for the participant. 5. In total, 20 studies reported walking parameters (n = 12) and walking functional tests (n = 13) separately for patients with tetraplegia:

		a. Among them, 4 studies focusing on walking parameters showed statistically significant improvements regarding walking speed, walking distance, walking time, 6MWT, and 10MWT b. One patient with tetraplegia improved his ASIA score and another one become a walker without the exoskeleton after the WPE rehabilitation program in two studies. c. One RCT showed similar improvements in walking functional tests between patients with incomplete tetraplegia and patients with paraplegia after a gait training program using two types of exoskeletons: and greater improvements in patients with paraplegia than in patients with tetraplegia with complete lesions.
Zhang et al. 2022 China Reviewed published articles up to August 2021 N = 12 **Level of evidence:** Cochrane collaboration's tool **Type of study:** N/A **AMSTAR:** 7	**Method:** A network meta-analysis of RCTs and non-RCTs to assess the clinical effects of two different types of RAGT (Lokomat and wearable EAW) in patients with SCI. **Database:** PubMed, Embase, and the Cochrane Library. **Outcome Measures:** 6MWT, 10MWT.	1. Effects of receiving wearable EAW (with sensitivity analysis to eliminate heterogeneity): a. 10MWT time was significantly improved relative to that of the baseline [0.65 (95% CI = 0.32, 0.99)]; heterogeneity was observed among these groups (I^2 = 0%). b. 10MWT speed significantly improved relative to that of the baseline [−0.82 (95% CI = −1.23, −0.40)]. Heterogeneity was observed among these groups (I^2 = 17%). c. 6MWT distance significantly improved relative to that of the baseline [−0.87 (95% CI = −1.16, −0.58)] and heterogeneity was observed among these groups (I^2 = 0%). 2. Effects of Lokomat: a. A meta-analysis of 3 studies (n = 91) showed that the 10MWT score was significantly improved [−0.08 (95% CI = 0.14, −0.03)] and the I^2 test for inconsistency was 0%.

		b. Three studies were included (n = 82), showing a significant increase in the WISCI II score [1.77 (95% CI = 0.23, 3.31)]. Heterogeneity was observed among these groups (I^2 = 3%). 3. Network meta-analysis: a. For the 10MWT speed showed that the probability of wearable EAW to ranking first was 89% and that of wearable EAW ranking second was 47%. b. For the WISCI II scores showed that the probability of Lokomat to rank first was 73% and that of wearable EAW to rank second was 63%. 4. After a meta-regression analysis for comparing baseline demographic and clinical characteristics, the results indicated that age, time after injury, and the AIS score had no impact on the outcomes of patients undergoing wearable EAW and Lokomat training (P > 0.05).
Tamburella et al. 2022 Italy Reviewed published articles up to December 2020 N = 41 **Level of evidence:** Downs and Black (D&B) tool **Type of study:** RCTs of parallel-group or cross-over design and n-RCTs (such as cohort studies, case–control, case series and pilot studies) **AMSTAR:** 8	**Method:** The aim of this systematic review was to explore the current state of the art of the overground powered lower limb exoskeletons and its effects on walking and on secondary health conditions in people with SCI. **Database:** MED-LINE, Embase, Scopus, Web of Science and Cochrane Library (CENTRAL). **Outcome Measures:** Walking domain (N = 27) (e.g., 10MWT, 2MWT, 6MWT, kinematics, WISCI II); muscle strength (N = 6) (e.g., LEMS); ADL (N = 5) (e.g., FIM, SCIM, Barthel Index).	1. Methodological quality was reflected as “poor” or “moderate”. 2. A total sample of 566 participants was analyzed. 3. Different overground powered lower limb exoskeletons devices were analyzed. 4. Thirteen studies reported different AEs during training, showing the skin lesions as the most frequent AEs. 5. The average total number of sessions across the studies ranged from 1 to 55; and for session frequency, 3 sessions per week were performed in 42% of the studies included. 6. Effects on walking domain (n = 27): a. The pattern of outcome measures employed in the enrolled studies was extremely different, thus making comparisons unreliable. b. Different group comparisons showed a positive trend in 10MWT

		and a positive effect in 2MWT and 6MWT. c. Group comparison through instrumental walking analysis varied according to the different characteristics employed. i. Overall Ekso training allowed walking speed improvement (significance was present only in 2 studies). ii. All studies assessing cadence parameters (n = 7) reported an improvement trend, and showed a significance reach after Ekso training in two studies with non-ambulatory persons and after HAL training in one study with ambulatory persons with SCI. iii. A trend of stride length improvement was observed after Ekso training (reaching significance only in 2 studies). iv. Overall, training allowed persons to walk with a longer step (reaching significance only for one study after Ekso training and for one study with HAL training). v. Only a single Ekso study addressed step width and showed that non-ambulatory persons with chronic SCI walked with a significantly larger step width after training. vi. Swing phase duration was evaluated only in one study, showing a trend of reduction after ReWalk training. vii. Significant positive effects in the reduction of trunk swing oscillation while wearing EXO were reported after ReWalk and HAL training in two studies. viii. The only study with GARS-M reported a significant improvement after HAL training in ambulatory persons with subacute SCI and the studies using WISCI II reported no

		significant improvements after HAL or Ekso. ix. Stance and double-time support phases duration alone or in combination were analyzed in 4 Ekso studies and showed ambiguous results. x. Kinematics of the lower limb range of motion (ROM) were analyzed in studies employing Ekso (N = 3), ReWalk (N = 2) or HAL devices (N = 1) and showed extremely heterogeneous results. 7. Effects on strength domain (n = 6): Only significant improvements were present for LEMS in persons with subacute lesion in three studies either with Ekso or HAL devices.
Yang et al. 2022 Taiwan Reviewed published articles up to August 2020 N = 15 **Level of evidence:** Cochrane risk of bias 2 tool **Type of study:** RCTs **AMSTAR:** 8	**Method:** This network meta-analysis approached for comparing the effectiveness of three strategies (BWSTT, RAGT and body-weight supported overground training [BWSOGT]) for ambulatory improvements in patients with SCI. Also, a comprehensive literature review was conducted to identify RCTs focusing on gait training for SCI. **Database:** PubMed, Cochrane Library, Scopus, and Embase. **Outcome Measures:** Walking ability, 6MWT, 10MWT, LEMS, and WISCI. *Control intervention: Conventional gait training, such as sit to stand, weight shifting, walking, turning, and stand to sit.	1. The overall risk of bias was uncertain for all studies. 2. The network meta-analysis included 497 participants. 3. The investigated interventions were relatively safe and well tolerated by participants as six studies reported on AEs, four of them did not observe AEs, and two reported that some participants experienced pain. 4. The pooled standard mean differences (SMDs) (95% CIs) of functional scores revealed that RAGT (0.30 [0.11, 0.50]) was significantly more favorable than the control intervention, whereas BWSTT (0.09 [-0.40, 0.58]) and body-weight supported overground training (0.09 [-0.55, 0.73]) did not result in significant differences compared with the control intervention. 5. The ranking probabilities indicated that RAGT was the most effective, followed by BWSOGT, BWSTT, and the control intervention. 6. There was no significant inconsistency between the results of direct and indirect comparisons. Furthermore, the differences between the traditional pairwise meta-analyses and

		network meta-analyses were determined and none of the differences were significant.
Alashram et al. 2021 Italy Reviewed published articles up to January 2021 N = 16 **Level of evidence:** PEDro scale **Type of study:** 13 RCTs 2 clinical controlled trials 1 pilot study **AMSTAR:** 6	**Method:** The present systematic review aimed to provide an overview of the immediate and long-term effects of the Lokomat on various impairments following SCI, to determine the optimal treatment dosage, and to define who most likely would benefit from the intervention. **Database:** PubMed, SCOPUS, PEDro, REHABDATA, MEDLINE, EMBASE, and web of science. **Outcome Measures:** Walking speed (10MWT), walking distance (6MWT, 2MWT, SCI-Functional Ambulation Profile [SCI-FAP]), walking capacity (SCI-FAP, 6MWT), Falls Efficacy Scale-International Version I [FES-I]), functional level (WISCI II, FIM-L, SCIM, SCIM-III – mobility section [SCIM-III-M], Ambulatory Motor Index), leg strength (LEMS), strength (maximum voluntary contraction [MVC]), and agility (Probe Reaction Time).	1. Quality of the included studies: a. The median score on the PEDro scale was 6 (ranged from 2 to 8). b. Overall, 6 studies met 8 criteria, 7 criteria (n = 1), 6 criteria (n = 3), 5 criteria (n = 2), 4 criteria (n = 2), 3 criteria (n = 1), and 2 criteria (n = 1) for low risk of bias. 2. A total of 658 patients with incomplete SCI were included. 3. The included studies did not demonstrate any AEs or uncomfortable issues following the Lokomat intervention. 4. Effects on walking speed (10MWT): 2 studies showed that the patients in the experimental groups improved significantly compared with the control groups; however, the remaining 8 studies did not show significant differences between groups. 5. Effects on walking distance: 4 studies reported significant improvements after the RAGT compared with the control groups at the end of intervention and follow-up; however, 4 studies did not show significant differences between groups. 6. Effects on strength: 3 studies showed significant improvements in the LEMS scores or MVC of dorsiflexors and plantar flexors after the RAGT 'Lokomat' compared with the control group; however, 2 studies did not show significance improvements in the LEMS scores in the experimental group. 7. Effects on agility: One study reported significant improvements in Probe Reaction Time after RAGT. 8. Effects on functional level and functional ambulation: a. WISCI II: One study reported significant improvements after the

		RAGT, compared with the control group. Two studies showed improvements in both groups; however, only in one study the experimental group showed greater and significant improvements. b. FIM-L scores: One study reported an improvement after RAGT. c. Functional ambulation category (FAC): One study reported significant improvements after the RAGT but in other study both groups showed improvements with no significant difference between groups.
Fang et al. 2020 Ireland Reviewed published articles up to November 2019 N = 18 (12 in the qualitative synthesis and 6 in quantitative synthesis) **Level of evidence:** The Cochrane risk of bias assessment tool for RCTs and the Newcastle Ottawa Scale for the cohort studies and clinical trials **Type of study:** 6 RCTs 1 RCT crossover 6 case reports 1 pre-post 3 single group **AMSTAR:** 6	**Method:** The purpose of this meta-analysis was to compare the effects of RAGT on spasticity, pain, LEMS and walking ability with those of other treatments after SCI. **Database:** PubMed, Scopus, Medline (Proquest), and Cochrane CENTRAL. **Outcome measures**: LEMS and walking ability (i.e., 6MWT, 10MWT).	1. Risk of bias: In all included RCTs, only one study had high risk of bias level; and all non-RCTs had general to good quality. 2. The apparatus used for RAGT in the studies included were Lokomat, HAL, Indego Exoskeleton, ReWalk, ARKE 2.0, and Ekso GT. 3. A total of 301 participants were included. 4. Walking distance (6MWT) increased significantly in favor of robotic group (RCTs: 95%CI = 4.394 to 106.628, p = 0.033; non-RCTs: 95%CI = 7.218 to 52.586, p = 0.010). The pooled MD (random effects model) of RCTs and non-RCTs were 55.511 m and 29.902 m, respectively. 5. Walking speed (10MWT) significantly improved in robotic group of non-RCTs (95%CI = 0.032 to 0.213, p = 0.008) but not of RCTs (p = 0.597). The pooled MD (random effects model) for non-RCTs was 0.123 m/s. 6. The results on WISCI II showed no significant difference (p = 0.265 for RCTs; p = 0.228 for non-RCTs).

Shackleton et al. 2019 South Africa Reviewed published articles up to April 2018 N = 27 **Level of evidence:** GRADE system **Type of study:** Prospective non-randomized, uncontrolled trials **AMSTAR:** 7	**Method:** This review aimed to examine the effectiveness of overground powered exoskeletons as a tool for SCI rehabilitation by investigating gait parameters, cardiovascular demands, secondary health outcomes, including spasticity, pain and user-satisfaction. **Database:** PubMed, Cochrane Library, Web of Science, Scopus, EBSCOhost (CINAHL and Health Source Nursing/Academic) and EI Compedex Engineering Village. **Outcome Measures:** Walking performance (6MWT, 10MWT)	1. The overall quality of evidence was judged to be very low. 2. 308 participants were included in the analysis. Most participants presented with complete SCI between T1 and T12. 3. The ReWalk™ powered exoskeleton was evaluated in 11 studies, Ekso® in 10 studies, Indego™ in 3 studies, WPAL in 2 studies and REX in one study. 4. The most common intervention length was 8 weeks and typically, training was conducted 3 times per week for 60 min per session. 5. Meta-analyses were performed on the 7 studies that assessed walking performance tests: a. Five studies reported a positive pooled effect of –0.94 (95% CI –1.53, –0.36) with moderate heterogeneity (I^2 = 27%, p = 0.002) for the distance achieved during the 6MWT. b. Six studies reported a positive pooled effect of –1.22 (95% CI –1.87, –0.57) with high heterogeneity (I^2 = 60%, p = 0.0002) for the speed achieved during the 10MWT. 6. Effects on walking velocity and distance: a. Six studies considered the mean distance and velocity achieved during a 6MWT showing a range from 47 to 129 m and 0.22 to 0.36 m/s, respectively. b. Six studies considered the velocity required to complete a 10MWT, ranging from 0.25 to 0.38 m/s across 4 studies. The remaining 2 studies indicated that different injury levels can affect walking velocity, as can the level of assistance provided while walking.
Aguirre-Güemez et al. 2019 México Reviewed published articles	**Method:** The aim was to contribute to the available evidence on the use of RAGT in people with SCI by incorporating the latest evidence from clinical trials as well as by widening the	1. From the 15 included RCTs, a total of 499 participants were registered and from the 5 included systematic reviews, a total of 1,227 participants were included.

up to December 2016 N = 20 included in qualitative synthesis and 6 included in quantitative synthesis (meta-analysis) **Level of evidence:** Cochrane Handbook for Systematic Reviews of Interventions **Type of study:** 15 RCTs 5 systematic reviews **AMSTAR:** 10	scope with the inclusion of additional indicators of effectiveness (improve gait, strength and functioning in people with SCI in comparison to other modalities of training). **Database:** Cochrane Injuries Group Specialized Register, Cochrane CENTRAL, MEDLINE (Ovid), EMBASE (Ovid), CINAHL and ISIWeb of Science: Science Citation Index Expanded (SCIEXPANDED). **Outcome Measures:** The analysis focused on speed (m/s), WISCI, strength (LEMS) and FIM-L.	2. Dose of intervention: a. The period of treatment was one day; three weeks; four weeks; eight weeks; and 12 weeks. b. The frequency was reported from three times per week for four weeks, up to five times per week for 12 weeks. c. The RAGT setup was initially prescribed for the amount of BWS at 60% and never less than 25%. d. The guidance force was set from 100% to 20%. e. The lowest initial speed was reported at 1.0 Km/h and in one trial the participants accomplished 3.4 Km/h. f. The length of the RAGT therapy varied from 20 min to 45 min. 3. Effects of interventions based on meta-analysis (n = 6): a. Five studies (n = 169 patients) of RAGT compared with control groups showed no effect in speed gait, with a MD of -0.00 (95% CI -0.05 to 0.04, P = 0.95). b. Four studies (n = 188 participants) showed a MD of 3.01 (95% CI -0.54 to 6.55, P = 0.10) for WISCI in favor of the RAGT.
Mehrholz et al. 2017 Germany Reviewed published articles up to September 2016 N = 13 **Level of evidence:** Cochrane Risk of Bias Tool **Type of study:** RCTs of parallel-groups or cross-over trials	**Method:** A systematic review and meta-analysis were performed to update the Mehrholz et al. (2012) review. Specifically, the aim was to compare the effectiveness of BWSTT and RAGT with OGT and other forms of physiotherapy on walking speed and walking distance in people with traumatic SCI: • Comparison no. 1: BWSTT vs. OGT and other forms of physiotherapy (not including RAGT). • Comparison no. 2: RAGT vs. OGT and other forms of	1. Thirteen RCTs involving 586 patients were included in the analysis. 2. Risk of bias: a. Six trials were rated as low risk of bias for random sequence generation, five trials were rated as low risk of bias for concealed allocation and eight trials were rated as low risk of bias for blinding of assessors. b. Two and five trials were rated as high risk of bias for concealed allocation and blinding of assessors, respectively. 3. Comparison no. 1:

AMSTAR: 9	physiotherapy (not including BWSTT). **Database:** Cochrane Injuries Group's Specialised Register; Cochrane CENTRAL; MEDLINE; EMBASE; CINAHL; Allied and Complementary Medicine Database; SPORTDiscus; PEDro; COMPENDEX; INSPEC. Online trials databases Current Controlled Trials (www.controlled-trials.com/isrctn) and Clinical Trials (www.clinicaltrials.gov) was searched. **Outcome Measures:** Walking speed, walking distance and AEs.	a. Walking speed: The pooled MD was − 0.03 $m \cdot s^{-1}$ favoring OGT (95% CI, − 0.10 to 0.04; P = 0.37; I^2 = 0%). Few clinicians or patients would consider a possible increase of 0.04 $m \cdot s^{-1}$ as clinically meaningful. Therefore, these results indicate that BWSTT does not have clinically important effects on walking speed when compared to OGT. b. Walking distance: The pooled MD was − 7 m favoring OGT (95% CI − 45 to 31; P = 0.73; I2 = 71%). Most would consider a possible increase of 31 m as clinically meaningful. Therefore, these results indicate that BWSTT may have clinically important effects on walking distance when compared to OGT, but these results are not certain because the 95% CI spans down to − 45 m, favoring overground training. c. AEs (Five trials involving a total of 309 participants): The rates of AEs were between 0 (n = 3) and 4% (n = 2). The risk difference (95% CI) of an AE was 0.03 (−0.01 to 0.07; P = 0.21; I^2 = 0%). 4. Comparison no. 2: a. Walking speed: The pooled MD was − 0.04 $m \cdot s^{-1}$ favoring OGT (95% CI − 0.21 to 0.13; P = 0.66; I^2 = 57%). Few would consider a possible increase of 0.13 $m \cdot s^{-1}$ as clinically meaningful. Therefore, these results indicate that RAGT does not have clinically important effects on walking speed when compared to OGT. b. Walking distance: The pooled MD was − 6 m favoring OGT (95% CI − 86 to 74; P = 0.88; I^2 = 68%). Most would consider a possible increase of 74 m as clinically meaningful. Therefore, these results indicate that RAGT may have clinically important effects on walking distance when compared to OGT,

		but these results are not certain because the 95% CI spans down to − 86 m, favoring overground training. c. AEs (four trials involving a total of 136 participants): The risk difference (95% CI) of an AE was 0.01 (−0.06 to 0.08; P = 0.79; I^2 = 0%).
Nam et al. 2017 South Korea Reviewed published articles up to January 2016 N = 10 **Level of evidence:** PEDro score **Type of study:** RCTs of parallel-groups or cross-over trials **AMSTAR:** 8	**Method:** A systematic review and meta-analysis were performed to assess the effects of RAGT (using Lokomat) on improving walking-related functional outcomes according to time since injury in patients with incomplete SCI. **Database:** MEDLINE, EMBASE, SCOPUS, Web of Science, Cochrane CENTRAL, the World Health Organization International Clinical Trials Registry Platform, and the clinical trials registry and database of the U.S. National Institutes of Health (ClinicalTrials.gov) were searched. **Outcome measures:** Walking speed (10MWT), walking distance (6MWT), leg strength (LEMS), level of functional mobility and independence (WISCI II), independence of gait (FIM-L), and spasticity (Modified Ashworth Score).	1. Of the 502 participants, 263 in four studies were assessed at < 6 months post-injury and 209 in five studies were assessed at > 12 months post-injury, and the remaining 30 participants in one study (mean 6.3 months post-injury) did not belong to any group. 2. The mean PEDro score of the studies was 5.7. 3. Among 10 comparisons, 3 investigated RAGT vs. conventional OGT, 2 investigated RAGT vs. BWS gait training, 2 investigated RAGT vs. non-gait-specific training (strength or bike), and finally, three trials compared RAGT with no intervention. 4. Effects on gait velocity: a. Gait velocity tended to be higher in the acute RAGT groups than in the OGT groups, albeit not significantly so (pooled MD = 0.08 m/s, 95% CI -0.00 to 0.15; P = 0.05; I^2 = 0%, two trials, 130 participants). b. In the chronic RAGT groups, significantly greater improvements were observed than in the no intervention groups (pooled MD = 0.07 m/s, 95% CI 0.01 to 0.12, P = 0.01, I^2 = 0%; three trials, 124 participants). 5. Effects on gait distance: a. Significantly greater improvements were observed in the acute RAGT groups than in the OGT groups (pooled MD = 45.05 m, 95% CI 13.81 to 76.29; P = 0.005; I^2 = 0%, two trials, 122 participants). b. However, there were no significant improvements in the chronic RAGT

		groups compared to the BWS or no- intervention groups (pooled MD = -4.92 m, 95% CI -11.96 to 2.11; P = 0.17; I^2 = 0%, two trials, 114 participants). 6. Effects on functional level of mobility and independence: a. Significantly greater improvements on the WISCI II and FIM-L were observed in the acute RAGT groups compared to the OGT groups (pooled MD = 0.5, 95% CI 0.02 to 0.98; P = 0.04; I^2 = 67%, three trials, 211 participants). b. There was no significant improvement in the chronic RAGT groups compared to the strength group (MD = 0.16, 95% CI -1.15 to 1.48, P = 0.81; one trial, 9 participants).
Louie et al. 2015 Canada Systematic Review AMSTAR = 8/11 N = 15	**Methods:** A systematic search in computerized databases was conducted to identify articles that reported on walking outcomes when using a powered exoskeleton. Individual gait speed data from each study was extracted. Pearson correlations were performed between gait speed and 1) age, 2) years post-injury, 3) injury level, and 4) number of training sessions. **Databases:** MEDLINE (1946 to May 6, 2015), EMBASE (1980 to May 6, 2015), Cochrane CENTRAL (1991 to May 6, 2015), and CINAHL (1982 to May 6, 2015).	1. Gait speed, ranged from 0.031m/s to 0.71m/s. The mean gait speed attained by the 84 participants in these 12 studies was 0.26m/s (SD: 0.15m/s) 2. An aggregate mean of 19.8 (SD= 18.6, n= 79) training sessions was calculated across all studies; training sessions were 60 to 120min in duration. 3. Participants ambulated on a body weight-supported treadmill while wearing the HAL. At the end of the intervention period, the participants improved their mean gait speed without the exoskeleton from 0.28m/s to 0.50m/s (p< 0.05, n= 8, effect size= 0.71). They also demonstrated an improvement in mean 6MWT distance from 70.1 m to 163.3 m (p< 0.05, n= 8, effect size= 0.64). 4. A significant correlation was found between increasing age and faster gait speed (r= 0.27, 95% CI 0.02–0.48, p= 0.03, n= 63). However, no relationship was found between injury duration and gait speed (r= 0.19, 95% CI−0.09–0.44, p= 0.18, n= 53) from 10 studies. From the 12 studies, we found a significant correlation between

		injury level and gait speed (r= 0.27, 95% CI 0.02–0.48, p = 0.03, n = 63). 5. Those who were able to practice longer with the powered exoskeleton achieved faster gait speeds (r= 0.27, 95% CI 0.003–0.49, p= 0.048, n= 56).

3.2 Systematic Reviews With Meta-Analysis Assessing Neuromodulation Strategies

Table 2. Systematic Reviews With Meta-Analysis Assessing Neuromodulation Strategies

Authors Year Country Date included in the review Number of articles Level of Evidence Type of Study AMSTAR Score	**Method Databases Outcome Measures**	**Conclusions**
Non-invasive Stimulation Methods		
Li et al. 2024 China Reviewed published articles up to April 2022 N = 14 (5 studies were pooled as having lower limb and gait outcome measures) **Level of evidence:** Cochrane risk-of-bias criteria **Type of study:** RCTs **AMSTAR:** 8	**Methods:** The study aimed to examine the effectiveness of NIBS (noninvasive brain stimulation) (transcranial magnetic stimulation [TMS] and/or transcranial direct current stimulation [tDCS]) in the treatment of motor dysfunction among those with incomplete SCI. **Databases:** PubMed, Embase and the Cochrane Library. **Outcome Measures:** Lower limb muscle strength and gait outcomes, among others.	1. Meta-analysis of muscle strength outcomes indicated a nonsignificant difference between the real NIBS and sham groups (SMD=0.35, 95% CI=-0.07 to 0.77, P=0.10, I^2=26%). However, significant effect was detected in the effect of NIBS versus sham groups on lower limb muscle strength at the one-month follow-up after intervention (SMD=0.69, 95% CI=0.11 to 1.28, P=0.02, I^2=0%). 2. Additionally, the pooled analysis of the gait outcomes showed a similar effect between the groups (SMD=0.16, 95% CI=-0.34 to 0.66, P=0.54, I^2=41%).

Shi et al. 2024 China Reviewed published articles up to December 2023 N = 6 (4 studies were pooled as having lower limb and gait outcome measures) **Level of evidence:** Cochrane Risk of Bias Tool **Type of study:** RCTs **AMSTAR:** 8	**Methods:** The study aimed to consolidate findings from available RCTs regarding the influence of transcutaneous spinal cord stimulation on extremity motor function in patients with SCI. **Databases:** Medline (PubMed), CENTER (Cochrane Library), Embase (Ovid), Web of Science, Wanfang, and China National Knowledge Infrastructure. **Outcome Measures:** Upper and/or lower extremity strength (UEMS/LEMS), and walking function (10MWT, 2MWT, 6MWT), among others.	1. Pooled results of two studies showed that transcutaneous spinal cord stimulation on the basis of conventional rehabilitation could significantly improve limb strength as evaluated by LEMS (MD: 5.28, 95% CI: 1.46 to 9.09, p = 0.007; I^2 = 0%). 2. Pooled results of four studies demonstrated that transcutaneous spinal cord stimulation significantly improved mobility as indicated by walking speed (MD: 0.13 m/s, 95% CI: 0.03 to 0.23, p = 0.009; I^2 = 0%) and walking distance (standardized MD: 0.62, 95% CI: 0.30 to 0.94, p < 0.001; I^2 = 0%). In addition, subgroup analysis for walking distance in studies with 2MWT and 6MWT showed consistent results.
Megía-García et al. 2020 Spain Reviewed published articles up to December 2018 N = 13 **Level of evidence:** GRADE, CARE (Case Report Guidelines) and PEDro Scale **Type of study:** 10 case-series studies 2 clinical trials with crossover designs **AMSTAR:** 6	**Method:** This review analyzed the feasibility and efficacy of transcutaneous spinal current stimulation (tSCS) to promote motor activity and function in patients with SCI. In addition, the range of stimulation parameters and spinal site of stimulation are also reviewed to understand the optimal protocol required to promote motor activity. **Database:** PubMed, Cochrane Registry, and PEDro. **Outcome Measures:** Motor response (electromyography [EMG], movement, force, assessment of active movement or function) and perceived clinical improvement.	1. Nine studies analyzed the lower extremities, three analyzed the upper extremities, and one assessed motor response in the trunk. 2. The total study sample comprised 55 persons with SCI. 3. Stimulation parameters: a. Level of stimulation: All studies that sought to induce muscle activation patterns in the lower extremities applied stimulation at the level of the T11-T12 interspinous space. Of these, 6 applied stimulation simultaneously at adjacent levels, such as L1-L2 or the first coccygeal vertebra. b. Type of current: i. All studies used a rectangular wave, with the waveform being reported as biphasic in five studies, monophasic in another five, and without specification in the remaining reports. ii. Eight studies applied stimulation currents applied at a carrier frequency of between 2.5 and 10 kHz with a burst frequency of 30 Hz. The

		remaining studies used isolated pulse protocol, with frequencies of bursts or pulses applied between five and 90 Hz. iii. All studies applied the stimulus with a pulse width of between 0.5 and 2.0 ms. c. Current intensity: There was great variability with most of the studies using high intensities close to the participants' tolerance threshold. Current was, thus, applied with an intensity that ranged from 10 to 250 mA. 4. Three studies recorded AEs, and in general, there was good tolerability of the intervention by patients, without any apparent AEs other than cutaneous irritation after repeated stimulation. 5. Effects on motor response during stimulation: a. All studies reported an increase in motor response. b. The reports that studied stimulation at several spinal levels observed a response dependent on the site of application of the current and a summation effect when the stimulus was simultaneously applied at various spinal levels. i. Spinal stimulation at T11- T12 → Quadriceps and hamstring ii. Spinal stimulation at L1-L2 → Triceps surae and tibialis anterior. c. Eight studies used functional variables: 6. Among other improvements in gait outcomes, a decrease in the time needed to cover 10 m has been shown in 4 studies.

Invasive Stimulation Methods		
McHugh et al. 2021 Ireland Reviewed published articles up to June 2020 N = 18 **Level of evidence:** The Modified Downs and Black Quality Checklist **Type of study:** 8 case reports 10 case series **AMSTAR:** 7	**Method:** The aim of the current review was to pool all of the currently available research regarding the efficacy of epidural spinal cord stimulation (ESCS) for regaining motor function in SCI, and systematically review existing methodologies and results. **Database:** CINAHL, Embase, Medline and Web of Science. **Outcome Measures:** Motor function was assessed with different outcome measures (e.g., ASIA, gait distance, gait speed, PLOA gait, PLOA standing, % body weight during gait, % body weight during standing, ground reaction force, joint/muscle force, joint kinematics [ROM], number of unassisted/assisted, OG walking unassisted/assisted, treadmill walking unassisted/assisted, unassisted/assisted standing [± time], EMG, intentional control of motor activity, muscle mass and action research arm test).	1. All the studies reviewed were categorized into the poor range (<14) of the Modified Downs and Black Quality Checklist. 2. Thirteen of these studies included patients with motor-complete SCI, with the remaining 5 reporting on motor incomplete patients. 3. The total number of study participants evaluated was 40. However, 7 of these were identified as repeat participants, resulting in cumulative data presented on only 24 persons. 4. Reported AEs in this review were very rare, with just one study reporting a hip fracture. However, 14 studies failed to report any information regarding AEs. 5. All studies reported some level of functional improvement, with 11 studies describing improved locomotor function and eight studies reporting improved standing ability: a. Improvements in ASIA scoring were reported in three studies and re-categorization of ASIA score post- ESCS was achieved by four participants. b. Independent ambulation with a gait aid was reported by four of the 18 studies. While these impressive results were achieved in motor incomplete persons. c. Inconsistencies in the reported methods and presentation of EMG data limit any meaningful interpretation.

3.3 Systematic Reviews With Meta-Analysis Assessing Biofeedback Techniques (Virtual Reality [VR])

Table 3. Systematic Reviews With Meta-Analysis Assessing Biofeedback Techniques (VR)

Authors Year Country Date included in the review Number of articles Level of Evidence Type of Study AMSTAR Score	**Method Databases Outcome Measures**	**Conclusions**
Abou et al. 2020 USA Reviewed published articles up to September 2019 N = 10 in the systematic review and 6 in the meta-analysis **Level of evidence:** Cochrane Risk of Bias Tool for RCTs and Quality Assessment Tool for pre-post studies with no control group **Type of study:** 3 RCTs 7 pre-post trials **AMSTAR:** 8	**Method:** The main objective of this systematic review and meta-analysis was to evaluate and synthesize the effects of virtual reality (VR) therapy on gait rehabilitation among people with SCI. **Database:** PubMed, Web of Science, Scopus, SportDiscus, and CINHAL. **Outcome Measures:** Gait outcomes (WISCI II, 10MWT, 2MWT, spatiotemporal gait parameters, 6MWT, and gait speed).	1. A total of 149 participants were included. 2. Five studies used only VR therapy and the other studies used a combination of VR therapy with balance or coordination training. 3. Methodological quality: a. Two of the three RCTs included in this review presented a low risk of bias and the third was rated as high risk of bias (and was not included in the meta-analysis). b. Four out of the seven pre-post studies included in this review presented an overall good quality and three studies were rated as fair overall quality (and were not included in the meta-analysis). 4. Effects of VR therapy assessed by meta-analysis (n = 6): a. After completion of VR therapy, results showed a trend toward improvement in overall gait function compared with baseline. The combination of the three meta-analyses (WISCI II and 10MWT) showed an overall statistically significant within-group difference (SMD = 0.34; 95% CI 0.02-0.66; P = .04).

3.4 Systematic Reviews With Meta-Analysis Assessing Mixed Physiotherapy Interventions

Table 4. Systematic Reviews With Meta-Analysis Assessing Mixed Physiotherapy Interventions

Authors Year Country Date included in the review Number of articles Level of Evidence Type of Study AMSTAR Score	**Method Databases Outcome measures**	**Conclusions**
Patathong et al. 2023 Thailand Reviewed published articles up to October 2022 N = 17 **Level of evidence:** Cochrane Risk of Bias Tool for randomized trials (RoB2) **Type of study:** RCT **AMSTAR:** 9	**Method:** This systematic review and network meta-analysis of RCTs aimed to find the best intervention for incomplete SCI, such as conventional physical therapy, treadmill, FES, and RAGT. The velocity improvement, distance and functional score of walking as well as safety issues were comprehensively assessed in this study. **Database:** PubMed and Scopus databases. **Outcome Measures:** The main outcome represented gait function including velocity (m/s), distance (m), WISCI, and WISCI II. The secondary outcomes were any adverse events during gait training such as fall and pressure ulcer.	1. For the quality assessment, the overall results were of medium quality (29% high, 59% moderate, and 12% low quality). 2. Direct meta-analysis involved 15 studies (601 patients) and three interventions (conventional physical therapy, treadmill, and RAGT).: a. Velocity: Conventional physical therapy insignificantly increased velocity compared to treadmill (pooled USMD − 0.03 m/s, 95% CI − 0.14, 0.19; I^2 = 0%, p = 0.69) and RAGT (pooled USMD 0.04 m/s, 95% CI − 0.04, 0.12; I^2 = 70%, p < 0.01). Subgroup analysis showed that RAGT improved velocity more than conventional physical therapy in acute-phase patients (time of injury < 6 months) (pooled USMD 0.1 m/s, 95% CI 0.05, 0.14; I^2 = 0%, p = 0.76) and underwent at least 2-month duration of intervention (pooled USMD 0.1 m/s, 95% CI 0.06, 0.14; I^2 = 0%, p = 0.91). Regarding to the level of SCI, subgroup analysis showed no significant difference of velocity between RAGT and conventional physical therapy. b. Distance: Conventional physical therapy was comparable with treadmill (pooled USMD 76.00 m,

		95% CI − 85.22, 236.96; I^2 = 99%, p < 0.01) and RAGT (pooled USMD 65.34 m, 95% CI − 36.26, 166.92; I^2 = 99%, p < 0.001). Regarding subgroup analysis for acute-phase, RAGT provided longer walking distance than conventional physical therapy (pooled USMD 64.75 m, 95% CI 27.24, 102.27; I^2 = 55%, p = 0.14). Moreover, subgroup analysis for the level of SCI showed that RAGT improved distance more than conventional physical therapy (pooled USMD 40.45 m, 95% CI 14.69, 66.20; I^2 = 0%, p = 0.89). c. WISCI: Compared to conventional physical therapy, RAGT significantly increased WISCI (pooled USMD 3.28, 95% CI 0.12, 6.45; I^2 = 90%, p < 0.01), whereas treadmill showed no significant differences (pooled USMD − 0.08, 95% CI − 0.93, 0.78; I^2 = 0%, p = 0.73). Regarding subgroup analysis for studies included cervical, thoracic, and lumbar SCI, RAGT improved WISCI score more than conventional physical therapy (pooled USMD 2.86, 95% CI 0.07, 5.66; I^2 = 28.09%, p = 0.24). 3. Network meta-analysis included 13 studies (709 patients), 5 interventions (conventional physical therapy, FES, treadmill, RAGT, FES + treadmill), indirect and 9 direct comparisons. a. Velocity: FES showed insignificant treatment benefit when compared to conventional physical therapy, treadmill, RAGT, and FES + treadmill with pooled USMD (95% CI) of 0.12 (− 0.07, 0.31), 0.07 (− 0.12, 0.25), 0.08 (− 0.10, 0.26), and 0.07 (− 0.12, 0.26) m/s, respectively. b. Distance: Treatment effect of FES was superior to conventional physical therapy, treadmill, RAGT and FES + treadmill with pooled USMD (95% CI) of 76.26 (− 59.68, 212.20), 2.90 (− 131.89, 137.70), 38.69 (− 95.66, 173.03), and 7.62 (− 132.66, 147.91) m, respectively.

Duan et al. 2021 China Reviewed published articles up to November 2018 N = 31 **Level of evidence:** PEDro scale **Type of study:** 28 RCTs 3 CTs **AMSTAR:** 9	**Method:** This study systematically compared the benefit of repetitive transcranial magnetic stimulation (rTMS), FES, activity-based therapy (ABT), and Robotic-assisted treadmill training on the walking capacity and motor function in persons with SCI in rehabilitation stage. **Database:** PubMed, Embase, Cochrane, the database of the U.S. National Institutes of Health, and World Health Organization International Clinical Trials Registry Platform. **Outcome Measures:** Patient independence (FIM scale and SCIM scale); lower or upper extremity functions (ASIA UEMS, UEFI, m-action research arm test, ASIA LEMS, Toronto rehabilitation institute hand function test, Jebsen–Taylor hand function test and rehabilitation engineering laboratory hand function test); walking speed (10MWT) and walking distance (6MWT); and total motor ability and functional level (Craig Handicap Assessment Report Technique, Tinneti scale, or WISCI II).	1. The averaged PEDro scale score of the included studies was 5.30. 2. A total of 1040 participants were included in present study (n = 4 articles of rTMS, n = 6 of FES, n = 9 of exercise or treadmill training, and n = 12 locomotor robot studies). 3. Interventions included studies with rTMS plus gait training vs. sham rTMS plus gait training (n = 81), FES hand therapy plus conventional occupational therapy vs. conventional occupational therapy alone (n = 174), exercise or treadmill training vs. overground walking or no intervention (n = 238) and robotic-assisted treadmill training vs. overground walking or no intervention (n = 547). 4. The efficacy of rTMS were confirmed by improvement in 10MWT (MD = 0.09, 95% CI [0.01, 0.16], I^2 = 50%, fixed-effects model; P = 0.03) and ASIA LEMS scores (MD = 4.41, 95% CI [1.55, 7.27], I^2 = 0%, fixed-effects model; P = 0.003) compared with controls (sham rTMS or plus gait training); however, rTMS did not induce significant WISCI II changes (MD = – 1.52, 95% CI [– 3.43, 0.40], I^2 = 25%, Fixed-effects model; P = 0.12) compared with control. 5. Meta-analysis indicated that FES did not provide an obvious difference in lower extremity independence (MD = – 0.02, 95% CI [– 1.18, 1.15], I^2 = 34%, Fixed- effects model; P = 0.98) between the experimental and control groups. 6. The ABT (activity-based therapies) including massed practice and treadmill training did not improve walking speed (10MWT) (MD = – 0.01, 95% CI [– 0.09, 0.06], I^2 = 0%, Fixed-effects model; P = 0.71) and walking distance (6MWT) (MD = 6.46, 95% CI [– 9.02, 21.94], I^2 = 64%, Random-effects model; P = 0.41) compared with control (no intervention, overground mobility therapy, self-regulated

		exercises, or conventional rehabilitation program). 7. Meta-analysis indicated that Robotic-assisted treadmill training did not increase walking speed (10MWT) (MD = 0.00, 95% CI [– 0.02, 0.03], I^2 = 3%, Fixed-effects model; P = 0.74) and walking distance (6MWT) (MD = 14.30, 95% CI [– 5.80, 34.41], I^2 = 85%, Fixed-effects model; P = 0.16) compared with control (no intervention, bike, and overground walking). However, Robotic-assisted treadmill training significantly increased ASIA LEMS score (MD = 5.00, 95% CI [3.44, 6.56], I^2 = 0%, Fixed-effects model; P < 0.00001) and lower extremity independence (MD = 3.73, 95% CI [2.53, 4.92], I^2 = 28%, Fixed-effects model; P < 0.00001).
Aravind et al. 2019 Australia Reviewed published articles up to January 2018 N = 26 **Level of evidence:** Cochrane Risk of Bias Tool **Type of study:** RCTs and randomized cross-over trials **AMSTAR:** 9	**Method:** The two primary objectives of this systematic review were to determine: • The effectiveness of any physiotherapy intervention compared to sham or no intervention for increasing muscle strength in people with SCI. • The relative effectiveness of any physiotherapy intervention compared to another physiotherapy intervention for increasing muscle strength in people with SCI. **Database:** Embase (via the Ovid search engine), Medline (via the Ovid search engine), the Cochrane CENTRAL and the PEDroGT. **Outcome Measures:** Voluntary strength of muscles directly affected by SCI (measured by force [kg or Nm], torque [Nm], results of a manual muscle testing [MMT] [points] or composite measures such as the LEMS [points]).	1. The number of participants in the trials included a median number (interquartile range) of 14 (10 to 29) per group. 2. Overall, 12 of the 26 trials were at high risk of bias on three or more items of the Cochrane Risk of Bias Tool. 3. Comparison of any two physiotherapy interventions to each other (n = 16): a. Ten trials compared one type of gait training with another type of gait training (or another type of physiotherapy intervention): BWSTT vs. OGT, robotic gait training vs. OGT (n = 3), robotic gait training vs. strength training (n = 1), swing-assisted robotic gait training vs. swing-resisted robotic gait training (n = 1), high-intensity BWSTT and OGT vs. low-intensity BWSTT and OGT (n = 1), BWSOGT vs. BWSTT (n = 1), and robotic gait training vs. stretch (n = 1). Only robotic gait training vs. OGT showed statistically significant between-group differences, favoring robotic gait training, in the meta-analysis (MD = 3.1/50

		points on the LEMS; 95% CI, 1.3–5.0; p = 0.0008) b. The remaining six trials compared one type of non-gait related therapy with another type of non-gait related therapy. Focusing lower limb function, only one study examined FES cycling vs. passive leg cycling and other study examined maximal intensity resistance training (RT) vs. conventional RT. None of these trials showed a statistically significant between-group difference.
Lam et al. 2007 Canada Systematic Review AMSTAR = 4 N = 41	**Methods:** Literature search for published literature evaluating the effectiveness of any treatment or therapy on functional ambulation in people with SCI. Interventions include BWSTT, FES, braces/orthoses and hybrid therapies. Outcome measures include FIM, WISCI II, walking distance, and walking speed. **Databases:** PubMed/MEDLINE, CINAHL, EMBASE, PsycINFO.	1. There is level 1 evidence of an overall enhancement of functional ambulation, as measured by overground gait speed, when BWSTT was combined with FES of the common peroneal nerve. 2. There is level 1 evidence that a combination of physical therapy and GM-1 ganglioside improved motor scores, walking distance, and walking speed in participants with chronic SCI. 3. There is level 1 evidence that different modes of gait training (BWSTT vs. overground) result in similar effects.

4 Predictors for Walking after SCI

Many people with SCI are interested in regaining the ability to walk to maintain independence in their lives. Considerable progress has been made in predicting who will or will not be able to walk post-SCI.

Defining Walking Recovery after SCI

To determine if someone with SCI can engage in walking training, you will need to know their neurological status, the completeness/incompleteness of their SCI, and some empirical data from their attempts to stand and/or maintain balance beforehand. There are of course ways to engage in these activities safely, with multiple spotters (i.e., nurses/physical therapists) present, and/or using assistive technologies like hydraulic lifts, body-weight support systems, standing frames, parallel bars, or walkers.

Functional ambulation has been defined as “the capacity to walk reasonable distances in and out of home unassisted by another person,” (Hussey & Stauffer 1973) and “the ability to walk, with

or without the aid of appropriate assistive devices (such as prostheses, orthoses, canes or walkers), safely and sufficiently to carry out mobility-related activities of daily living" (Stroke Engine 2025).

Regaining the ability to walk after SCI is not a 'one size fits all' prospect; there are many things for the health care professional and the person with SCI to consider. For example, there may be differences in strength, sensation, and motor ability between the right leg and the left leg, which could compromise step length/cadence, walking symmetry, and balance putting the person with SCI at risk for falling and further injury. Someone with incomplete SCI who can walk may be safe to stand and walk in their own home, but may not be able to walk far enough to get from where their car is parked to their place of work, or they may not be able to walk fast enough to cross a street before the traffic lights change.

Tests Used to Measure Walking Ability in People with SCI

A number of tests, or Outcome Measures, have been validated to test walking ability in people with SCI.

Timed tests include:

- Timed Up & Go (TUG) test measures the time in seconds it takes someone to stand up from an armchair, walk 3 meters, return to the chair, and sit down. This test was originally developed as a clinical measure of balance in elderly people.13
- Ten Meter Walk Test (10MWT) measures the time in seconds that it takes a people to walk 10 meters (i.e., assessing short-duration walking speed).
- Six Minute Walk Test (6MWT) measures the distance in meters walked within 6 minutes. This test is useful in assessing how far people can walk safely continuously (i.e., walking duration) in addition to getting an approximation of cardiovascular exercise capacity.

Functional walking tests include:

- Walking Index for Spinal Cord Injury II (WISCI-II) an ordinal scale that quantifies a person's walking ability; the lowest score of 0 indicates that a person cannot stand and walk and the highest score of 20 is assigned if a person can walk more than 10 meters without walking aids or assistance.
- SCI Functional Ambulation Inventory (SCI-FAI) – walking ability is measured by three components: gait parameter (weight shift, step width, step rhythm, step height, foot contact, step length), assistive devices use (degree of assistance provided by each device (e.g., cane, walker, parallel bars)), and walking mobility (walking distance, speed, and walking frequency).
- The Spinal Cord Independence Measure (SCIM) – Scale developed to measure the functional abilities of people with SCI and their level of independence when performing basic activities of daily living. The walking related items comprise the SCIM-Mobility subscale, useful for functional walking determination because they are scored based on

the level of assistance need by the walker (e.g., 0 = total assistance; 1 =electric wheelchair or partial assistance to operate manual wheelchair; to 6 = walks with 1 cane; 7 = needs leg orthosis only; and 8 = walks without aid).

There is some research to show what walking speeds are safe for different levels of ambulation. Van Hedel et al. (2009) created 5 functional ambulation categories from the SCIM Mobility items and subsequently timed all participants to determine threshold times for grouping walkers with SCI. They found:

1. With a minimum walking speed of 0.09 ± 0.01 m/s, a person with SCI would be considered a "supervised walker."
2. With a minimum walking speed of 0.15 ± 0.08 m/s, a person with SCI would be considered an "indoor walker."
3. With a minimum walking speed of 0.44 ± 0.14 m/s, a person with SCI would be considered an "assisted walker."
4. To be considered a "walker who does not use a walking aid", a minimal walking speed of 0.70 ± 0.13 m/s is required. This is also the threshold that clinicians may consider a person with SCI “functional ambulation” or safe for walking in the community.

Severity of Spinal Cord Injury Lesion and ASIA Impairment Scale

The most important variable in determining walking capabilities will be neurological level and completeness/severity of injury. The standard assessment of the severity and level of SCI is the International Standards of Neurological Classification of Spinal Cord Injury (ISNCSCI). The ISNCSCI is (ideally) performed within 72 hours of a SCI to allow clinicians to determine the neurological level and completeness of injury through testing of voluntary movements and pinprick/light touch sensation. The ASIA Impairment Scale (AIS) defines complete and incomplete spinal cord lesions, remaining sensory or motor function, and classifies people on a 5-level ordinal scale:

- A: Complete. No sensory or motor function is preserved in the sacral segments S4-S5.
- B: Sensory incomplete. Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5 (light touch, pin prick at S4-S5 or deep anal pressure), AND no motor function is preserved more than three levels below the motor level on either side of the body.
- C: Motor incomplete. Motor function is preserved below the neurological level and more than half of key muscle functions below the single neurological level of injury (NLI) have a muscle grade less than 3.
- D: Motor incomplete. Motor function is preserved below the neurological level and at least half of key muscle functions below the NLI have a muscle grade of 3 or greater.

- E: Normal. If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

In a review of all walking-related predictor literature in people with SCI, Scivoletto et al. (2014) provided the following conclusions:

- AIS A:
  - Limited possibilities of achieving walking, however of people who convert from complete to incomplete injury, 14% may regain some walking function (usually limited to those with injuries from T12 to L3, orthoses/braces or other devices may be required, and the speed at which they may walk will likely be slow and require great energy, so may not be 'functional.' (van Middendorp et al. 2009; Ditunno et al. 2008; Vaccaro et al. 1997).
- AIS B:
  - An estimated 33% of people may recover walking ability. Pinprick preservation seems to be a positive factor compared to light touch sensitivity, suggesting less extensive damage to the spinothalamic tracts and posterior column (Foo et al., 1981; Crozier et al. 1991; Waters et al. 1994; Katoh and el Masry 1995; Oleson et al. 2005).
- AIS C:
  - Around 75% have a positive prognosis for walking, especially in those with lower thoracic and lumbar level injuries, though orthoses/braces or other assistive devices will likely be necessary. Age is a stronger predictor at AIS C than in other levels, with 80-90% of people younger than 50 more likely to walk versus 30-40% in those over 50 (Maynard et al. 1979; Crozier et al. 1991; Waters et al. 1994; van Middendorp et al. 2009; Waters et al, 1994; Perot and Vera 1982; Foo, 1986; Burns et al. 1997; Scivoletto et al. 2003).
- AIS D:
  - Very good likelihood of walking at rehabilitation discharge and at 1-year post-injury (Burns et al. 1997; Scivoletto et al. 2003; van Middendorp et al. 2009).

Specific Walking Prediction Models in People with SCI

Some research provides more precise prediction models for walking in people with SCI based on remaining neural activity in specific myotomes and muscles. Van Middendorp (2011; N=640) produced a prediction rule using the motor scores and light touch scores at both L3 (quadriceps femoris – knee extensor) and S1 (gastrocsoleus – plantar flexor) and age of the person with SCI. This data had excellent discrimination and accurately distinguished independent walkers, dependent walkers, and non-walkers (area under the curve 0.956, 95% CI 0.936–0.976, $p<0.0001$). Hicks (2017; N= 278) tested a simplified model of Van Middendorp's prediction rule on Rick Hansen Spinal Cord Injury Registry (RHSCIR) data set, using only L3 motor score, S1

light touch score, and age as a dichotomized variable (older/younger than 65 years). The simplified Hicks three variable model had an overall classification accuracy of 84%, with 76% sensitivity and 90% specificity.

More recently, two additional prediction models have emerged using similar variables. Draganich et al. (2023; N=3721) used L3 motor score, L5 motor score (big toe extensor), and S1 light touch as inputs and they were able to predict outdoor walking capabilities at 1-year post-SCI 84.9% of the time. Cathomen et al. (2023; N=361) used L2 and L3 myotomes to differentiate between walkers and non-walkers. They found that 85% of patients with a motor score in the L2 myotome of 1 or higher achieved ambulatory capacity throughout rehabilitation, and for the L3 myotome the proportion was 88%.

Accurately assessing someone's SCI level of injury and completeness, as well as using these prediction rules may useful for clinical decision-making in rehabilitation. For example, if someone with SCI is more likely to walk based on these parameters, then intensive walking training would more likely be useful to be prescribed. Conversely, if someone is less likely to walk based on these parameters, then a rehabilitation program focusing on wheelchair skills, transfers, and other compensatory strategies would likely be the most useful course of action (Draganich et al. 2023).

Key Points

After spinal cord injury, people may or may not be able to walk. The level and completeness of injury (i.e., AIS level) will be the best indicator; people with lower and incomplete injuries will have greater chances of regaining walking ability. Research suggests that the odds of recovering walking ability for people with AIS A, B, C, and D will be roughly: less than 15%, 33%, 75%, and >90%.

Outcome Measures like the 10-meter walk test (10MWT), the 6-minute walk test (6MWT), the Walking Index for SCI (WISCI-II), and the mobility subscale of the Spinal Cord Independence Measure (SCIM) are good for benchmarking walking speed, duration, and functionality in people with SCI.

Some clinical prediction rules have been established by research showing that responsiveness in specific myotomes and dermatomes like L3 and S1 can accurately predict walking types (i.e., none/indoor/outdoor) approximately 85% of the time.

Table 5. Predictors of Walking

Author, Year Study Design Setting	Population Characteristics	Methods	Outcomes
Cathomen et al. 2023 Cohort Study Switzerland	**N:** 361 **Level:** Paraplegia **Mean age:** 40 **% Female:** 20.5%	**Objective:** To assess walking function using an established outcome measure featuring a continuous scale. **Outcome Measure:** 6-minute walk test, 10-m walk test, Spinal Cord Independence Measure III, mobility items 12-14, Walking Index for Spinal Cord Injury	**Results:** The group of non-walkers showed no muscle function early after injury in any myotome (motor score median [range] = 0 [0-1]), compared to indoor walkers with residual muscle function in myotomes L2 (motor score median [range] = 1 [0-5]) and L3 (motor score median [range] = 2 [0-4]). Indoor walkers were thereby characterized by a lack of muscle function of the MI leg in distal myotomes L4, L5, and S1 (motor score median [range] = 0 [0-4]) ≤15 days after injury.

Van Middendorp et al. 2011
Longitudinal Cohort Study
Europe
	N: 640
	Level: AIS - 241 A; 63B; 82C; 171D; 5E
	Mean Age (SD): 45 ± 17 (18-92)
	% Female: 21%
		Study Duration:
		longitudinal cohort study of adult patients with traumatic spinal cord injury, with early (within the first 15 days after injury) and late (1-year follow-up) clinical examinations, who were admitted to one of 19 European centres between July 2001, and June 2008
		Outcome Measures: SCIM
		A clinical prediction rule based on age and neurological variables was derived from the international standards for neurological classification of spinal cord injury with a multivariate logistic regression model
		Objective:
		Developed a simple clinical prediction rule derived from data from a large prospective European
			Results:
			A combination of age, motor scores of the quadriceps femoris (L3), gastrocsoleus (S1) muscles, and light touch sensation of dermatomes L3 and S1 showed excellent discrimination in distinguishing independent walkers from dependent walkers and non-walkers
			The prediction rule distinguished well between those patients who were able to walk independently and those who were not (AUC 0·956, 95% CI 0·936–0·976, p<0·0001)
			Prediction Rule:
			- Four neurological predictors:
			  - Quadriceps femoris muscle grade (L3)
			  - Gastrocsoleus muscle grade (S1)

		database that can be used by physicians to counsel patients with traumatic spinal cord injury and their families during the initial phase after injury	- Light Touch Score at L3 - Light Touch Score at S1 - Age
Burns et al. 1997 Inception Cohort Study USA	**N:** 1191 (105) **Level:** AIS: 64 C, 41 D **Mean Age (SD):** 45 + 17 (18-92) **% Female:** 21%	**Objective:** To determine the effect of age and initial neurologic status on recovery of ambulation in patients with motor incomplete tetraplegia. **Study Duration:** Inception cohort study of acute SCI patients admitted between January 1984 - January 1993, within 72 hours of admission. **Outcome Measure:** Ambulatory Status at time of discharge from inpatient rehab. For this study, a patient was considered ambulatory if able to walk 50 feet without assistance from another person. The use of ambulatory aids and orthoses was permitted.	**Results:** Age and initial ASIA classification are associated with recovery of independent ambulation. - All ASIA D patients have a good prognosis for ambulation, regardless of age. - Older patients with ASIA C tetraplegia demonstrate less functional motor recovery than younger patients. Results ($p < 0.0001$, x2 test): ● 30/33 ASIA C subjects younger than 50 became ambulatory by discharge ● 13/31 ASIA C subjects older than 50 became ambulatory by discharge ● All ASIA D subjects became ambulatory by discharge
Van Hedel et al. 2009 Prospective cohort Europe	**N:** 886 **Level:** AIS - 413 A, 113 B, 137 C, 223 D **Mean Age (SD):** ASIA A, 39 (18) ASIA B, 42 (18) ASIA C, 48 (20) ASIA D, 47 (17) **% Female:** ASIA A 19%; ASIA B 27; ASIA C 32; ASIA D 22	**Objective:** The aim of the present study was to assess gait speeds that distinguished between levels of functional ambulation in subjects with a spinal cord injury. **Study duration:** Patients within 2 weeks of injury were prospectively assessed across 18 European centres between 2001 - 2007. Assessments occurred at 1, 3, 6, and 12 months after SCI **Outcome Measures:** SCIM II	**Results:** 1. In general, participants in a higher category walk at higher speeds. For each time point, the walking speed differed between the ambulatory categories (for all, $P < .001$) 2. Speeds that separate ambulation Categories: a. Indoor walker, wheelchair dependent: 0.15 ±0.08m/s b. Assisted walker: 0.44±0.14m/s c. No aid walkers: 0.70±0.13m/s

		10MWT 6MWT	3. Distinguishing between minor and strong dependence on walking aids categories: a. Minor dependence for aids (1 cane, leg orthosis): 0.64 m/s @ 3 months, 0.68 m/s @ 6 months b. Strong dependence for aids: 0.44 m/s
Zörner et al. 2010 Prospective cohort Europe	**N:** 90 **Level:** Tetraparesis: 4 C2; 5 C4; 17 C4; 20 C5; 5 C6 AIS (subacute phase): 20C, 31 D AIS (chronic phase): 1B, 5C, 45 D Paraparesis: 20 thoracic; 19 lumbar AIS (subacute phase): 19 C, 20 D AIS (chronic phase): 2 C, 35 D, 2E **Etiology:** Tetraparesis: 43 traumatic, 5 ischemic, 1 hemorrhagic, 1 disk herniation, 1 other Paraparesis: 28 traumatic, 6 ischemic, 1 hemorrhagic, 4 disk herniation **Mean Age (SD):** Tetraparesis**:** 50.27 ± 16.17 Paraparesis: 42.38 ± 16.46 **% Female:** Tetraparesis: 19.6% Paraparesis: 30.8%	**Objectives:** The aims of this study on people with motor incomplete SCI (miSCI) were: (1) to rank the strongest single predictors and predictor combinations of later walking capacity; (2) to develop a reliable algorithm for clinical prediction; and (3) to identify subgroups with only limited recovery of walking function **Study Duration:** Participants were selected from a prospectively gathered European database and admitted between 2001 and 2005 to acute care and rehabilitation hospitals **Outcome Measures:** WISCI II, 6MWT, lower extremity motor score (LEMS)	**Results:** 1. Participants with tetra- or paraparesis achieved average WISCI II scores of 13.6 ± 8.4 (median = 20) or 17.9 ± 4.1 (median = 20) respectively, six months after injury. 2. Within 6 min (6MWT), participants with tetraparesis were able to walk a mean distance of 284 ± 235 m; paraparetic subjects: 376 ± 209 m. 3. For participants with tetraparesis, results of the 6MWT (57% "functional" walkers) were very similar to the WISCI II outcome (53% "independent" walkers) 4. In contrast, 79% of the participants with paraparesis were scored as "functional" (6minWT), but only 64% as "independent" walkers (WISCI II) 5. Strongest correlations between single predictors + outcome measures for walking function in tetra + paraplegia a. Pin prick: r=0.80 i. WISCII: tetra: p<0.01, para: p<0.01 ii. 6MWT: tetra: p<0.01, para: p>0.01 b. Light touch: r=0.69

			i. WISCI II: tetra: p<0.01, para p>0.01 ii. 6MWT: tetra p<0.01. Para p>0.01 6. LEMS = best predictor of walking outcomes - correct prediction rates: a. Tetraparesis = 90% for WISCI II, 90% for 6MWT (p<0.01 both) b. Paraparesis = 67% for WISCI II, 90% for 6MWT (p<0.01) 7. Strongest combined predictors a. 6MWT (functional vs non-functional walkers): LEMS and AIS most predictive
Phan et al. 2019 Prospective Cohort Study Canada	**N:** 675 **Level:** AIS A&D 515; B&C 160 **Etiology:** Assault 17; Fall 302; Sports 129; Transport 181; Other 34; Surgery 97 **Mean Age (SD):** AIS A&D 47.2(18); B&C 45.1 (18.6) **% Female:** A&D 22%; B&C 21%	**Objective:** To compare independent ambulatory outcomes in AIS (ASIA [American Spinal Injury Association] Impairment Scale) A, B, C, and D patients, as well as in AIS B+C and AIS A+D patients by applying two existing logistic regression prediction models **Study duration:** Individuals with traumatic SCI enrolled in the pan-Canadian Rick Hansen SCI Registry (RHSCIR) between 2004 and 2016 with complete neurologic examination and Functional Independence Measure (FIM) outcome data **Outcome Measures:** FIM locomotor score was used to assess independent walking ability at 1-year follow-up.	**Uses prediction models from (see above extractions):** **1. Van Middendorp** **2. Hicks** **Van Middendorp model:** 1. AUCs for AIS A, B, C, and D were 0.730 (0.622–0.838), 0.691 (0.533–0.849), 0.850 (0.771–0.928), and 0.516 (0.320–0.711), respectively. 2. AUCs for A+D = 0.954 (95% confidence interval [CI]0.933–0.975 3. AUCs for B+C 0.833 (95% CI 0.771–0.895 **Hicks model:** 1. AUC for AIS A, B, C, and D were 0.730 (0.621–0.839), 0.714 (0.565–0.863), 0.840 (0.747–0.933), and 0.519 (0.307–0.731), respectively 2. AUCs for A+D = 0.950 (95% CI 0.928–0.971)

			3. AUCs for B+C = 0.821 (95% CI 0.754–0.887) Comparing Models: 1. The difference in AUC between AIS A+D and AIS B+C cohorts was statistically significant using both the van Middendorp and Hicks models (p=.00038) 2. When comparing between the two models, the difference of AUCs was not statistically significant for AIS A+D (p=.131) or AIS B+C(p=.448)
Kay et al. 2007 Retrospective Study USA	**N:** 343 **Level** AIS A or B tetraplegia 135 A or B paraplegia 84 C tetraplegia 44 C paraplegia 16 D 64 **Mean Age (SD):** 42.1 **Avg time post injury (SD):** 24 days **% Female:** 30%	**Objective:** To investigate how injury level and American Spinal Injury Association Impairment Scale (AIS) grade at rehabilitation admission are related to walking at discharge after traumatic spinal cord injury (SCI). **Study duration:** Traumatic SCI Inpatients between January 1998 to May 2004 were retrospectively studied **Outcome Measures:** FIM instrument walking rating of 3 (moderate assistance) or higher at discharge	**Results:** 1. Significantly more participants admitted with AIS grade C than AIS grade A or B injuries walked at discharge (P<.001) 2. No AIS grade C tetraplegics at admission walked at discharge, a significant difference (P<.001) 3. Fewer AIS grade A or B patients walked at discharge than AIS grade C (P<.001) 4. Injury level was not significantly associated with walking at discharge for participants with AIS grade C injuries (P=.756) 5. A logistic regression model showed that injury level was not associated with walking (P=.946) when data were adjusted for age and onset time. 6. The presence of Central Cord Syndrome was not associated with walking at discharge with an AIS grade C injury in this sample. 7. Participants with AIS grade D injuries at admission were

			more than twice as likely to walk as subjects with AIS grade C injuries (67.2% vs 28.3%, P.001) 8. A logistic regression model showed that admission AIS grade (D vs C) was associated with walking at discharge (P.001) when data were adjusted for age and onset time. 9. Among participants aged >50, non-significant association between age and walking while adjusting for neurological level and onset time (P=.810) 10. Significantly more participants younger than 50 walked than participants older than 50 (P=.0401)
Hicks et al. 2017 Prospective cohort Canada	**N:** 278 **Level** AIS A 113 B 30 C 55 74 D **Mean Age (SD):** 44(18) **Avg time post injury (SD):** n/a **% Female:** 20%	**Objective:** To revalidate an existing clinical prediction model for independent ambulation (van Middendorp et al. 2011) using acute and long-term post-injury follow-up data, and to investigate **Study duration:** Acute (0-15 days) and long term follow up data (>12 months) were extracted for traumatic SCI patients were prospectively obtained from the RHSCIR, between 2004 and 2014. **Outcome Measures:** The FIM locomotor score was used to assess independent walking ability	Proposed simplified prediction model: three variables: - age at injury (<65 years vs. ≥65 years), - L3 motor score at admission, and - S1 light touch sensory score at admission. - The AUC was calculated to be 0.866 (95% confidence interval 0.816–0.916, p<.001), which is only slightly lower than that of the five-variable LR model The fitted model yielded 85% overall classification accuracy, 79% sensitivity, and 90% specificity. The AUC was calculated to be 0.889 (95% confidence interval 0.846–0.933, p<.001)
Buehner et al. 2012 Prospective cohort study	**N:** 224 **Level** AIS C 57	**Objective:** To determine the effects of locomotor training on: (1) the International Standards for Neurological	**Results:** 1. Post-locomotor training, a significant number of participants (28.1%) classified as AIS grade C

USA	D 167 **Mean Age (SD):** 42.5 (15.9) **Avg time post injury (SD):** 2.45 (3.79) **% Female:** 26%	Classification of Spinal Cord Injury examination; (2) locomotion (gait speed, distance); (3) balance; and (4) functional gait speed stratifications after chronic incomplete spinal cord injury (SCI). **Study duration:** Acute (0-15 days) and long term follow up data (>12 months) were extracted for traumatic SCI patients were prospectively obtained from the RHSCIR, between 2004 and 2014. **Outcome Measures:** AIS classification, lower extremity pin prick, light touch and motor scores, 10MWT, 6MWT, and the Berg Balance Scale	improved to AIS grade D (9/32; P.001) 2. 92% of the overall sample remained unchanged (n=23 AIS grade C; n=109 AIS grade D) 3. Significant gains in gait speed, ambulation distance, and balance occurred after locomotor training regardless of initial AIS classification (n225) (P<.01) 4. Gains in gait speed resulted in significant conversion between these functionally stratified groups after locomotor training (P<.001) 5. LEMS at enrolment did not correlate well with gait speed, endurance, or balance after locomotor training
Wirz et al. 2006 Longitudinal and cross-sectional analysis Europe	**N:** 178 **Level:** A (motor complete, walking) tetra 49 para 68 B (motor incomplete, non-walking) tetra 24 para 22 C (motor incomplete, standing or walking) tetra 3 para 12 1 (limited walking function) Tetra 16 Para 33 2 (unrestricted walking function) Tetra 24	**Objective:** To relate locomotor function improvement within the first 6 months after spinal cord injury (SCI), to an increase in Lower Extremity Motor Score (LEMS) and to assess the extent to which the level of lesion influenced the outcome of ambulatory capacity. **Study duration:** Retrospective study on an electronic database in 2005 over a 20-month period. Traumatic or ischemic injuries were included. **Outcome Measures:** WISCI, Gait speed, LEMS LEMS = voluntary muscle strength of hip flexors, knee extensors, ankle dorsiflexor, toe extensor, ankle plantar flexor	**Results:** 1. Walking function (i.e., WISCI, gait speed) did not change. 2. For the total group, the overall improvement in LEMS, WISCI, and gait speed was significant (P<0.001). 3. No difference was evident between the relative improvements of LEMS and gait speed (P=0.54). 4. Group C (motor incomplete, standing or walking) the overall improvements of LEMS, WISCI, and gait speed was significant (P=0.001).

	Para 13 **Mean Age (SD):** A 35.3 (14.1) B 44.1 (16.4) C 42.1 (14.4) 1 tetra 46.2 (12.8) 1 para 37.7 (15.4) 2 tetra 42.2 (14.1) 2 para 37.1 (10.6) **% Female**: 33%		
Draganich et al. 2023 Retrospective Study USA	**N:** 3721 participants' data **Level:** AIS A: 446 AIS B: 145 AIS C: 255 AIS D: 337 **Mean age:** 47.2 **% Female:** 21.4%	**Objective:** Retrospective analysis of USA SCI Model Systems data from 12 centers. **Outcome measures:** L3 motor score, L5 motor score, and S1 sensory score	1. Clinical Prediction Rule (CPR) ≥ 33 was identified as the optimal predictive CPR threshold to predict outdoor walking one year after SCI. 2. We were also able to predict outdoor walking one year after SCI with high accuracy in the testing dataset using the optimal CPR threshold determined by cross-validation (CPR ≥ 33) 3. Prediction performance-area under the curve: 0.900 (95% CI: 0.890 – 0.910; p < 0.0001), classification accuracy of 82.9% (95% CI: 81.6% – 84.1%; p < 0.0001), balanced accuracy of 83.8% (95% CI: 82.6% – 85.0%; p < 0.0001), sensitivity of 88.1% (95% CI: 0.890 – 0.910; p < 0.0001), and specificity of 79.4% (95% CI: 0.890 – 0.910; p < 0.0001)
Silfhout et al. 2016 Retrospective Study Europe	**N:** 184 **Level:** ABC C1-C4 – 45; ABC C5-C8 – 58; ABC T1-T6 27 ABC T7-S5 31 D 23 **Mean Age (SD):** 42 (18) **% Female:**	**Objective:** To determine the accuracy of a previously described Dutch clinical prediction rule for ambulation outcome in routine clinical practice (Van Middendorp study). Study duration: Traumatic SCI patients were retrospectively studied	4. The AUC was 0.939, 95% CI (0.892, 0.986) 5. There was no significant difference between those who did and those who did not walk in terms of gender or whether the patients had spinal surgery 6. Analyses comparing the patients with a 1-year follow-up, a 6-month follow-

	26%	from hospital records (2006 - 2014) **Outcome Measures:** Ability to walk independently at 1 year post injury	up and a missing follow-up showed significant differences (Po0.05) in time hospitalised.

5 Gait Retraining Strategies to Enhance Walking

5.1 Overground Training

Overground gait training (OGT) has been the predominant approach for regaining walking function, until recent years when the emphasis shifted to other forms of locomotor training (LT) (Mehrholz et al. 2017). Overground walking training (OWT) does not require expensive devices, and it more closely resembles natural walking conditions in daily life compared to walking on a treadmill (Yu et al. 2019). It is most likely in people with motor incomplete SCI and is used when there is improved neuromuscular capacity and/or a readiness to walk at home and in the community. Though overground training is often used as a control group for other types of treatment (e.g., treadmill training), some studies assessed a progressive approach to overground training.

Table 6. Overground Training for Gait Rehabilitation

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Amatachaya et al. 2021 Thailand RCT PEDro = 6 Level 1 N = 54	**Population:** 54 ambulatory persons with SCI, with the ability of independent walking over at least 17 m with or without assistive devices (or a FIM-L score of 5-7); 36 males and 18 females; mean (± SD) age 51.7 (± 15.4) years; paraplegia (n = 34) and tetraplegia (n = 20); AIS C (n = 15) and D (n = 39); and mean (± SD) time since injury 88.3 (± 79.6) months. **Treatment:** Participants were randomly stratified into: • Participants in the control group (n = 26) performed an overground walking training	1. All participants in the experimental group could safely walk on a track with different surfaces without any AEs. 2. Functional outcome measures: a. Only the participants in the experimental group showed significant improvements after 2- and 4-week training for the 10MWT, 6MWT, and FTSTS test (P < 0.001). b. There were no significant differences after 6 months follow-up for both training programs.

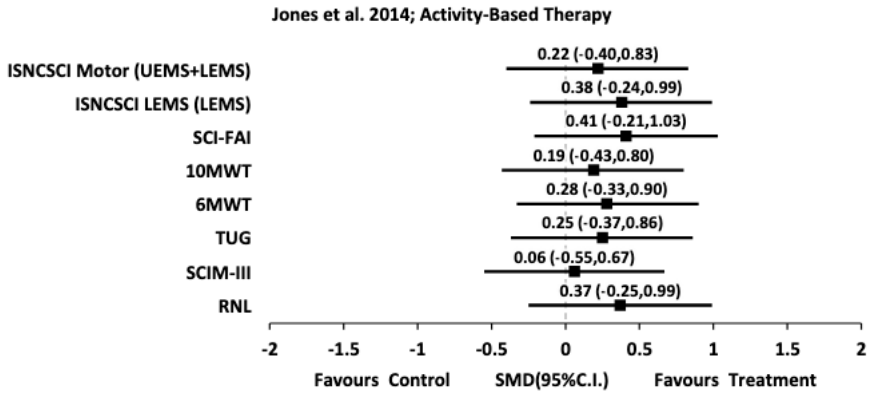
	(OWT) over a hard flat, and smooth surface. • Participants in the experimental group (n = 28) performed a walking training on a walking track (10m long) with different surfaces (walking track with different surfaces consisted of artificial pebbled, grass, and soft areas). Training program was performed for 30 min/d, 5 d/wk over 4 weeks; and participants walked at their usual speed without fatigue. **Outcomes Measures:** 10MWT, FTSTS test, 6MWT, and fall data were assessed at baseline, after 2- and 4-week training, and at 6 months follow-up.	3. During 6-month follow-up, 5 participants (9 falls in total) in the experimental group and 12 participants (39 falls in total) in the control group experienced falls, with a relative risk of 0.39 for participants in the experimental group as compared to those in the control group.
Lotter et al. 2020 USA RCT PEDro = 6 Level 1 N = 16	**Population:** 16 participants with motor incomplete SCI and the ability to walk overground at self-selected speeds <1.0 m/s without physical assistance but with devices and bracing below the knee as needed; 10 males and 6 females; mean age 48.5 years; injury level C1-C4 (n = 6), C5-C8 (n = 4) and T1-T10 (n = 6); and mean time since injury 4.1 years. **Treatment:** Participants were randomized to receive up to 20 sessions of either task-specific or impairment-based training (both of 40 min sessions) over less than 6 weeks followed by the alternate training paradigm after a break of 4 weeks: • Task-specific training consisted of stepping practice in variable contexts (i.e., speed-dependent treadmill training, skill-dependent treadmill training, overground training, and stair climbing) within 1-hour sessions. • Impairment-based training consisted of nonwalking interventions, including strengthening, aerobic conditioning and practice of	1. Task-specific training group had significant higher stepping parameters during the training; however, average number of sessions completed, was similar between groups. 2. Significantly greater increases in fastest overground and treadmill walking speeds, and 6MWT were observed following task-specific vs. impairment-based training; with moderate associations between differences in amount of practice and outcomes. 3. There were no differences for self-selected speed, FTSTS test, or LEMS in either group. 4. Changes in peak recumbent stepping power favored impairment-based vs. task-specific training. 5. There were no serious AEs during the intervention; however, there were significantly greater incidence of minor AEs, including a greater number of falls, during task-specific (n = 23) vs. impairment-based training (n = 8), P < .01).

	transfers to improve lower extremity and trunk strength and coordination. A primary intent of both strategies was to achieve high cardiovascular intensities (e.g., 70%-80% HRR and rate of perceived exertion [RPE] >14). **Outcome measures:** Fastest speed over short distances, peak treadmill speed, self-selected speed, 6MWT, Berg Balance Scale (BBS), FTSTS test, activity-specific balance confidence (ABC) scale, PROMIS-Mobility score, LEMS, and incidence of AEs were assessed prior to and following each training protocol.	
Brazg et al. 2017 USA RCT cross-over PEDro = 6 Level 1 N = 15	**Population:** 15 participants with a chronic motor incomplete SCI at neurological injury level of T10 or above; 11 males and 4 females; mean (± SD) age 49 (± 8.1) years; injury level high cervical (C1-C4) (n = 4), low cervical (C5-C8) (n = 6), and thoracic (T1-T10) (n = 5); AIS C or D (n = 15); and mean (± SD) time since injury 7.7 (± 7.9) years. **Treatment:** Participants were randomized to receive sessions of either a high- or low-intensity LT over 4 to 6 weeks, followed by a 4-week wash-out. Both high- and low-intensity LT consisted of up to 20 one-hour sessions at a frequency of 3 to 5 days/week over ≤ 6 weeks. The goals of sessions were to achieve 40 min of stepping practice while maintaining the desired HRs or RPEs (high-intensity training [70%-85% HR_{max}, 15 to 17 {"hard" to "very hard"}] vs. low-intensity training [50%-65% HR_{max}, 11 to 13 {below "somewhat hard"}]). Each session was composed of 4 different stepping tasks practiced over ~10 min per session, including speed-dependent treadmill training, skill-dependent treadmill training, overground training, and stair climbing.	1. No significant AEs were noted. 2. The average number of sessions completed and number of steps within sessions were not significantly different between groups. 3. Significant main effects of time (P < .01) but not time × intensity interactions were observed for 6MWT (changes following high- vs. low-intensity LT: 26 ± 27 vs. 14 ± 30 m; P = 0.16). 4. For peak treadmill speed, main effects of both time and time × intensity interactions were significant (0.18 ± 0.14 vs. 0.02 ± 0.02 m/s, P = 0.02 and P < 0.01, respectively). 5. No significant interaction effects of order were observed for 6MWT or peak treadmill speed (P > 0.30). 6. Significant main effects of time and time × intensity interactions were observed for fastest-possible speeds (0.12 ± 0.10 vs. 0.03 ± 0.13 m/s, P = 0.01), with a trend for significant time × intensity interactions for self-selected speed (0.04 ± 0.08 vs. −0.01 ± 0.07 m/s; P = 0.02).

	Outcome Measures: 6MWT, peak treadmill speed, walking speed over short distances at self-selected speeds and fastest-possible speeds, BBS, and LEMS were assessed prior to and following each 4- to 6-week training paradigm.	7. No significant main or interaction effects were observed for BBS or LEMS.
Evans & Field-Fote 2024 USA Prospective controlled trial Level 2 N = 25	**Population:** 25 participants with chronic motor-incomplete SCI, able to stand for ≥5 minutes, and able to advance each leg independently ≥ 3 steps. Mean (SD) age: 48.4 (13.2) years 18M, 7F Level of injury: Cervical (n = 22), thoracic (n = 3) AIS C (n = 2), D (n = 23) Mean (SD) time since injury: 86.7 (87.2) months Sample stratification by baseline walking speed resulted in 15 participants being identified as slow walkers and 10 participants as fast walkers. **Treatment:** The study was carried out over 5 consecutive days (intervention on days 2, 3, and 4) of a motor skill training (MST) intervention. MST consisted of 6 exercises performed as a circuit (60sec/exercise) with each session comprised of 4 cycles of the circuit. Participants were encouraged to complete each exercise as quickly as possible to ensure at least a moderate exercise intensity was achieved (i.e., ≥40% HRR). The average time to complete the MST circuit was 37±6.1 minutes, including transition time between exercises. **Outcome Measures:** Overground walking speed (WS), step length (SL), step frequency (SF), and walk ratio (WR) were measured during the 10MWT completed each day (baseline, day 1; pre-intervention, day 2, day 3, and day 4; and 24 hours post-intervention, day 5).	1. Among the full sample, MST was associated with increases in walking speed, step length, step frequency, and a decrease in the walk ratio. a. Relative change in walking speed and step frequency was higher among slow walkers (ΔWS=↑46%, ΔSF=↑28%) vs fast walkers (ΔWS=↑16%, ΔSF=↑8%). b. Change in te WR differed between groups (slow: ΔWR=↓10%; fast: ΔWR=0%). c. Twenty-six percent of the variability observed in ΔWR among slow walkers could be explained by ΔSF, while ΔSL did not contribute to ΔWR. Among fast walkers, ΔSL accounted for more than twice the observed ΔWR (43%) compared to ΔSF (15%).
Liu et al. 2021	**Population:** 320 patients with acute and complete (AIS A) SCI; 271 males	1. The intervention was safe, as none of the patients' postoperative

China Pre – post Level 4 N = 320	and 49 females; mean (± SD) age 35.4 (± 9.6) years; level of injury cervical (C4-C5 was the most frequent), thoracic (T10-T12 were the most frequent), and lumbar (L1-L2 was the most frequent); and mean (± SD) time from injury 8.3 (± 7.4) days. **Treatment:** Participants received a combination treatment involving surgical intervention and, 15 days post-surgery, weight-bearing walking training: • Surgical intervention involved intradural decompression (via durotomy), and, in some cases, intramedullary decompression (via myelotomy). • Weight-bearing walking training (3-5-6 Kunming Locomotor Training Program was performed in 3 1-h sessions, 5 days per week, for 6 months, and with protection of a tailored chest-waist cast. The program was made up of 8 progressive steps from 1) training to stand with weight support when a trainer fixes the knees, to, 8) training to walk without any support. • In addition, patients received physical and occupation therapies on a daily basis. **Outcome Measures:** Kunming Locomotor Scale (10-point locomotor assessment scale) was assessed at baseline, at 15 days after surgery, and at 3 and 6 months after rehabilitation.	conditions were worsened after the intervention, compared to pre-operative conditions. 2. There were significant improvements in mean Kunming Locomotor Scale between comparisons of time points of 15 days, 3 months or 6 months (P < 0.001) for lumbar and thoracic injuries, while for cervical injuries, significant increase in scores was seen only from 15 days to 3 months.
Senthilvelkumar et al. 2015 India RCT PEDro = 7 Level 1 N = 16	**Population**: 16 participants; motor incomplete tetraplegia; 0-2yrs post injury. **Treatment**: Participants were randomized to one of two groups: body weight-supported overground training on level ground and BWSTT. Both groups received 30 min of gait training per day, five days a week for eight weeks. In addition, both groups received regular rehabilitation which	1. There was not statistically significant between group differences in the WISCI [MD=0.3 points; 95% CI (-4.8 to 5.4); p=0.748]. 2. No statistically significant between group differences in the LEMS [MD=0.2 points; 95% CI (-3.8 to 5.1); p=0.749]. 3. In Group A, the mean Walking Index score increased from 2.1±0.7 to 12.1±4.6 [mean change = 10; 95%CI

	included flexibility, strength, self-care and functional training. **Outcome Measures:** WISCI and LEMS.	(6.6 to 13.4)] and in Group B, it increased from 3±2.3 to 12.7±5.8 [mean change=9.7; 95%CI (5.1 to14.3)]. 4. In Group A, the mean Lower Extremity Muscle Score increased from 18.8±5.3 to 28.3±6.6 [mean change=9.5; 95%CI (3.2 to15.8)] and in Group B, in increased from 19.8±6.5 to 28.6±8 [mean change=8.9; 95%CI (1.2 to 16.6)].
Pramodhyakul et al. 2016 Thailand RCT PEDro = 5 Level 2 N = 32	**Population**: 32 participants - 26 males and 10 females; incomplete SCI; 26 AIS D and 10 AIS C; mean age= 41.69 ± 10.90y; months post injury= 35.00 ± 24.40 months. **Treatment**: Participants were randomly assigned to the experimental or control groups using stage of injury, severity of SCI, and baseline walking ability as criteria for group arrangement (16 participants per group). The participants were trained to walk over level ground at their fastest safe speed with or without a visuotemporal cue, 30 min/day, for 5 consecutive days. **Outcome Measures:** 10MWT, 6MWT, and FTSTS test.	1. The participants demonstrated significant improvement in all functional tests after the 5 days of training. The improvement in the group trained using the visuotemporal cue was significantly better than that trained without using the cue.
Jones et al. 2014a USA RCT PEDro = 5 Level 2 N = 38	**Population**: 38 participants - 27 males and 11 females; chronic, motor incomplete SCI; AIS C or D; age range= 22-63y; years post injury= >12 months. **Treatment**: A total of 9h/wk of ABT for 24 weeks including developmental sequencing; RT; repetitive, patterned motor activity; and task-specific LT. Algorithms were used to guide group allocation, FES utilization, and LT progression. **Outcome Measures:** Neurologic function (ISNCSCI), 10MWT, 6MWT, and community participation (SCIM-III, and Reintegration to Normal Living Index), metabolic function (weight, body mass index, and Quantitative Insulin Sensitivity Check).	1. ABT had a positive effect on neurologic function (ISNCSCI total motor score and LEMS). 2. ABT had a positive effect on 10MWT speed and 6MWT total distance.

<table>
<tr>
<td rowspan="2">Jones et al. 2014b
USA
Secondary analysis of results from an RCT
PEDro = 5
N = 38</td>
<td>Population: 38 participants - 27 males and 11 females; chronic, motor incomplete SCI; AIS C or D; age range= 22-63y; years post injury= >12 months.
Treatment: A total of 9h/wk of ABT for 24 weeks including developmental sequencing; RT; repetitive, patterned motor activity; and task-specific LT. Algorithms were used to guide group allocation, FES utilization, and LT progression.
Outcome Measures: Walking speed and endurance (10MWT and 6MWT).</td>
<td>1. On the basis of the most conservative estimate, 18%, 26%, and 32% of the participants demonstrated clinically significant improvements on the 10MWT, and the 6MWT, respectively.
2. This secondary analysis identified likely responders to ABT on the basis of injury characteristics: AIS classification, time since injury, and initial walking ability.
3. Training effects were the most clinically significant in AIS grade D participants with injuries <3 years in duration.</td>
</tr>
<tr>
<td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data.
 
</td>
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</table>

Discussion

Overground training provides an important mode of exercise for improving walking function, other physical and mental functions (e.g., muscle strength, bone health, cardiovascular function, or depression symptoms), and is helpful for ambulating at home and in the community.

In a systematic review, Mehrholz et al. (2017) compared the effectiveness of 13 trials of BWSTT and RAGT with OGT and other forms of physiotherapy on walking speed and walking distance in people with traumatic SCI. The results indicated that neither BWSTT nor RAGT increases walking speed more than OGT and other forms of physiotherapy (Mehrholz et al. 2017). The authors noted that an increase in walking speed of 0.04 and 0.13 m s^{-1} was sufficiently meaningful to justify the additional cost of BWSTT and RAGT (Mehrholz et al. 2017). The results for walking distance were similar, so it was not possible to rule out that BWSTT or RAGT improve walking distance more than OGT and other forms of physiotherapy (Mehrholz et al. 2017).

Several studies have indicated that overground training benefits functional walking capacity for people with motor-incomplete SCI (Forrest et al. 2014; Amatachaya et al. 2021; Senthilvelkumar

et al. 2015). Overground training has also been integrated with a wider variety of other exercises to provide more comprehensive therapy (Jones et al. 2014a), and others have suggested the additive benefits of providing visuotemporal cues during walking training (Pramodhyakul et al. 2016). Lotter et al. (2020) included 10 patients with tetraplegia and 6 with paraplegia who were randomly allocated to an intervention training consisting of 20 training sessions of up to 40 min over < 6 weeks and in either task-specific or impairment-based training. Task-specific training consisted of stepping practice in variable contexts (such as overground), and impairment-based training consisted of non-walking interventions (including strengthening, aerobic conditioning and practice of transfers) (Lotter et al. 2020). During the intervention, the task-specific training group achieved higher stepping parameters than impairment-based training, but average and maximum rate of perceived exertions (RPEs) were similar between groups (Lotter et al. 2020). After the intervention, significantly greater gains in the fastest speed over short distances, peak treadmill speed, and 6MWT were observed following task-specific vs. impairment-based training, while Berg Balance Scale (BBS), FTSTS test or LEMS showed similar improvements in both groups (Lotter et al. 2020). Although there were no serious adverse events (AEs) during training, minor AEs during task-specific training were significantly higher than in impairment-based training, with specific differences including a greater number of falls (Lotter et al. 2020). The authors noted that, as training specificity may be an important component of rehabilitation interventions, therapists must educate patients on strategies to minimize the AEs shown in the trial (Lotter et al. 2020).

Additionally, it should be noted that most of the overground LT in ambulatory persons with incomplete SCI was performed over a flat, smooth, and firm surface, and this training condition is different from the irregular, unstable areas that patients encounter in their daily living after discharge (Amatachaya et al. 2021). In an RCT, Amatachaya et al. (2021) showed that a walking training program for 4 weeks (5 d/w) on a walking track with different surfaces (including artificial grass, pebbles, and soft areas) provided significant improvements at the end of the program on walking speed (10MWT), walking distance (6MWT), and risk of falling; conversely, the control intervention (OWT) did not provided significant improvements. However, there were no significant differences after 6 months of follow-up for both training programs (Amatachaya et al. 2021).

Evans and Field-Fote (2024) explored the relationships among walking outcomes in a subgroup analysis of slow (n = 15) vs fast (n = 10) walkers. Over three consecutive days, participants performed an MST intervention (Evans & Field-Fote 2024). Among the full sample, MST was associated with increases in walking speed, step length, step frequency, and a decrease in the walk ratio (step length/step frequency) (Evans & Field-Fote 2024). In addition, a relative change in walking speed and step frequency was higher among slow vs fast walkers (Evans & Field-Fote 2024).

In a pre-post study, Liu et al. (2021) tested whether 320 patients with acute and complete (AIS A) SCI after intradural decompression surgery and assessed the effects of a weight-bearing walking training program, called 3-5-6 Kunming Locomotor Training Program. This program was performed in 3 1-h sessions, 5 days per week, for 6 months, and was made up of 8 progressive steps from 1) training to stand with weight support when a trainer fixes the knees, to 8) training to walk without any support (Liu et al. 2021). The authors reported that the

intervention was safe, as none of the patients' postoperative conditions worsened after surgery and weight-bearing walking training. There were significant improvements in locomotor scores at 15 days, 3 months, and 6 months for people with lumbar and thoracic level injuries; people with cervical level injuries showed improvements at 15 days and 3 months only (Liu et al. 2021).

Despite the established role of cardiovascular intensity in the field of exercise physiology, its role in the physical rehabilitation of patients with neurologic injury has emerged only in the past 15 to 20 years (Fahey et al. 2022). Regarding walking recovery, the RCT of Brazg et al. (2017) included people with chronic motor incomplete SCI compared high (70%-85% HR_{max}) vs. low intensity training (50%-65% HR_{max}) by altering the biomechanical demands of walking, with equivalent total stepping practice. Consistent with previous studies in patients' post-stroke (Ivey et al. 2015), significantly greater improvements in peak treadmill speed, peak velocity, and VO_2peak-match were observed following high-intensity training, while changes in self-selected speeds and 6MWT approached significance, but LEMS or BBS did not change. It should be noted that there were no AEs during both interventions and that the intensity of stepping exercise can be readily manipulated and indirectly monitored using cardiopulmonary and subjective measures in clinical settings (Brazg et al. 2017).

Conclusions

There is level 1 evidence (from 1 RCT: Senthilvelkumar et al. 2015) that overground and treadmill-based training are comparable.

There is level 1 evidence (from 1 RCT: Lotter et al. 2020) that task-specific training (stepping practice in different contexts such as overground training) provides more improvements in fastest speed over short distances, peak treadmill speed, and 6MWT compared with impairment-based training in patients with chronic motor incomplete SCI.

There is level 1 evidence (from 1 RCT: Amatachaya et al. 2021) that a walking training program for 4 weeks (5 d/w) on a walking track with different surfaces (including artificial grass, pebbles, and soft areas), compared to OWT yields better results on walking speed (10MWT), walking distance (6MWT), and a lower risk of falling during 6-month follow-up in patients with chronic motor incomplete SCI.

There is level 1 evidence (from 1 RCT: Brazg et al. 2017) that high-intensity (70%-85% HR_{max}) LT (composed of speed-dependent treadmill training, skill-dependent treadmill training, overground training, and stair climbing) provides significantly greater improvements in selected locomotor variables (peak treadmill speed and fastest-possible speeds) and combined metabolic capacity and efficiency (VO_2peak) compared to low-intensity (50%-65% HR_{max}) LT in participants with chronic and motor incomplete SCI.

There is level 2 evidence (from 1 prospective controlled trial: Evans & Field-Fote 2024) that three consecutive days of moderate-intensity MST (overground exercises performed as a circuit) provides significant increases in walking speed, step length, and step frequency, and a significant decrease in the walk ratio (step length/step frequency) in patients with motor-incomplete and chronic SCI.

Key Points

Community-based walking training that is progressively challenging, including walking over different surfaces, may result in long-lasting benefits in patients with incomplete and complete SCI.

Mobility improvements of overground and treadmill-based training are comparable in patients with SCI.

5.2 Body-Weight Supported Treadmill Training (BWSTT)

Body-weight support treadmill training (BWSTT) was introduced years ago as a promising approach to improve walking function in people with SCI (Barbeau & Blunt 1991). In this approach, partial BWS is provided by a harness suspended from the ceiling or a frame, while limb stepping movements are assisted by a moving treadmill belt. Because body weight is partially supported, often with a harness attached to the ceiling or a supported beam, walking can be practiced safely even when a person cannot stand or walk independently (SCIRE Community, 2017). Body-weight-support walking training can before patients have developed appropriate motor control, and as well as with better safety and less fear of falling (El Semary & Daker 2019). It is believed that locomotor circuitries within the spinal cord below the level of injury can be activated by repetitive and intensive LT, which provides appropriate afferent feedback (Rossignol et al. 2011). Currently, LT with a body-weight-support system is among the most widely used rehabilitation strategies to retrain standing and walking abilities after SCI (Yu et al. 2019).

In a systematic review and meta-analysis, Duan et al. (2021) compared the benefits of different interventions to affect walking ability/lower limb function in people with SCI. Results show that robotic-assisted treadmill training did not increase walking speed (10MWT) or walking distance (6MWT) better or worse than control (no intervention, bike, and overground walking); however, robotic-assisted treadmill training significantly increased ASIA LEMS score and lower extremity independence (Duan et al. 2021).

In this review, we focus on the BWSTT intervention studies (including RAGT interventions, mainly using Lokomat) that report functional ambulation (such as walking speed or endurance), and strength-related outcome measures (such as LEMS). These studies tend to focus on people with motor-incomplete SCI lesions, but some more recent studies have included patients with AIS A level injuries (Çinar et al. 2021; Çinar et al. 2020; Jansen et al. 2017b; Okawara et al. 2020; Sawada et al. 2021; Yildirim et al. 2019). For the purposes of this review, we defined SCI <12 months post-injury as acute/sub-acute and SCI >12 months post-injury as chronic.

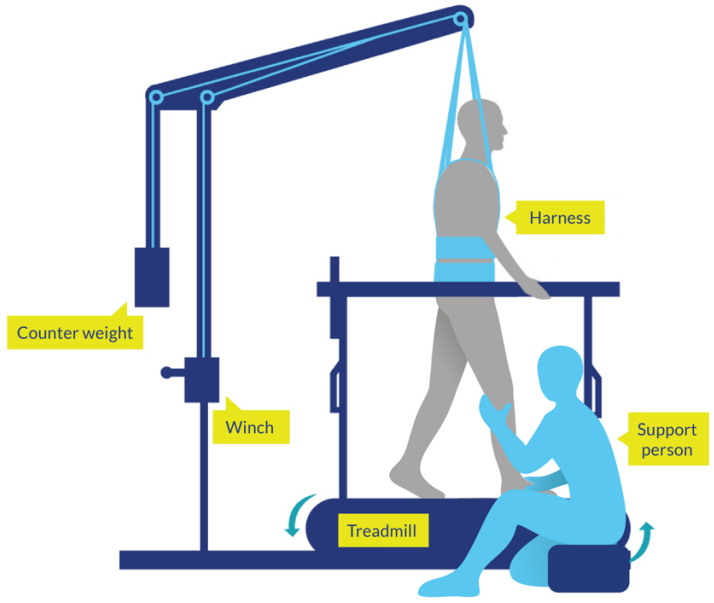


Figure 1. Body-Weight Supported Treadmill Training (BWSTT)

5.2.1 Body-Weight Supported Treadmill Training (BWSTT) in Patients With Acute/Sub-Acute SCI

Table 7. BWSTT in Patients With Acute/Subacute SCI (<12 Months Post-Injury)

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Çinar et al. 2021 Turkey RCT PEDro = 6 Level 1 N = 37	**Population:** 37 patients with complete (AIS A) paraplegic SCI and with a maximum of 6 months after the injury; 15 males and 22 females; mean age 34.9 years; injury level thoracic (n = 20), and lumbar (n = 17); and mean duration of injury 3.7 months. **Treatment:** Patients were divided into two groups: • Group 1 (n = 17): Received both RAGT with Lokomat and conventional therapy.	1. No significant difference was noted in WISCI II admission–discharge change scores between the two groups (P > 0.05). However, intra-group evaluations revealed significant increase in the discharge WISCI II scores in groups I and II compared with admission scores (P < 0.05). 2. At the time of discharge, 5 of the 17 patients in group 1 improved to ASIA B and 4 patients improved to ASIA C; 7 of the 20 patients from

	• Group 2 (n = 20): Received only conventional therapy. Conventional treatment included training in the ROM, stretching, strengthening, coordination, and walking once a day, 5 days a week for 8 weeks. **Outcome Measures:** WISCI II was evaluated at the beginning and at the end of the treatment.	group 2 improved to ASIA B and 6 patients improved to ASIA C level.
Yildirim et al. 2019 Turkey RCT PEDro = 6 Level 1 N = 88	**Population:** 88 participants with SCI; 55 males and 33 females; mean age 34.25 years; injury level cervical (n = 18), thoracic (n = 53), and lumbar (n = 19); tetraplegia (n = 16) and paraplegia (n = 72); ASIA complete (n = 39) and ASIA incomplete (n = 49); and mean time since injury 3 months. **Treatment:** All participants received conventional therapy (joint ROM, stretching, strengthening and gait training) for 5 days a week (twice a day). Also, they were randomized into 2 groups: • The RAGT group (n = 44) underwent 30-min sessions of robotic therapy training using Lokomat for 8 weeks twice a week. BWS was progressively increased to full body weight at the end of treatment. • The control group (n = 44) underwent only conventional treatment. **Outcome Measures:** WISCI II was assessed at baseline and at the end of training.	1. Between groups comparisons: a. The improvement in functional ambulation (as measured by the WISCI II score) was significantly higher in the robotic group (median WISCI II score went from 5.0 to 9.0) than in the control group (median WISCI II score went from 5.0 to 6.5; P = 0.011). b. The improvement in functional independence (as measured by the FIM score) was significantly higher in the robotic group (median FIM score went from 69.0 to 85.0) than in the control group (median FIM score went from 67.0 to 77.0; P = 0.022). 2. Within groups improvements were observed in both groups according to the WISCI II scores (P < 0.001).
Khande et al. 2024 India Prospective controlled trial Level 2 N = 30	**Population:** 30 participants with complete (ASIA A) and dorsolumbar SCI • Conventional group (n = 15): Mean (SD) age: 34.60 (10.22) years 12M, 3F	1. Intervention group results (within-group): Robotic group demonstrated a significant improvement at the end of 12 weeks in terms of WISCI II score (p = 0.0001), LEMS score (p = 0.007), and SCIM-III score (p = 0.0001).

	Mean (SD) time since injury: 7 (3) days • Intervention group (n = 15): Mean (SD) age: 30.93 (7.90) years 12M, 3F Mean (SD) time since injury: 4 (2) days **Treatment:** Joint ROM & muscle strengthening physiotherapy/ exercises was given to both groups for initial 2–3 weeks. After 3 weeks, participants were stood erect (90°) gradually on inclination table and as the participants achieved 90° of inclination with stable vitals, they were taken on Robotic machine or movement started by using KAFO, depending upon the rehabilitation group, for 12 weeks: • In robotic assisted rehabilitation group, BWSTT with Lokomat was performed. During treatments, initial velocity of the treadmill was kept at 1.5 km/h and 0.3 km/h gain was achieved in further walking sessions depending upon the muscle power in lower limbs and step length was kept fixed (40 cm). At the beginning, 100% of each participant's body weight was supported. During the subsequent walking sessions, the BWS was reduced gradually to the minimum as tolerated without substantial knee buckling or toe drag and it was dependent upon the muscle power in lower limbs. Guidance force was maintained at 100%. • In conventional group, participants were stood with the help of KAFO and bipedal movement was done on parallel bars. 100% body weight was on lower limbs from starting to end of	2. Conventional group (within-group): Conventional group demonstrated a significant improvement at the end of 12 weeks in terms of WISCI II score (p = 0.0001), LEMS score (p = 0.023), and SCIM-III score (p = 0.0001). 3. Comparison of functional outcome scores and parameters between conventional and robotic group at the end of 12th week of Rehabilitation: In terms of the WISCI II score (p = 0.0001) and SCIM-III score (p = 0.0001), there was a statistically significant improvement in the robotic group compared to the conventional group. However, LEMS score (p = 0.052) was not statistically significant.

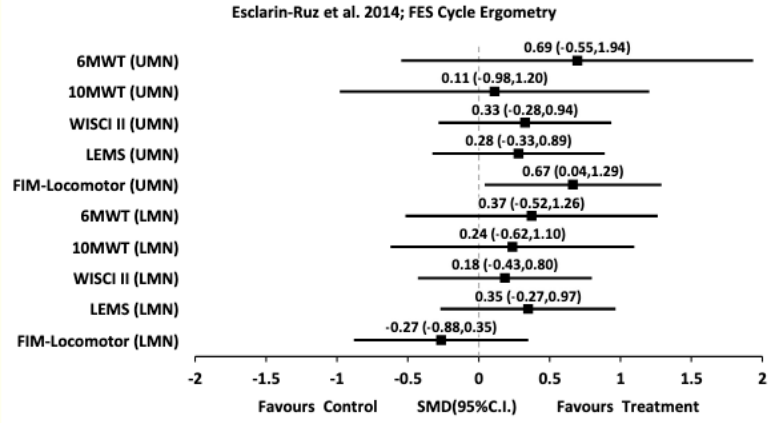
	conventional rehabilitation and velocity and step length varied participants to participants. **Outcome Measures:** WISCI II, LEMS, and SCIM-III were assessed pre- and post-rehabilitation.	
Çinar et al. 2020 Turkey Prospective controlled trial Level 2 N = 34	**Population:** 34 patients with SCI; 23 males and 11 females; mean age 32.8 years; injury level from C6 to L1, cervical (n = 6), thoracic (n = 21), and lumbar (n = 7); complete injury (AIS level A) (n = 17) and incomplete injury (AIS level B, C, or D) (n = 17); and mean duration of injury 3.5 months. **Treatment:** All participants performed a robotic treatment training (Lokomat) for a total of 10 sessions for 5 weeks, twice a week; and received conventional treatment (ROM, stretching, strengthening, and walking training) for 5 days a week (twice daily). The patients were divided into two groups as complete and incomplete patients. **Outcome Measures:** WISCI II was evaluated at the beginning and at the end of the treatment.	1. WISCI II: a. For complete injury patients, the after-treatment scores showed a significant increase compared to the scores at baseline (p = 0.008). b. In incomplete patients, after-treatment scores demonstrated a significant increase compared to the baseline scores (p = 0.002). c. WISCI II score improvement did not exhibit a significant difference between the incomplete and complete injury patients (p = 0.364).
Zieriacks et al. 2021 Germany Prospective controlled trial Level 2 N = 121 (47 acute)	**Population:** 121 patients with SCI and existing motor function of hip and knee extensor and flexor muscle groups to operate the exoskeleton; 89 males and 31 females; mean age 44.3 (16 – 74) years; AIS A with zones of partial preservation (n = 24), AIS C (n = 61) and AIS D (n = 36); injury level cervical (n = 32), thoracic (n = 55) and lumbar (n = 34); and mean (± SD) time since injury 65.3 (± 89.5). Participants were divided into two subgroups: • Acute group (n = 47): < 12 months of SCI. • Chronic group (n = 74): > 1 year of SCI.	1. There were no AEs (e.g., falls). 2. HAL associated outcomes: Participants could significantly extend walking time with the exoskeleton on the treadmill and the ambulated distance after 12 weeks (p ≤ 0.0001); with no significant difference time observed between the subgroups (p = 0.16). 3. Functional outcomes: a. All participants significantly improved in the functional assessments performed without the exoskeleton. b. Participants significantly improved in 10MWT from baseline to after 12 weeks (p ≤ 0.0001); with no significant

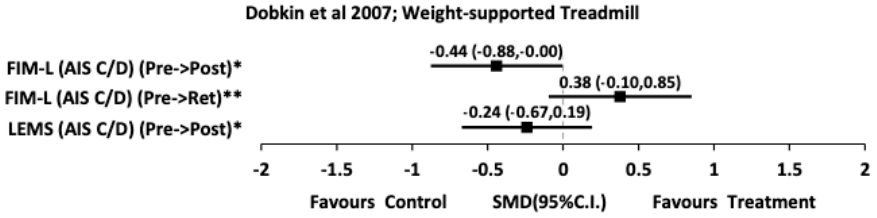
	Treatment: Participants performed BWSTT with the HAL robot suit exoskeleton 5 times a week for 90 – 120 min for 3 months. In addition to this, participants regularly performed a 10MWT and 6MWT without the exoskeleton with individual walking aids. **Outcome Measures:** 10MWT, 6MWT and WISCI II were measured at the beginning, and after 6 and 12 weeks of training; LEMS was measured before and after the training program; and the parameters of walking time and distance were recorded each training session.	differences between groups (p = 0.72). c. The distance ambulated (6MWT), WISCI II, and LEMS increased significantly in all participants from baseline to after 12 weeks (p ≤ 0.0001); however, acute participants improved significantly more than chronic participants (p ≤ 0.0001).
Alcobendas-Maestro et al. 2012 Spain RCT PEDro = 8 Level 1 N = 75	**Population:** 75 participants with SCI in total; all <6 months post-injury. For the Lokomat group (N=37), mean (SD) age = 45.2 (15.5); 62%M, 38%F; 68% AIS C, 32% AIS D. For the conventional treatment group (N=38); mean (SD) age= 49.5 (12.8); 63%M, 37%F; 71% AIS C, 29% AIS D. **Treatment:** Randomized to 2 groups: Lokomat and conventional treatment. **Outcome Measures:** 10MWT; WISCI II; 6MWT; walking and stairs tasks of the FIM-L section; LEMS subscale; Ashworth Scale and visual analogue scale for pain.	1. The Lokomat treatment group showed statistically significant differences in favor of Lokomat treatment over conventional treatment in the following outcome measures: a. WISCI II: Lokomat [16 (8.5-19)], Conventional [9 (8-16)]; p < 0.05. b. 6MWT (m): Lokomat [169.4 (69.8-228.1)], Conventional [91.3 (51.4-178.7)]; p < 0.05. c. LEMS lower limb strength: Lokomat [40 (35-45.5)], Conventional [35 (29.7-40)]; p < 0.05. d. FIM-L: Lokomat [10 (6-12)], Conventional [7 (5-10)]; p < 0.05. 2. There were no differences between the Lokomat and conventional treatment group in the variables: speed (10MWT), spasticity (Ashworth scale), and pain (visual analogue scale).
Dobkin et al. 2006 USA RCT PEDro = 7 Level 1	**Population**: 117 males and females; age 16-69 yrs; AIS B-D; <8 weeks post-injury. * These data showed that 15% of patients classified as ASIA B, 40% as ASIA C, and 75% as ASIA D at the time of admission were	1. There were no significant statistical difference in FIM-L score between ASIA B and C participants. 33% (7/21) of ASIA B participants in the BWSTT group were ambulatory at 6 months and 58% (14/24) in the control

N = 292 (enrolled) N = 117 (analyzed)	able to walk 150 feet at a supervised or better level of function at discharge. **Participants were subgrouped into: • Upper motor neuron, participants with a cervical to T10/T11 lesion. • Lower motor neuron, participants with a T112 to L3 lesion and no upper motor neuron signs. **Treatment:** BWSTT vs. overground mobility training: 5x/wk, 9-12 wks, 30-45 min/session. Each participant engaged in equal amounts of either BWSTT or overground walking training. **Outcome Measures:** BBS, FIM-L, walking speed, 6MWT, WISCI at 3 and 6 months. Primary outcomes were FIM-L for ASIA B and C participants and walking speed for ASIA C and D participants at 3 months and 6 months after SCI.	group. The majority of ASIA C participants recovered independent walking; 92% of BWSTT and control participants (24/26 in each group) had a FIM-L score ≥6 at 6 months. ASIA C participants were significantly more likely than ASIA B participants to walk independently and both ASIA B and C participants who were randomized earlier (<4 weeks after SCI) had a greater probability of recovery to a FIM-L score >5. 2. ASIA C and D – Walking speed: Primary outcome measures showed no statistical differences between treatment groups in walking velocity at 6 months for the combined upper motor neuron/lower motor neuron participants or the upper motor neuron participants alone. The median measures for velocity in the ASIA C and D participants demonstrated a remarkably high level of walking ability and fell within the range of functional community ambulation. 3. Secondary analyses; ASIA C and D at 6 months: The median quartile walking velocities at 6 months for upper motor neuron ASIA C and D participants were unexpectedly high in both arms (1.1 m/s). No significant differences between the two interventions for FIM-L, walking speed, endurance, LEMS, BBS, or WISCI score. Walking speed at the end of treatment was highly correlated (r = 0.91) with the speed at 6 months, but speeds continued to increase between 3 and 6 months. Earlier time of entry (<4 weeks) into the study after onset of SCI was associated with faster walking speeds (p = 0.001) and longer walking distances (p = 0.0001) in both

		arms at 6 months for each ASIA group compared to velocities attained in participants in that group who were randomized >4 weeks after SCI.
Wirz et al. 2017 Switzerland, Germany, Spain and UK RCT PEDro = 6 Level 1 N = 18	**Population:** 18 participants with acute SCI and limited walking ability (WISCI II < 5); 16 males and 2 females; mean age 34.9 years; level of injury C4 to T12; AIS B (n = 9) and AIS C (n = 9); and study inclusion was set at maximum of 60 days post-trauma. **Treatment:** Patients performed 3–5 days of training per week of RAGT using Lokomat for a period of 8 weeks. Patients were randomly allocated to one of two groups: • Intervention group (n = 9): 50 min of RAGT training • Control group (n = 9): 25 min. of RAGT training. **Outcome Measures:** SCIM subscore mobility was assessed at baseline and at 8 weeks of training.	1. For the SCIM mobility subscore, within-groups comparisons show that both groups improved after 8 weeks of RAGT training (intervention= from 3.0 to 20.0; p = 0.008; control= 4.0 to 10.0; p=0.012).
Sadegui et al. 2015 Iran RCT PEDro = 3 Level 2 N = 20 (enrolled) N = 17 (analyzed)	**Population:** 20 males with incomplete SCI; mean (± SD) age 32.30 (± 1.50) years; paraplegia (n = 20); and time since injury > 6 months. **Treatment:** Both groups participated in traditional training consisting of a 10-min warm up with passive stretch exercises; 45-min mobilization exercises of the hip, knee, and ankle joints and overground walking assisted, functional exercises, and strengthening and stretching activities; and 10-min cool down. Over a 12-week period, participants were randomly assigned to one of two groups: • BWSTT group (n = 10): Participants also performed BWSTT 4 times per week, 60	1. In the traditional group, 3 participants left the study because of bedsores (n = 2) and operation (n = 1). 2. LEMS tended to increase to a greater extent following BWSTT compared to other intervention training (P = 0.000). 3. There were significant differences between two groups with respect to improvements of WISCI II (43.85% vs. 0%, P = 0.002). 4. A comparison of the changes in scores suggested that there was greater improvement in 10MWT (40.12% vs. 7.40%, P = 0.001) and 6MWT (88.23% vs. 18.74%, P = 0.001) after BWSTT compared to conventional training. *It should be noted that baseline scores in WISCI II, 10MWT and 6MWT seem to be different (no statistical analysis was

	min each session. BWS was progressively decreased to ensure full weight bearing at the end of the study. • Traditional group (n = 10): Traditional training only. **Outcome Measures:** LEMS, WISCI II, 10MWT, and 6MWT were assessed at baseline and at post treatment.	done) and better for the traditional group.
Shin et al. 2014 Seoul RCT PEDro = 5 Level 2 N = 53	**Population**: 53 participants- 34 males and 19 females with incomplete SCI; 31 with cervical injuries and 22 with thoracic & lumbar injuries; 36 with traumatic SCI and 16 with non-traumatic SCI; mean age= 48.15 ± 11.14y; months post injury= 3.33 ± 2.02 months. **Treatment**: Patients were included in a prospective, randomized clinical trial by comparing RAGT to regular physiotherapy. • The RAGT group received RAGT with Lokomat three sessions per week at duration of 40 min with regular physiotherapy in 4 weeks. • The conventional group underwent regular physiotherapy twice a day, 5 times a week. **Outcome Measures:** LEMS, ambulatory motor index, SCIM-III mobility section (SCIM-III-M), WISCI II.	1. At the end of rehabilitation, both groups showed significant improvement in LEMS, Ambulatory Motor Index, SCIM-III-M, and WISCI II. 2. Patients in the RAGT group showed significant greater gain (from 3 [IQR, 0-14] to 11 [IQR, 0-19]) compared to controls in the WISCI-II (from 4 [IQR, 0-16] to 9 [IQR, 0-20]). P=0.01.
Esclarín-Ruz et al. 2014 Spain RCT PEDro = 7 Level 1 N = 88	**Population**: 88 participants; 44 with upper motor neuron SCI (group A) and 44 with lower motor neuron SCI (group B); 59 AIS C and 25 AIS D; mean age= 43.6 ± 12; days post injury= 125.6 ± 65.2. **Treatment**: Participants with UMN and LMN were randomized into 2 training groups: • Condition 1: Subgroups A1 and B1 were treated with	1. The distance covered in the 6MWT was statistically greater for the robotic plus overground therapy group than for the conventional OGT group (p = 0.047). 2. For the 10-MWT, there were no differences between conditions (p = 0.09). 3. For the WISCI II, there were no differences between conditions (p = 0.10).

<table>
<tr><td rowspan="2"></td><td>robotic LT plus overground therapy for 60 min.
• Condition 2: Subgroups A2 and B2 received 60 min of conventional OGT 5 days per week for 8 weeks.
Outcome Measures: 10MWT, 6MWT, WISCI II, LEMS, and the FIM-L were assessed.</td><td>4. Patients who underwent robotic LT plus overground therapy therapy obtained higher LEMS strength values than did patients in conventional OGT therapy.
5. In group A: upper SCI patients who underwent robotic LT plus overground therapy (A1) obtained higher FIM-Locomotor scores than did patients who underwent coventional OGT therapy (A2) (p = 0.013).</td></tr>
<tr><td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data.
 
</td></tr>
<tr><td>Tang et al. 2014
China and Japan
RCT
PEDro = 4
Level 2
N = 30</td><td>Population: 30 male participants with incomplete SCI; mean (± SD) age 38.6 (± 7.6) years; AIS D (n = 30); and time since injury 189 days.
Treatment: Participants were randomly assigned to two groups:
• Lokomat group (n = 15): Participants trained using Lokomat with an initial training speed of 1.5 km/h (and progressively raised to 1.8 km/h while maintaining gait quality), with a BWS initiated at 35%, and with a 70% guidance force.
• Ergo_bike group (n = 15): Participants were instructed to pedal at a pedaling rate of 45 rpm with a workload of 60 W during 40 min in each session.</td><td>1. Post-intervention, the Lokomat group had a significantly shorter Probe Reaction Time than the Ergo_bike group, but there was no difference in the 10MWT between the Lokomat group and the Ergo_ bike group.
2. The Probe Reaction Time and the 10MWT decreased significantly in the Lokomat group, while 10MWT (but not Probe Reaction Time) decreased significantly in the Ergo_bike group.</td></tr>
</table>

	Outcome Measures: Probe Reaction Time and 10MWT were assessed at baseline and after the training.	
Dobkin et al. 2007 USA and Canada PEDro = 5 RCT Level 2 N = 112	**Population:** 112 males and females; 29 participants with diagnosis of AIS B, 83 participants with diagnosis of AIS C-D; age 16-70 yrs; mean 4.5 wks post-injury. **Treatment:** BWSTT vs. overground mobility training (control): 5x/wk, 9-12 wks, 30-45 min/session. **Outcome Measures:** FIM-L (range from 1 (total physical dependence) to 7 (independence to walk > 150 feet)), walking speed, 6MWT, LEMS.	1. At 12 weeks, no differences were found between patients who received BWSTT vs. control in FIM-L, walking speed, LEMS, or distance walked in 6 min. 2. FIM-L ≥ 4 was achieved in < 10% of AIS B patients, 92% of AIS C patients, and all of AIS D patients; few AIS B and most AIS C and D patients achieved functional walking ability by the end of 12 weeks of BWSTT and control. 3. Time after injury is an important variable for planning interventions to lessen walking disability. Patients who started their rehabilitation sooner (<4 weeks after onset) had better outcomes. Thus, entry within 4 weeks allowed some patients to start at a lower level of function. 4. By 6 weeks after entry, most patients with SCI who will recover have improved their FIM-L to >3 and are improving in walking speed.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- to post-intervention data and pre-intervention to retention/follow-up data.  *SD of post-intervention measurements used for calculation *SD of follow-up/retention measurements used for calculation	
Hornby et al. 2005a USA RCT	**Population**: 30 patients with SCI (ASIA classification of B, C, or D)	1. Mean changes in all groups improved significantly during the training regimen, with significant changes in FIM-L subscores, WISCI

PEDro = 5 Level 2 N = 30	Inclusion Criteria: traumatic or ischemic SCI above the T10 spinal cord level experienced between 14 and 180 days prior to study enrollment, partial preservation of voluntary motor control in at least one muscle of the lower extremities. **Treatment**: Randomly assigned to one of three 8-week training regimens: Robotic-assisted BWSTT, therapist-assisted BWSTT, and overground ambulation with a mobile suspension system. **Outcome Measures:** LEMS, WISCI II, FIM.	scores, and LEMS. 2. Significant difference in the total distance ambulated over ground: mean (SD) distance walked 1282 (606) m vs. both robotic-assisted (2859 (111) m) and therapist-assisted (2759 (215) m) BWSTT groups. 3. The number of therapists required to provide gait training on the treadmill or over ground was significantly greater than that required for the robotic-assisted group for the first 5 weeks of training. 4. There were no significant differences noted between therapist- and robotic-assisted BWSTT groups for the final 3 weeks of training.
Schwartz et al. 2011 Israel Case control (single experimental group with matched historical control). Level 3 N = 56	**Population:** 56 participants with SCI as a result of traumatic (57%) or non-traumatic causes; 37 males and 19 females; mean age 42.5 years; level of injury cervical (n = 26), thoracic (n = 16), and lumbar (n = 14); AIS A (n = 6), AIS B (n = 7), AIS C (n = 13), and AIS D (n = 2); and mean time since injury 24 days. **Treatment:** Participants in the intervention group were prospectively included and those in the control group were retrospectively matched. • Intervention group (n = 28): Participants received 30-min sessions of RAGT with Lokomat with individualized progression in speed and BWS, and 30-45 min of regular physiotherapy sessions; for 2-3 times a week and 12 weeks. • Control group (n = 28): Participants were treated by regular physiotherapy for 30–45 min five times a week using Bobath principles. **Outcome Measures:** FAC scale and WISCI II were assessed upon	1. Though there were no significant differences between groups on walking ability after 12 weeks of RAGT or regular physiotherapy training, both groups showed a significant improvement in ambulation ability according to FAC (Wilcoxon signed ranks test $Z = -5.21$, $P < 0.01$). 2. During the rehabilitation period both groups achieved a significant improvement in WISCI II with no significant interaction effect between groups over time.

	admission and upon discharge from the rehabilitation department.	
Benito-Penalva et al. 2010 Spain Case control Level 3 N = 42	**Population:** 29 patients with motor incomplete SCI (24 males, 5 females, mean age 47; Group A < 3 months post-injury (n=16), Group B > 3 months post-injury (n = 13), and 13 healthy volunteers (10 males, 3 females, mean age 32) with pre-test only. **Treatment:** Gait training using either the Lokomat or Gait Trainer GT1 (based on availability of the system), 20-45 min per sessions (5 days a week for 8 weeks). **Outcome Measures:** LEMS, WISCI II, 10MWT, H reflex modulation by TMS.	1. After gait training, there was a significant improvement in LEMS, WISCI and 10MWT for both group A and B, with a significantly greater improvement in 10MWT for group A vs. group B. 2. After gait training, Group A showed significantly greater H reflex facilitation with TMS at 20 ms than Group B (170.7 + 10.2% vs. 125.3 + 5.6%), with no significant differences at 50 and 80 ms.
Benito-Penalva et al. 2012 Spain Pre-post Level 4 N = 105	**Population:** 105 participants with SCI. 39 randomized to Lokomat treatment and 66 to Gait Trainer GT I treatment. Mean age for both groups = 45 yrs. • For the Lokomat group, 26M 13F and 5 AIS A&B, 18 AIS C, 16 AIS D. • For the Gait Trainer GT I group, 45M 21F, and 6 AIS A&B, 26 AIS C, 34 AIS D. Majority of participants were <1 year post-injury. **Treatment:** Patients received LT with one of the electromechanical devices [Lokomat or Gait Trainer GT I System], 5 days/wk for 8 wks. **Outcome Measures:** LEMS, WISCI, 10MWT were collected at baseline, midpoint (4wks) and end of program (8 wks).	1. Compared to conventional standard of care from the EM-SCI database, both ASIA grade C and D patients receiving electromechanical device system gait training had a significantly greater rate of change in motor function when compared to matched patients from EM-SCI group. 2. Rate of clinical change across the training period was not significantly different between the two treatment groups for any of the three outcomes. 3. For the total sample, all 3 clinical outcomes showed statistically significant improvement after the use of electromechanical systems: a. LEMS: pre= 22.07(1.08), post=30.56(1.15). b. WISCI: pre=3.97(0.49), post=9.16(0.68). c. 10MWT: pre=0.082(0.01), post=0.26(0.03).
Harkema et al. 2012 USA Pre-post	**Population**: 196 participants (148 male, 48 female) with incomplete	1. Scores on the BBS significantly improved by an average of 9.6 points.

(subacute and chronic) Level 4 N = 196	SCI; mean age 41±15 yrs; YPI- <1 yrs (n=101), 1-3 yrs (n=43), >3 yrs (n=52). **Treatment:** LT with three components: (1) 1 hour of step training in the body-weight support on a treadmill environment, followed by 30 min of (2) overground assessment and (3) community integration. **Outcome Measures**: BBS, 6MWT, and 10MWT.	2. 6MWT distances and 10MWT speeds of all patients significantly improved by an average of 63m and 0.20m/s, respectively. 3. 168 (86%) patients (66 of 66 AIS grade C, 102 of 130 AIS grade D) scored lower than 45, the reported threshold for risk for falls for the BBS: a. Patients with AIS grade C had significantly lower scores at enrollment than those with AIS grade D. b. Patients with AIS grade D walked significantly farther than those with AIS grade C.

Discussion

We found 18 studies that have examined the effect of Lokomat-assisted, therapist-assisted BWSTT, or hybrid assistive limb (HAL) exoskeleton walking on a treadmill in people with incomplete SCI (aggregate N = 1167) and six studies in people with complete SCI (aggregate N = 134) who were within 12 months of incurring their SCI (i.e., the acute/subacute phase).

RAGT + Physical Therapy vs. Physical Therapy

The addition of a BWSTT program to conventional rehabilitation typically improves walking outcomes more than conventional rehabilitation programs alone.

During an 8-week RCT, twice weekly RAGT sessions added to 5 days per week of conventional rehabilitation sessions (twice daily - joint range of motion, stretching, strengthening, and gait training) resulted in improved functional walking significantly more than conventional rehabilitation only (median WISCI II score improvement: 4.0 points vs. 1.5 points; P = 0.011) (Yildirim et al. 2019). Additionally, people in the RAGT group improved their functional independence significantly more than those in the conventional rehabilitation only group (median FIM score improvement: 16.0 points vs. 10.0 points; P = 0.022). Both groups improved their functional walking and independence, but the RAGT improved significantly more.

Similarly, Shin et al (2014) found that the RAGT group showed significantly greater gains in functional walking than those in the standard rehabilitation program (median WISCI II score: RAGT: from 3 to 11 vs. Controls: 4 to 9; P =0.01). Members of both groups improved in other walking outcomes, like LEMS and SCIM-III mobility scores, but the only significant difference between the two groups was on functional walking. Alcobendas-Maestro et al. (2012) also found that a Lokomat treatment showed statistically significant improvements vs. conventional treatment in functional walking (WISCI II scores: 16 vs. 9), walking distance (6MWT: 169.4 m vs. 91.3 m), lower limb strength (LEMS: 40 vs. 35) and functional independence (FIM-L: 10 vs. 7).

Conversely, Çinar et al. (2021) found no significant differences between the RAGT group and conventional physical therapy groups in pre- and post-treatment FIM and WISCI II change scores.

RAGT vs. OGT (With or Without Physical Therapy)

Studies that compared RAGT to OGT in people with acute SCI are inconclusive as to whether RAGT or OGT is superior. Nam et al. (2017) performed a meta-analysis, pooling the studies where RAGT was compared directly to OGT in people with acute SCI (only 3 trials; N=211 qualified). The RAGT groups improved significantly more than the OGT groups on a few outcomes: distance walked (pooled mean difference 45.05m; P=0.005), leg strength (2.54 points on LEMS; P=0.04), and in functional/walking independence (0.5 on WISCI-II or FIM-L; P=0.04). Walking speed tended to be higher in RAGT groups than OGT groups but the differences were not significant (pooled mean difference 0.08 m/s).

In one of the highest quality RCTs we found, Dobkin et al. (2006; n=117) provided 12 weeks of equal time of BWSTT or OGT and found no differences in FIM-L scores or in walking speed; in fact, these two variables in both groups improved roughly in parallel over the course of the intervention. One smaller RCT (Hornby et al. 2005a; n = 30) similarly found that there were no differences in motor (LEMS) or functional recovery (FIM-L sub-score or WISCI II score) between those who trained overground, with BWSTT, or with robotic-assisted treadmill training.

Some Better Results in Acute/Subacute SCI

Dobkin et al. (2006) found that participants who entered walking training earlier (< 4 weeks post-injury) had greater gains in walking speeds and endurance post-training, particularly for participants who improved their AIS classification within 4-6 works post-injury. A case-control study by Zieracks et al. (2021) found that 6MWT (performed without the exoskeleton), WISCI II scores and LEMS improved more in acute patients than in chronic patients. Authors have suggested that greater walking improvements during acute/subacute phase could be accounted for by being earlier in the process of regaining function (Dobkin et al. 2006).

Level of Injury Seems to be the Biggest Predictor

Dobkin et al. (2006) reported that the amount of function and movement that the person has before starting training is an important indicator of locomotor recovery. Among the participants who were initially classified as AIS B, those who improved to AIS C within 8 weeks post-injury showed improved walking function while those who remained as AIS B did not (Dobkin et al. 2006). Additionally, 15% of their participants classified as ASIA B, 40% as ASIA C, and 75% as ASIA D at the time of admission were able to walk 150 supervised and at a better level of function at discharge. Dobkin et al. (2006) also found that people classified as ASIA C were significantly more likely than people classified as ASIA B to walk independently (P = 0.001).

In another RCT, Dobkin et al. (2007) confirmed that level of injury/AIS classification is an important variable predicting walking ability. After 12 weeks of BWSTT vs. OGT, < 10% of AIS B, 92% of AIS C and 100% of AIS D notably improved their walking function. Based on these results, they recommend that future trials may reduce the number needed to treat by entering

patients with FIM-L < 4 at > 8 weeks after onset if still graded ASIA B and at > 12 weeks if still ASIA C (Dobkin et al. 2007).

Robot-assisted rehabilitation may be superior to conventional rehabilitation in people with AIS A SCI, where voluntary movement is limited, and attempting walking presents more of a safety concern (Khande et al. 2024).

How Much? How Long?

In the studies we found in people with acute SCI, walking training varied from 30 minutes, twice per week, for 4 weeks (Shin et al. 2014) to 30-60 minutes, five times per week, for 8-12 weeks (Dobkin et al. 2006; Esclarin-Ruz et al. 2014). A small RCT (n=18) found that people who performed BWSTT training for 50 minutes per session improved their SCIM-mobility scores from entry to discharge more than those who engaged in 25-minute sessions (SCIM-mobility subscores: 50-minute group: 3 to 20; 25-minute group: 4 to 10; no between-groups significance reported) (Wirz et al. 2017).

There is as of yet no consensus on how much, how long, or how often someone with SCI should be engaging in walking training However, there have been enough studies to suggest that an intensive locomotor program is feasible and could be beneficial in patients with acute SCI, assuming that all medical restrictions and precautions are taken into account (Wirz et al. 2017; SCIRE Community, 2017). A reasonable guiding principle is that the specific amount of time spent in walking training should vary based on what other therapies they are engaged in, as well as each person's level of exercise-induced fatigue (Dobkin et al. 2006).

Conclusions

There is level 1 evidence (from 2 RCTs: Alcobendas-Maestro et al. 2012; Yildirim et al. 2019) that BWSTT is effective in improving ambulatory function compared to conventional rehabilitation.

There is level 1 and level 2 evidence (from 2 RCTs: Dobkin et al. 2006; Hornby et al. 2005a) demonstrating that BWSTT has equivalent effects in walking outcomes when an equivalent amount of overground mobility practice is used in patients with acute/sub-acute SCI.

There is level 1 evidence (from 1 RCT: Wirz et al. 2017) that intensive sessions (walking time per session > 50 min) of Lokomat-assisted BWSTT for 8 weeks could provide more improvement in the SCIM mobility subscores than non-intensive sessions (walking time per session < 25 min) in patients with acute SCI.

There is level 2 evidence (from 1 prospective controlled trial: Çinar et al. 2020) that Lokomat-assisted BWSTT is effective in improving walking ability (WISCI II) in patients with complete and incomplete (without significant differences between both groups) and subacute SCI.

There is level 2 evidence (from 1 prospective controlled trial: Khande et al. 2024) that Lokomat-assisted BWSTT plus conventional therapy provides significantly larger improvements in walking ability (WISCI II), but not in LEMS, in comparison with standing-walking training using KAFOs plus conventional training in participants with complete (AIS A) and acute (mean time since injury: 6 days).

There is level 3 (from 1 case control study: Zieriacks et al. 2021) that BWSTT with the HAL robot exoskeleton provides similar improvements in walking time and distance on the treadmill with the exoskeleton and walking speed without the exoskeleton (10MWT) in patients with acute and chronic SCI; although 6MWT (performed without the exoskeleton), WISCI II and LEMS improved more in the acute subgroup than in the chronic subgroup.

Key Points

For patients less than 12 months post-SCI, Body-Weight Supported Treadmill Training (BWSTT) is superior to conventional physical therapy in improving walking outcomes.

BWSTT and Overground Gait Training (OGT) appear roughly equivalent in their effectiveness, though BWSTT may have an advantage in earlier mobilization and safety.

The effects of BWSTT may be superior during the acute/subacute phase of SCI owing largely to earlier mobilization and coincidental timing of neurorecovery.

There is no consensus on intensity or duration of BWSTT training, though durations of up to 60 minutes per session may provide more improvements if the patient is able to tolerate without too much exercise-induced fatigue.

5.2.2 Body-Weight Supported Treadmill Training (BWSTT) in Patients With Chronic SCI

Table 8. Treadmill Training in Patients With Chronic SCI (>1 Year Post-Injury)

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Midik et al. 2020 Turkey RCT PEDro = 4 Level 2 N = 30	**Population:** 30 males with traumatic incomplete SCI and a LEMS of ≥ 10; mean (range) age 36.6 (19-53) years; AIS C (n = 16) and AIS D (n = 14); injury level T12 (n = 7) and L1-L3 (n = 23); median time since injury for the RAGT and control groups was 5 and 24 months, respectively.	1. Both groups improved in LEMS and WISCI II (within group changes between T2-T1 and T3-T1 [but not between T3-T2] were statistically significant in both groups). Only the improvement between T3-T1 was significantly (p = 0.049) higher in RAGT group (2.1 ± 0.5) than in control group (0.6 ± 0.2) for LEMS.

	Treatment: All patients received regular physiotherapy (consisting of ROM exercises, strengthening exercises, body stabilization, self-care ability, and ground walking training) for 5 times a week for a total of 5 weeks. Participants were randomized into two groups: • RAGT group (n = 15): Received additional RAGT (using Lokomat) for 3 times a week (each session lasted 30 min) for a total of 5 weeks. Treadmill speed and BWS was increased individually. • Control group (n = 15). Nothing additional – regular PT only. **Outcome Measures:** LEMS and WISCI II were assessed at baseline (t1), at the end of the treatment (t2), and at three months after the treatment (t3).	2. The improvement in the LEMS scores and the SCIM-III scores was significantly higher in the RAGT group at the end of the fifth week and at three months (p=0.017; p=0.038).
Piira et al. 2019a Norway RCT PEDro = 7 Level 1 N = 20	**Population:** Participants with chronic and motor incomplete SCI; 15 males and 5 females; mean age 50 years; level of injury cervical (n = 8), thoracic (n = 8) and lumbar (n = 4); AIS C (n = 6) and AIS D (n = 14); and median time since injury 4 years. **Treatment:** Participants were randomly divided in two groups: • Control group (n = 10): Participants received usual care (which might include overground walking). • Intervention group (n = 10): A treadmill with BWS system was used for 60 days training, with 2 daily sessions of BWSTT with manual assistance for a total of 90 min per day, 5 days per week for 3 4-weeks periods; with the aim of reducing the BWS to <40% and/or increase walking speed towards normal (3–5 km/h). BWSTT also included overground training. The participants performed home exercises between the training periods. **Outcome Measures:** 10MWT, distance walked with use of necessary walking	1. The training intervention was well tolerated with no AEs, and there were only minor side-effects, such as superficial abrasions, which did not interfere with the regular training program. 2. In each group, 2 participants with AIS grade C were unable to walk at baseline and did not gain independent walking post-intervention. Thus, only 7 participants in each group were available for post-intervention walking testing: a. Both groups walked faster at post-test; however, the difference between the groups was small (0.1 m/s [95% CI –0.2, 0.4], p > 0.05). b. Distance walked improved approximately the same amount in both groups. c. There was no significant difference in change between the groups for BBS, –1.2 points 95% CI (–4.3, 1.9), *p* = 0.42. 3. In the intervention group, LEMS increased by a mean of 2.1 points (± 2.8, p = 0.05), whereas there was little change in the control group (mean change –0.6 (± 5.1), p = 0.75). The

	aids (6MWT), LEMS, BBS, and mFRT were assessed at baseline and 2–4 weeks after program.	difference in mean changes between the groups was 2.7 (95% CI –1.4, 6.8, p = 0.19).
Piira et al. 2019b Norway RCT PEDro = 7 Level 1 N = 24	**Population:** 24 participants wheelchair-dependents with or without some walking function and with chronic incomplete SCI; 9 males and 15 females; mean age 50.5 years; level of injury cervical (n = 10), thoracic (n = 9); and mean time since injury 18 years. **Treatment:** Participants were randomized to either intervention (n = 7) or control group (n = 12). • Intervention participants received 60 days of RALT (with the use of Lokomat®), with 3 training sessions per week over a period of 6 months. Each session included preparation (≈ 20–30 min), stepping on a treadmill (20–60 min) with BWS <40% of the participants' initial weight, and a few minutes of overground walking and/or exercises on the treadmill. • Control participants received low-intensity usual care, usually 1–5 times per week. **Outcome Measures:** Full or partial recovery of walking function, walking speed and endurance (10MWT and 6MWT); LEMS; BBS; and mFRT were assessed within 30 days before randomization, and post-evaluation within 14–30 days after completion of the trial.	1. The intervention was well tolerated with no AEs, except for minor issues such as small leg abrasions. 2. The recovery of walking function was not achieved in any participant. 3. Walking speed and endurance: Despite randomization, the groups differed in several aspects: All participants in the intervention group had some walking function, whereas 3 in the control group were unable to walk. Also, the controls with some baseline walking function had twice the walking speed and endurance compared with the intervention group. a. Both groups improved or maintained their walking speed (10MWT) at post-test. However, the group difference in improvement was small and not statistically significant. b. Mean endurance (6MWT), improved more in the control group (23.1 vs. 6.6 m, p > 0.05) than the intervention group. 4. In the intervention group, LEMS increased by 5.4 points, vs. 0.2 in controls.
Wu et al. 2018 USA RCT PEDro = 6 Level 1 N = 14	**Population:** 14 participants with incomplete SCI; 10 males, 4 females. • Robotic group: Mean age: 48.4 years; level of injury C2-T7; ASIA C (n=2) and ASIA D (n=5); and mean time since injury: 5.8 years • Treadmill only: Mean age: 48.1 years; level of injury C3-T10; ASIA C (n=0) and ASIA D (n=7); and mean time since injury: 9.4 years	1. Between-group comparisons indicated that gains in 6MWT distance were greater for the robotic training group than that for treadmill-only training group (P = 0.03), although gains in self-selected and fast walking speeds were not significantly different between the two groups (P = 0.06 and P = 0.12 for self-selected walking speed and fast walking speed, respectively).

	Treatment: Participants were randomly assigned to one of two groups: • Robotic treadmill training (n=7): A custom-designed cable-driven robotic gait training system (3DCaLT) was used to provide controlled forces to the pelvis and legs during treadmill walking. A bilateral pelvis assistance load was applied to the pelvis from heel strike to mid-stance on the ipsilateral leg for facilitating weight shifting. The peak force was set at approximately 9% of body weight (a constant magnitude force was applied during the loading period), although adjusted based on the tolerance of participants. In addition, an assistance load was applied to both legs from toe off to mid-swing to facilitate leg swing with magnitude of the force was determined using an adaptive control algorithm. • Treadmill only training (n=7): No assistance force was applied during treadmill training. Participants were fitted with an overhead harness that attached to a counterweight support system. BWS was provided as necessary for both groups to prohibit knee buckling or toe dragging during treadmill walking. Treadmill training speed was set at the participant's comfortable walking speed. Training was conducted 3 times/week for 6 weeks with the training time for each visit set to 45 minutes (i.e., 35 minutes of treadmill training and followed by 10 minutes of overground walking practice), excluding set up time. The targeted RPE was 12 to 16 (somewhat hard to hard levels). **Outcome Measures:** Self-selected and fast walking speeds (using a 10-m instrumented mat) and 6MWT were assessed before, after 6 weeks of	2. 6MWT significantly increased after robotic treadmill training (P = 0.02) (from 120 ± 37 m to 157 ± 59 m) after robotic training (P = 0.04) and remained to be significantly greater than baseline levels at the follow-up test, that is, 151 ± 60 m. The gain in 6MWT was greater than the MCID of adults with pathology (i.e., >14.0–30.5 m and is unknown for patients with SCI [Bohannon & Crouch 2017]). a. Self-selected walking speed tended to increase after robotic treadmill training, that is, from 0.33 ± 0.15 m/sec to 0.39 ± 0.20 m/sec after training, although this was not significant (P = 0.07) and was 0.38 ± 0.19 m/sec at the follow-up test. The gain in self-selected walking speed exceeded the MCID of patients with SCI, that is, ≥0.05 m/sec (Musselman et al. 2009). b. There were no significant changes in fast walking speed (P = 0.16) after robotic treadmill training and at follow-up tests. 3. Treadmill only training group: c. 6MWT, self-selected walking speed, and fast walking speed had no significant change after treadmill-only training and at follow-up test.

	treadmill training, and 8 weeks after the end of training.	
Tarnacka et al. 2023 Poland RCT PEDro = 5 Level 2 N = 105	**Population:** 105 participants with SCI • Control group (n = 33): 28 males, 5 females Median age: 36.5 years AIS A (n = 14), AIS B (n = 4), AIS C (n = 11), AIS D (n = 4) Level of injury: Cervical (n = 7), thoracic (n = 17), and lumbar (n = 9) Median time since injury: 13 months • Experimental group (n = 72): 58 males, 14 females Median age: 36.5 years AIS A (n = 27), AIS B (n = 7), AIS C (n = 13), AIS D (n = 25) Level of injury: Cervical (n = 17), thoracic (n = 32), and lumbar (n = 23) Median time since injury: 13 months **Treatment:** The therapeutic program consisted of two phases: first, 3 weeks, then, after a 1-week break, 3 weeks in the second phase. The program was conducted six days per week. Participants were allocated into two groups: • The control group received conventional physiotherapy and 30 min dynamic parapodium training. • The experimental group received 30 min sessions of RAGT with exoskeleton EKSO-GT or Lokomat Pro with the general exercise program and ground gait training. *The dynamic parapodium is a piece of individualized uprighting equipment (a combination of thoracolumbosacral orthosis and hip-knee-ankle-foot orthosis (HKAFO) device of the dynamic type) that allows the patient to stand and walk by swinging the trunk. All participants from the Lokomat group with incomplete SCI started with 60% BWS and an initial treadmill	1. Patients with incomplete SCI assigned to the rehabilitation group achieved significantly more improvement in motor score [2.58 (SE 1.21, $p < 0.05$)] and WISCI II [3.07 (SE 1.02, $p < 0.01$)] scores in comparison with patients assigned to the control group. 2. A nonsignificant improvement between the groups for SCIM-III was found.

	speed of 1.5 km/h; patients with complete SCI started with 100-90% BWS. Patients with a thoracic level of injury were mostly enrolled in the EKSO-GT group, and with a cervical level, in the Lokomat group. **Outcome Measures:** The American Spinal Cord Injury Association Impairment Scale Motor Score (LEMS), SCIM-III, WISCI II, and Barthel Index were conducted before the start of the therapy and after 7 weeks of therapy.	
El Semary & Daker 2019 Egypt RCT PEDro = 3 Level 2 N = 20	**Population:** 20 males with traumatic motor-incomplete SCI and paraplegia; mean (± SD) 32.53 (± 1.80) years; level of injury T9-T12; AIS B, C or D (n = N/A); and time since injury > 1 year. **Treatment:** The participants performed BWSTT (divided into a 15-min warm-up on a stationary bicycle, 45-min BWSTT, and a 10-min cool down) for 1h every session, twice a week, for 6 weeks. The participants were assigned randomly into two groups: • Group A (n = 10) performed BWSTT with a 30% of BWS. • Group B (n = 10) performed BWSTT with a 40% of BWS. **Outcome Measures:** 2MWT and 6MWT were performed prior to and following the training intervention and were assessed using the force platform or video camera optional including walking speed, step length, stride length, cadence, and step width.	1. Between-groups (40% vs. 30% of BWS) analyses revealed that there were significant distinctions among groups, with the 40% group experiencing superior improvements in: walking speed (89.36% vs. 23.84%, p = 0.001), step length (17.23% vs. 0.89%, p = 0.001), stride length (51.81% vs. 13.66% p = 0.001), and in cadence (16.07% vs. 4.69%, p = 0.009). 2. Within groups analysis showed that all the parameters (walking speed, step length, stride length and cadence width) except step width were improved in both groups.
Malik et al. 2019 Canada Case control Level 3 N = 13	**Population:** 8 participants with motor-incomplete and chronic SCI and able to walk on a treadmill with BWS but without manual assistance; 5 males and 3 females; AIS C (n = 1) and AIS D (n = 7); level of injury C1/2 (n = 1), C4/C5 (n = 1), C4-C5 (n = 1), C4 (n = 1), C5 (n = 1), T3 (n = 1), T4 (n = 1), and T10 (n = 1); and median time since injury 3.5 (range: 2-15) years.	1. Following training, improvements in skilled walking (SCI-FAP score) were significantly related to changes in hip-ankle coordination ($\rho = -.833$, p = 0.010) and knee ROM ($\rho = .833$, p = 0.010) of the weaker limb. 2. Inter-joint coordination tended to revert towards normative patterns, but not completely.

	5 non-SCI controls (median age 26 [range: 22-29] years) were recruited to provide normative kinematic data. **Treatment:** Kinematic data from participants who participated in the previous RCT by Lam et al. (2015) were included. Participants underwent 45min of Lokomat-based training 3 times per week for 3 months. **Outcome Measures:** Kinematic data from the lower limbs were recorded during treadmill walking before and after a 3-month training program. It was assessed: • The change in skilled walking and walking speed (based on the percent change of SCI-FAP and 10MWT, respectively). • ROM (sagittal plane hip, knee, and ankle joint angles). • Inter-joint (of hip-knee, hip-ankle and knee-ankle) coordination. Normative data from the non-SCI control participants were collected during a single session of treadmill walking.	3. No relationships were observed with walking speed.
Sawada et al. 2021 Japan Prospective controlled trial Level 2 N = 19	**Population:** 19 participants with chronic SCI; 14 males and 5 females; mean (± SD) age 42.9 (± 17.0) years; AIS A (n = 2), AIS B (n = 4), AIS C (n = 8) and AIS D (n = 5); level of injury cervical (n = 10), thoracic (n = 8), and lumbar (n = 1); and mean (± SD) time since injury 6.8 (± 11.0) years. Participants were divided into two groups according to their walking ability: • Low group; WISCI II scores 0–5 (n = 8). • High group; WISCI II scores 6–20 (n = 11). **Treatment:** All participants underwent BWSTT with voluntary driven exoskeleton (using the HAL) for 20 sessions (60 min, 2–5 times/week). During the training, the velocity of the treadmill was individually set to a comfortable and maximum tolerated speed with approximately 50% of	1. There were no serious AEs. 2. WISCI II and FIM motor score did not show significant differences after the voluntary driven exoskeleton-BWSTT program. 3. Furthermore, there was no significant improvement in any of the outcomes between pre-intervention and post-intervention in both low and high group. 4. In terms of individual data, WISCI II improved in four persons, while FIM motor score did not change in any participants.

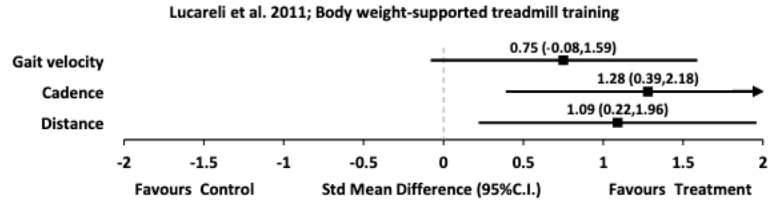
	each BWS; and the training intensity was progressively increased by changing the walking speed (from 0.5 to 2.5k/m), time, and amount of assist torque by voluntary driven exoskeleton, depending on each participant's ability. In persons unable to walk, only weight shifting or stepping training was performed on the treadmill with voluntary driven exoskeleton. **Outcome Measures:** WISCI II and FIM motor subscore were evaluated at baseline and post-intervention.	
Okawara et al. 2020 Japan Prospective controlled trial Level 2 N = 20	**Population:** 20 participants with chronic SCI who had reached a plateau in recovery from paralysis symptoms; 15 males and 5 females; mean (± SD) age 43.3 (± 16.6) years; level of injury cervical (n = 10), thoracic (n = 9) and lumbar (n = 1); AIS A (n = 2), AIS B (n = 4), AIS C (n = 8) and AIS D (n = 6); and mean (± SD) time since injury 80.4 (± 128.8) months. Based on baseline WISCI II score, 8 participants were categorized into the low walking ability group (n = 8) and into the high walking ability group (n = 12). **Treatment:** Participants underwent 20 sessions of BWSTT with voluntary driven exoskeleton (using the HAL) (2–5 sessions per week [mean frequency 2.6 ± 1.1 sessions] with 60 min of duration) on a treadmill with 50% BWS. The velocity of the treadmill was individually set to the participant's comfortable walking speed, and there was no inclination. **Outcomes Measures:** The speed, distance, and duration walked, and RPE were recorded in each session. WISCI II, 10MWT*, 2MWT), and LEMS were evaluated at pre and post intervention.	1. There were no AEs. 2. Gait performance on the treadmill with voluntary driven exoskeleton: a. The speed, distance, and total duration of walking in one training session increased significantly from the first to the last training session in all participants. b. Five participants who initially had difficulty walking with voluntary driven exoskeleton were analyzed afterwards, when they were able to walk with voluntary driven exoskeleton for the first time. 3. Overground walking ability without voluntary driven exoskeleton: a. In the high group, there was a significant improvement in 10MWT time (134.0 to 88.3 s, p = 0.01), and speed (0.26 to 0.34 s/m, p < 0.01) and number of steps (44.8 to 36.5 steps, p = 0.05) (this decrease in number of steps indicates an extension of step length); but not in the WISCI score (10.5 to 11.5, p = 0.11). b. There were significant differences between participants in the high/low groups at enrollment; there were more people with cervical level injuries and people classified as AIS B in the 'low' group. In addition, no participants in the low group were able to complete the 10MWT at any time point.

		4. Compared to baseline, LEMS did not change after training neither in the whole group nor in the low and high walking ability groups.
Jansen et al. 2017b Germany and USA Pre-post N = 21	**Population:** 21 participants with chronic SCI and some residual motor function of hip and knee extensor and flexor muscle groups; 15 males and 6 females; mean (± SD) age 44.8 (± 13.8) years; neurologic lesion level between C4 and L3 (paraplegia, n = 18; tetraplegia, n = 3); AIS A (n = 10), AIS B (n = 1), AIS C (n = 7) and AIS D (n = 3); and mean (± SD) time since injury 6.5 (± 5.8) years. **Treatment:** All participants underwent BWSTT 5 times per week using the HAL robot suit exoskeleton for a 12-week period (5 sessions per week). Overall, each training session lasted approximately 90 min, divided into 30 min for preparation, 30 min of functional testing, and 30 min of HAL-BWSTT. During the intervention, training intensity was increased progressively by changing walking speed, time, and level of BWS, depending on each patient's abilities. Additionally, the training was supplemented by specific task exercises such as downhill/uphill/backwards walking and climbing stairs, using a mobile BWS system. **Outcome Measures:** LEMS was assessed biweekly. 10MWT (gait speed, total time, and number of steps), 6MWT, and WISCI II were assessed without the exoskeleton at baseline, 6 weeks midtraining, and 12 weeks after training. The treadmill training performance parameters (walking distance, speed, and walking time) were recorded continuously.	1. There was only temporary skin reddening at the site of the skin electrodes, leg cuffs, and shoes in four patients, but without causing an interruption of the training. 2. Treadmill training performance parameters were significantly improved from at baseline to at 6 weeks and at 12 weeks. 3. A significant reduction of the time needed for 10MWT and in the number of steps in 10MWT from baseline (61.17 ± 44.27 sec and 30.90 ± 8.71 steps, respectively) to 6 weeks (43 ± 31.99 sec and 24.45 ± 6.47 steps, respectively; P < 0.001), from baseline to 12 weeks (32.18 ± 25.53 sec and 20.70 ± 5.51 steps, respectively; P < 0.001), and from 6 weeks to 12 weeks (P = 0.001) was shown. 4. The WISCI II score increased from 10.7 ± 4.95 at baseline to 11.7 ± 4.5 after the intervention (ns). 5. Before the training, the average walking distance covered in the 6MWT was 90.81 ± 110.18 min. All patients improved their walking distance significantly to 118.71 ± 134.89 m (6 weeks, P = 0.001) and 149.76 ± 144.28 m (12 weeks, P < 0.001). 6. LEMS showed a statistically significant improvement (P < 0.001) from 22.38 ± 10.7 to 25.71 ± 10.21.
Grasmücke et al. 2017 Germany and USA	**Population:** 55 participants with chronic SCI and some residual motor function of hip and knee extensor and flexor muscle groups; 43 males and 12 females; mean (± SD) age 44.3 (± 13.9)	1. Participants demonstrated an overall significant increase (p ≤ 0.001) in mean walking speed and cumulative walking time from at baseline to at 12 weeks of

Prospective controlled trial Level 2 N = 55	years; and mean (± SD) time since injury 6.85 (± 5.12) years. Participants were divided by age (< 50 or ≥ 50 years), independent of lesion level, and into 4 homogeneous groups according to lesion level: • Subgroup 1, participants with incomplete SCI and tetraplegia (n = 13) (C2–8, AIS C [n = 8] and AIS D [n = 5]). • Subgroup 2, participants with incomplete SCI, with paraplegia, and with spastic motor behavior (n = 15) (T2–12, AIS C [n = 8] and AIS D [n = 7]). • Subgroup 3, participants with SCI, complete motor paraplegia and absence of spastic motor behavior (n = 18) (T11–L4 [AIS A], and ZPP from L-3 to S-1). • Subgroup 4, participants with incomplete SCI, with paraplegia, and with absence of spastic motor behavior (n = 9) (T12–L3, AIS C [n = 8] and AIS D [n = 1]). **Treatment:** All participants underwent BWSTT 5 times per week using the HAL robot suit exoskeleton for a 12-week period. Overall, each training session lasted approximately 90 min. Additionally to the exoskeleton's weight, up to 30% of the participants bodyweight was neutralized during the initial training sessions. A 10MWT without the HAL was performed before and after each session in addition to regular physiotherapy. **Outcome Measures:** Gait speed, number of steps, and required assistance to walk were assessed using the 10MWT in self-selected speed (10MWTsss); 6MWT; and WISCI II were evaluated without the exoskeleton at baseline, at 6 weeks, and at 12 weeks of training. Treadmill-associated data (walking distance, speed, and time) acquired while using	training; without significant differences between subgroups. 2. An increase in the mean ambulated distance ($p \leq 0.001$) on the treadmill while using the HAL suit was observed across all groups. The mean ambulated distance in Subgroups 1, 3, and 4 showed relatively greater improvement than that in Subgroup 2. 3. The mean time for the 10MWT significantly decreased ($p \leq 0.001$) from baseline (70.45 ± 61.50 s) to 12 weeks (35.22 ± 30.80 s). There were no significant differences between subgroups. 4. A significant increase ($p \leq 0.001$) in the mean ambulated distance in the 6MWT from 97.81 ± 95.80 m to 146.34 ± 118.13 m was observed. There were no significant differences between subgroups. 5. The WISCI II scores improved significantly across all participants (baseline mean score, 9.35 ± 5.12; 12-week mean score, 11.04 ± 4.52; $p \leq 0.001$). A significant improvement in the WISCI II score was detected in Subgroups 1 and 3 ($p \leq 0.001$). Subgroups 2 and 4 presented no significant differences in pre- and postintervention assessments.

	the HAL exoskeleton were recorded continuously.	
Wu et al. 2016 USA RCT PEDro = 6 Level 1 N = 14	**Population:** 14 participants with incomplete SCI; the ability to ambulate overground with/without assistive device as necessary, and with orthotics that do not cross the knee; walking with impaired walking function (self-selected walking speed < 1.0 m/s); mean age: 51.9 years; 10 males, 4 females; level of injury C1-T10; ASIA C (n=1) and ASIA D (n=13); and time since injury: more than one year. **Treatment:** Participants were blocked by gait speed into slow (<0.5 m/s) or fast (<0.5 m/s) and randomly assigned to 1 of 2 groups of robotic treadmill training with resistance (n=7) or assistance (n=7) training. Training was performed 3 times per week for 6 weeks, with the training time for each visit set to 45 minutes (35 minutes of treadmill followed by 10 minutes of overground walking practice) as tolerated. For each training session, participants were fitted with an overhead harness attached to a counterweight support system. BWS was only provided in the instance that a counterweight was necessary to prohibit knee buckling or toe dragging during stepping. Treadmill speed was consistent with the participant's maximum comfortable walking speed, determined on the treadmill at the beginning of each training session. The RPE was monitored during the course of training and was 12 to 16. * A custom-designed cable-driven robotic gait training system (CaLT) was used to provide controlled bilateral resistance or assistance load to the leg at the ankle of participants during treadmill training. **Outcome Measures:** Step length (using the GaitMat recording system, gait speed (self-selected and fast walking speeds, assessed using a 10-m instrumented walkway), walking	1. Six participants in the resistance training group and six in the assistance training group completed all the 18 training sessions and three evaluation sessions. 2. A significant increase in step length was observed after resistance training (P = 0.04), but not after assistance training (P = 0.18). 3. The changes in self-selected walking speed were not significantly different between the 2 groups after resistance and assistance training (P = 0.37), and at the 8-week follow-up (P = 0.90). The gain in self-selected walking speed exceeded the MCID (i.e., > 0.05 m/s) of patients with SCI (Musselman et al. 2009). 4. The changes in fast walking speed were not significantly different between the two groups after resistance and assistance training (P = 0.61) and at the 8-week follow-up (P = 0.43). 5. The changes in 6-MWT were not significantly different between the two groups after resistance and assistance training (P = 0.78) and at the 8-week follow-up (P = 0.84). 6. Muscle strength, including peak torque, rate of torque development, and torque impulse, had no significant changes (P > 0.05) after treadmill training for both the resistance and assistance training group.

	endurance (6MWT), LEMS, and maximum voluntary isometric joint torques of the hip, knee, and ankle joints were assessed before, after 6 weeks of treadmill training, and 8 weeks after the cessation of treadmill training.	
Labruyère & van Hedel 2014 Switzerland RCT cross-over PEDro = 6 Level 1 N = 9	**Population**: 9 participants- 5 males and 4 females; SCI ranging from C4 to T11; mean age= 59 ± 11y; months post injury= 50 ± 56m. **Treatment**: Participants with a chronic incomplete SCI were randomized to group 1 or 2. Group 1 received 16 sessions of RAGT with Lokomat (45 min each) within 4 weeks followed by 16 sessions of strength training (45 min each) within 4 weeks. Group 2 received the same interventions in reversed order. Data were collected at baseline, between interventions after 4 weeks, directly after the interventions and at follow-up 6 months after the interventions. Pain was assessed repeatedly throughout the study. **Outcome Measures:** 10MWT at preferred and maximal speed, walking speed under different conditions, gait symmetry, WISCI, LEMS, and SCIM.	1. There were no significant differences in changes in scores between the 2 interventions, except for maximal walking speed (10MWT), which improved significantly more after strength training than after RAGT.
Lucareli et al. 2011 Brazil RCT PEDro = 7 Level 1 N = 30	**Population:** 14 males and 10 females with incomplete SCI; mean age 31.5; mean YPI 9.8. **Treatment:** Group A – treadmill gait training with BWS + conventional physiotherapy; Group B – conventional physiotherapy; both groups underwent 30 semi-weekly sessions lasting 30 min each. **Outcome Measures:** Spatial temporal gait variables and angular gait variables.	1. Group B showed no within group differences for spatial-temporal gait measures. Group A showed within group improvements ($p < 0.05$) in gait speed (47%), step length (17%), and cadence (16%). 2. There were no statistically significant improvements for Group B for any angular measure. However, group A showed a significantly greater ROM after intervention compared to Group B for maximum hip extension during stance and maximum plantar flexion during pre-swing. There were no significant group differences after treatment in other angular gait variables.

	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data.  	
[Yang et al. 2014](#) Canada RCT PEDro = 6 Level 1 N = 22	**Population**: 22 participants; 16 males and 6 females; Level of injury between C2 and T12; mean age= 48 ± 13y; years post injury= 5.7 ± 10.5y. **Treatment**: Twenty-two participants, ≥7 months post injury, were randomly allocated to start with Precision or Endurance Training. Each phase of training was 5 times per week for 2 months, followed by a 2-month rest. • Precision Training: Participants had to step over obstacles of different heights and onto targets of different sizes. • Endurance Training: Participants walked on the treadmill, with BWS and manual assistance if needed. **Outcome Measures:** Walking speed- 10MWT, distance- 6MWT, skill, confidence- Activities specific, depression- Centre for Epidemiologic Studies- Depression Scale (before training and monthly afterwards), WISCI II, SCI-FAP.	1. Both forms of training led to significant improvements in walking, with Endurance Training inducing bigger improvements in walking distance than Precision Training, especially for high-functioning walkers who had initial walking speeds >0.5 m/s. 2. The largest improvements in walking speed and distance occurred in the first month of Endurance Training, with minimal changes in the second month of training. 3. In contrast, improvements in walking skill occurred over both months during both types of training. Retention of over ground walking speed, distance, and skill was excellent for both types of training.
[Wu et al. 2012](#) USA RCT crossover PEDro = 5 Level 2 N = 10	**Population:** 10 participants with chronic SCI (8M 2F); mean (SD) age: 47(7); mean (SD) DOI: 5.8(3.8) yrs; level of injury: C2-T10. **Treatment:** Group 1: BWSTT with 4 wks assistance training, then 4 weeks RT. Group 2: BWSTT with 4 wks RT, then 4 wks assistance training. Resistance provided by a cable-driven robotic LT system. Sessions were 45 min, 3x/wk x 8 weeks. **Outcome Measures:** Self-selected and fast walking speed, 6MWT, BBS,	1. A significant improvement in both walking speed (increased from 0.67(0.20) at baseline to 0.76(0.23) m/s post-intervention) was observed after robotic treadmill training. 2. Following robotic training, stride length, step length, and cadence during self-selected walking significantly improved. 3. There was no significant difference in walking functional gains after resistance vs. assistance training, although RT was more effective for higher functioning patients.

	muscle strength tests, WISCI II, and Physical SF-36.	
Lam et al. 2015 Canada RCT PEDro = 8 Level 1 N = 15	**Population**: 15 participants - 9 males and 6 females; chronic motor incomplete SCI; 5 AIS C and 10 AIS D; age range= 26-63y; years post injury> 1y. **Treatment**: Participants were randomly allocated to BWSTT with Lokomat resistance (Loko-R group) or conventional Lokomat-assisted BWSTT (controls). Training sessions were 45 min, 3 times/wk for 3 months. **Outcome Measures:** Skilled walking capacity (SCI-FAP), 10MWT, 6MWT, were measured at baseline, post-training, and 1 and 6 months follow up.	1. Training was well tolerated by both groups, although participants in Loko-R tended to report higher levels of perceived exertion during training. 2. The Loko-R group showed a significantly greater improvement in the SCI-FAP at posttraining than the control. Compared with baseline, posttraining SCI-FAP scores decreased by 204 points (SD: 207, 95% CI: -348 to -61) in the Loko-R group but only by 18 points (SD: 36, 95% CI: -50 to 14) in the control group. Improvements were retained at 1 and 6 months follow-up. In the Loko-R group, SCI-FAP scores at 1 and 6 months follow-up were 217 (SD: 213, 95% CI: -364 to -69) and 220 (SD: 249, 95% CI: -404 to -36) points less than baseline, respectively. In the control group, the SCI-FAP scores at 1 and 6 month follow-up were 36 (SD: 70, 95% CI: -97 to 25) and 50 (SD: 131, 95% CI: -165 to 65) points less than baseline, respectively. 3. Both groups showed improvements in walking speed (10MWT) and distance (6MWT) with training, but there were no between-group differences.
Field-Fote & Roach 2011 USA RCT PEDro = 8 Level 1 N = 64	**Population:** Patients with chronic SCI at least 1-year post-injury, mean ages between 38 and 45; TM group (14 males, 3 females), TS group (14 males, 4 females), OG group (11 males, 4 females), LR group (12 males, 2 females). **Treatment:** Training 5 days/week for 12 weeks with: treadmill-based training with manual assistance (TM), treadmill-based training with stimulation (TS), overground training with stimulation (OG), or treadmill-based training with robotic assistance (LR). **Outcome Measures:** 10MWT, 2MWT, LEMS.	1. Walking speed: There were no significant between-group differences; however, the improvement in walking speed was statistically significant for the OG (moderate effect size, d=0.43), TS (small effect size, d=0.28), and TM small effect size, d=0.28) groups but not for the LR group. 2. Walking distance: There were significant between-group differences ($P < 0.01$) as the increase in the OG group was significantly greater than that in any treadmill-based training group. The increase in walking distance was statistically significant for the OG (moderate effect size, d=0.40) and TS (small effect size, d=0.16) groups but not for the TM and LR groups.

		3. LEMS: LEMS scores of all participants significantly increased 8-13%, with no significant between-group differences.
Alexeeva et al. 2011 USA RCT PEDro = 7 Level 1 N = 35	**Population:** 35 participants; 30 males and 5 females; chronic SCI; 8 AIS C and 27 AIS D; level of injury: C2-T10. mean age= 38.5y; median years post injury= 4y. **Treatment:** Patients participated in a 13-week training program, with three 1-hour sessions per week. The physiotherapy group is a structured rehab program individualized for each participant. The TRK group consisted of body weight supported ambulation on a fixed track. The TM group involved body weight supported ambulation on a treadmill. **Outcome Measures:** 10MWT, LEMS and total MMT score (sum of UEMS and LEMS), and the motor domain component of the FIM measure.	1. All three training groups showed significant improvements in maximal walking speed, muscle strength, and psychological well-being, with no between group differences.
Niu et al. 2014 USA RCT PEDro = 5 Level 2 N = 40	**Population**: 40 participants - 27 males and 13 females; spastic hypertonia in lower extremities. All participants were injured within their cervical or upper thoracic (above T10) vertebrae. *Growth Mixture Modeling was used to subdivide participants into multiple latent classes based on the recovery patterns (i.e., the change over time) of their walking measures, and subsequently inspect gait improvement within each class: • Class 1, low walking capaticity class: Participants with longer 10MWT and TUG times and shorter 6MWT distances at baseline. • Class 2, high walking capacity class: Participants with shorter 10MWT and TUG times and a longer 6MWT distance at baseline. **Treatment**: Each participant was assigned either to the control (no intervention) or intervention (Lokomat training) group. Each participant received a one-hour	1. The baseline (i.e., pre-training) measures of MVC torque (dorsiflexion torque and plantarflexion torque) could predict the differential treatment response, i.e., participants with high plantarflexion and dorsiflexion torques were more likely to have both high walking capacity and receive significant benefit from Lokomat training. 2. Lokomat training in participants with low walking capacity did not show significant improvements. By contrast, participants with a high walking capacity at baseline presented a consistent linear trend in time for speed over the 4-week training period.

	training session three times per week for four consecutive weeks; as it took 15-20 mins to set up the participant, the gait training lasted up to 45 mins per session. **Outcome Measures:** 10MWT, 6MWT, isometric torque resulting from MVC, Modified Ashworth Score, EMG, WISCI II.	
Gorassini et al. 2009 Canada Prospective Controlled Trial Level 2 N = 23	**Population:** 17 participants with incomplete SCI, mean (SD) age 43.8(16.5), injury level C3-L1, and 6 participants without SCI. Participants were divided into 2 groups: those who improved in walking ability (responders, n=9, 4 AIS-C, 5 AIS-D) and those who did not (non-responders, n=8, 7 AIS-C, 1 AIS-C). **Treatment:** BWSTT, on average for mean (SD) 3.3(1.3) days/week for 14(6) weeks. **Outcome Measures:** EMG; WISCI II.	1. Responders had an average WISCI II increase of 4.6pts, compared to no increase in the non-responders. 2. The amount of EMG activity increased significantly after training in responders, whereas no change was observed in non-responders.
Behrman et al. 2012 USA Cohort Level 2 N = 95	**Population:** 95 participants with SCI (75M, 20F); <1 yr (n=47), 1-3 yrs (n=24), ≥3 yrs (n=24) since injury; level of injury: T11 or above; Mean (SD) age: 43(17); median time since injury: 1 year; 31 AIS C, 64 AIS D. **Treatment:** At least 20 sessions of the NRN Locomotor Training Program consisting of manual-facilitated BWS standing and stepping on a treadmill and overground. Training consisted of 1hr of treadmill training, 30 min overground assessment, and 15-30 min of community reintegration. Frequency: 5 days/wk for non-ambulators, 4 days/wk for ambulators with pronounced assistance, 3 days/wk for independent walkers. Participants split into phases 1-3 depending on level of ability to perform task-specific movements relative to the preinjury capability (higher ability = larger numerical phase). **Outcome Measures:** ISNCSCI AIS, BBS, 6MWT, 10MWT.	1. For those were classified phase 1 at enrollment and were still classified phase 1 after NRN training, no change was seen in BBS, 6MWT or 10MWT scores. 2. For those who enrolled in phase 1 and were classified phase 2 after NRN training, mean change scores were 1 for BBS, 10 for 6MWT and 0 for 10MWT. 3. For those enrolled at Phase 1 and classified as Phase 3 after NRN training, mean change scores were 38.5 for BBS, 265.5 for 6MWT and 0.7 for 10MWT. 4. For those enrolled in Phase 2 and classified as Phase 2 after training, mean change scores were 7 for BBS, 46 for 6MWT and 0.1 for 10MWT. 5. For those enrolled in Phase 2 and classified as Phase 3 after training, mean change scores were 15 for BBS, 82.3 for 6MWT and 0.3 for 10MWT.

Buehner et al. 2012 USA Prospective cohort Level 2 N = 225	**Population:** 225 participants with chronic incomplete SCI (167M, 58F); mean (SD) age=42.5 (15.9); Median DOI=2.45; 57 AIS C, 167 AIS D. **Treatment:** NRN Locomotor Training Program. Training consisted of 1 hr of treadmill training, 30 min overground assessment, and 15-30 min of community reintegration. Frequency: 5 days/wk for non-ambulators, 4 days/wk for ambulators with pronounced assistance, 3 days/wk for independent walkers. **Outcome Measures:** LEMS, 10MWT, 6MWT, BBS.	1. Significant gains occurred in LEMS scores (Pretraining: 31.85 (13.98); Post-training: 38.61 (12.29)). 2. Although 70% of participants showed significantly improved gait speed after LT, only 8% showed AIS category conversion. 3. Significant gains in gait speed (72%) and ambulation distance (74%) after NRN training regardless of initial AIS classification.
Lorenz et al. 2012 USA Longitudinal Level 2 N = 337	**Population:** 337 participants with SCI (255M, 82F); mean (SD) age: 40 (17); 99 AIS C, 238 AIS D. **Treatment:** At least 20 sessions of the NRN Locomotor Training Program. Training consisted of 1hr of treadmill training, 30 min overground assessment, and 15-30 min of community reintegration. Frequency: 5 days/wk for non-ambulators, 4 days/wk for ambulators with pronounced assistance, 3 days/wk for independent walkers. **Outcome Measures:** BBS; 6MWT; 10MWT.	1. Participants varied significantly across groups defined by recovery status and AIS grade at enrollment with respect to baseline performance and rates of change over time. 2. Distances for the 6MWT significantly improved from enrollment at an attenuated rate ($p < 0.001$). 3. Speeds for the 10MWT significantly improved from enrollment at an attenuated rate $p < 0.001$). 4. BBS scores significantly improved from enrollment at an attenuated rate $p < 0.001$). 5. Time since SCI was a significant determinant of the rate of recovery for all measures.
Varoqui et al. 2014 USA RCT PEDro = 3 Level 2 N = 30	**Population**: 30 participants; ambulatory chronic incomplete SCI; mean age= 50.80 ± 2.12y; years post injury= 11.80 ± 2.54y. **Treatment:** • 15 participants with incomplete SCI performed twelve 1-hour sessions of Lokomat training over the course of a month. The voluntary movement was qualified by measuring active ROM, maximal velocity peak and trajectory smoothness for the spastic ankle during a movement from full plantar-	1. For the training group, the 10MWT resulted in a significant increase in mean gait speed of 13.4 ± 2.8% after training ($P < 0.05$); however, the control group did not show significant improvement ($P = 0.36$). 2. No significant improvements were found for the 6MWT in either group. 3. Results of MVC tests showed an improvement in the strength of dorsi- and plantar-flexor muscles during isometric voluntary contraction after the experimental training. On the other hand, for the control group, no change was observed between the two tests in MVCPF ($P = 0.09$) and MVCDF ($P = 0.81$).

	flexion to full dorsi-flexion at the patient's maximum speed. • 15 participants with incomplete SCI were included in a control group. **Outcome Measures:** Active ROM, maximal velocity peak and trajectory smoothness from full plantar-flexion to full dorsi-flexion at patient's maximum speed, isometric MVC (dorsi- and plantar-flexor muscle strength), 10MWT, 6MWT, and Modified Ashworth Scale were assessed before and after the training.	
Harkema et al. 2012 USA Pre-post (subacute and chronic) Level 4 N = 196	**Population**: 196 participants (148 male, 48 female) with incomplete SCI (AIS C, n = 66; AIS D, n = 130); mean age 41±15 yrs; YPI- <1 yrs (n=101), 1-3 yrs (n=43), >3 yrs (n=52). **Treatment**: At least, 20 training treatment sessions of LT with three components: (1) 1 hour of step training in the body-weight support on a treadmill environment, followed by 30 min of (2) overground assessment and (3) community integration. **Outcome Measures**: BBS, 6MWT, and 10MWT.	1. 6MWT distances and 10MWT speeds of all patients significantly improved by an average of 63m and 0.20m/s, respectively. 2. Significant increases also occurred in the AIS grade C and AIS grade D groups (P<.001) and were significantly different from each other (P<.001). Patients with AIS grade D had a greater magnitude of increase than those with AIS grade C. However, those with AIS grade C and already ambulatory improved their walking distances to a greater extent than the AIS grade D group, indicating potential for recovery.
Winchester et al. 2009 USA Pre-post Level 4 N = 30	**Population:** Mean (SD) age = 38.3(13.6); 22 males; 23 participants with tetraplegia, 7 with paraplegia; mean (SD) time since injury = 16.3(14.8) months. **Treatment:** LT, including: robotic assisted BWSTT (with Lokomat), manually assisted BWSTT, and over ground walking. 3 times per week for 3 months. **Outcome Measures:** WISCI II and 10MWT.	1. 22 participants showed improvement in walking speed; 8 showed no change post-training. 2. Pre-training, 16 participants could not walk. Post-training, 5 remained unable to ambulate, 7 recovered ambulation but needed assistance, and 4 recovered independent ambulation. 3. Step-wise regression analysis showed that time post-injury, voluntary bowel and bladder voiding, functional spasticity, and walking speed before training were the strongest predictors of post-training overground walking speed.

Discussion

BWSTT vs. Physical Therapy (Usual Care)

Most research that we found testing BWSTT vs. 'usual care' (i.e., some combination of range of motion training, stretching, strengthening, and/or some overground walking training) found that BWSTT was superior for walking-based outcomes. The most common improvement was in lower limb muscle strength (i.e., LEMS scores), but some studies also found improvements in functional walking (i.e., SCIM-III mobility scores or WISCI-II scores). Midik et al. (2020) found that participants in usual care group and the BWSTT group both improved with regular physiotherapy, but the improvement in the LEMS scores and SCIM-III mobility scores was significantly higher in the RAGT group at the end of the fifth week and at three months ($p=0.017$; $p=0.038$). In a relatively large RCT, Tarnacka et al. (2023; N=105) found that people with incomplete SCI who performed RAGT plus conventional PT had significantly more improvements in motor scores [2.58 (SE 1.21, $p < 0.05$)] and functional walking [WISCI II - 3.07 (SE 1.02, $p < 0.01$)] than those who did conventional PT and balance training.

Conversely, two studies by Piira et al. (2019a; 2019b) comparing Lokomat training to usual care found that all participants improved LEMS scores with no differences between groups in either walking speed or walking endurance.

BWSTT vs. OGT

When comparing BWSTT vs. OGT in people with SCI, the results are mixed, suggesting that neither method is superior to the other, but that the decision to use BWSTT may be more based on partially helping people to walk or providing a safer method to do so.

In a larger RCT, Field-Fote and Roach (2011; N=64) enrolled participants into a 5 days/week, 12 week walking training program, using either: treadmill-based training with manual assistance (TM), treadmill-based training with stimulation (TS), overground training with stimulation (OG), or treadmill-based training with robotic assistance (LR). For speed, they found no significant between-group differences; however, distance gains were greatest with OGT. They calculated effect sizes of each training method and found that they were largest for the OG group for speed and distance ($d=0.43$ and $d=0.40$, respectively). Authors suggested that a robotic training method that requires more active participation would possibly yield different results. In one small RCT, Wu et al. (2018) found that gains in 6MWT distance were greater for the robotic training group than that for treadmill-only training group ($P = 0.03$), although gains in self-selected and fast walking speeds were not significantly different between the two groups ($P = 0.06$; $P = 0.12$ respectively).

BWSTT vs. Other Types of BWSTT

There are multiple variations in how BWSTT or robotic gait training can be delivered; for example, the amount of support can be a smaller or larger percentage of body-weight, a BWSTT-assistance or -resistance mode can be used, or a hybrid assistive limb (HAL) wearable exoskeleton that assists walking and lower limb movements via real-time actuator controls may be combined with BWSTT (Kubota et al. 2018).

Three small RCTs (Lam et al. 2015; Wu et al 2016; Wu et al. 2012) tested different variations of BWSTT where one group used a robotic training method with resistance, and the other condition used robotic training with assistance. All three studies reported that both Lokomat-resistance and Lokomat-assistance groups improved walking speed (10MWT) and walking distance (6MWT), but that there were no between-group differences. Wu et al. (2012) hypothesized that robotic resistance training would be more effective for higher functioning patients, based on their results that people with better initial walking capacity had greater gains in walking speed over the course of their trial.

Multiple studies have shown walking training benefits using a hybrid assistive limb (HAL) wearable exoskeleton in people with chronic SCI. HAL uses power units and biofeedback sensors mounted on and around hip and knee joints to detect bioelectric signals and movement information to assist with (Koda et al. 2023). Although the HAL exoskeleton is not a walking aid for use during daily activities, it could represent a temporary training tool to improve functional mobility without the device in patients with SCI. Four pre-post trials from the same clinical setting reported significant improvement in gait performance following a program of 3-5 days per week of treadmill- progressing to overground-based BWST (Behrman et al. 2012; Buehner et al. 2012; Harkema et al. 2012; Lorenz et al. 2012).

Which Walking Training Type is Best?

Several systematic reviews with or without meta-analysis have been conducted to establish the effectiveness of different gait training interventions for people with SCI and the results have been mixed as to whether there is a 'best' walking training method (Aguirre-Güemez et al. 2019; Arroyo-Fernández et al. 2024; Huang et al. 2024; Mehrholz et al. 2017; Nam et al. 2017; Wan et al. 2024; Wall et al. 2015; Yang et al. 2022; Zhang et al. 2022). Systematic reviews and meta-analyses conducted by Mehrholz et al. (2017), Cheung et al. (2017), Nam et al. (2017), and Alashram et al. (2021) have indicated that neither BWSTT nor robot-assisted BWSTT increased walking ability, strength, or independence more than OGT and other forms of physiotherapy in patients with SCI. However, other systematic reviews and meta-analyses have shown positive results regarding these effects of RAGT (e.g., Lokomat) compared to different therapeutic interventions (such as conventional therapy, no intervention, or strength training, among others) (Aguirre-Güemez et al. 2019; Arroyo-Fernández et al. 2024; Fang et al. 2020).

In a network meta-analysis including 15 RCTs (and 497 participants), Yang et al. (2022) compared the effectiveness of three strategies (BWSTT, RAGT and BWSOGT) for ambulatory improvements. RAGT was found to be significantly more favorable than the control intervention (i.e., versus conventional gait training, such as sit-to-stand, weight shifting, walking, turning, and stand-to-sit), whereas BWSTT and BWSOGT provided similar effects and did not result in significant differences compared with the control interventions (Yang et al. 2022). An RCT by Niu et al. (2014) showed that Lokomat training in participants with lower walking capacity (i.e., longer TUG, lower 10MWT and shorter 6MWT) at baseline did not show significant improvements, in contrast with participants with a higher walking capacity who improved walking speed over the 4-week training period. It is reasonable to expect that walking training therapy works better and faster for people who are already better at walking.

There has been some specificity established by research in walking training intervention types; it would depend on what skills you are hoping your patient will develop. In a network meta-analysis, Zhang et al. (2022) showed that wearable EAW were most likely to be superior for improving walking speed (10MWT; the probability ranking first: EAW=89%; Lokomat=47%) but that Lokomat training was mostly likely to improve functional walking (WISCI-II: probability of ranking first: Lokomat=73%; EAW=63%).

Who For? How Much? How Long?

As with most research in SCI, there is a great degree of variability in what is tested, to the point where it is difficult to determine what is evidence-based and how you would build a program for your patient. For example, the duration of walking training in studies for people with SCI has a large range. In all studies we found, treatment session times ranged from 60 (Lucareli et al. 2011) to 600 (Behrman et al. 2012; Buehner et al. 2012; Lorenz et al. 2012; Harkema et al. 2012) min per week, and treatment duration lasted between 5 (Midik et al. 2020) and 24 (Piira et al. 2019b) weeks. In a systematic review and meta-analysis, Wan et al. (2024) found 8 studies testing RAGT and its effects on improving lower limb muscle strength; they found that studies that implemented the intervention for longer than 6 weeks found significant improvements in LEMS, but not for those who tested shorter durations of RAGT training.

Another variable in walking training for people with SCI is what percentage of body-weight support is most ideal. A systematic review by Ettema et al. (2024) found that in 33 studies involving 156 people with SCI the BWS levels ranged from 17-78% and the median level was 30%, suggesting it is the most common starting point in RAGT studies in neurological populations. We found one small RCT (N=20) that randomly assigned 20 males with incomplete SCI to receive BWSTT twice per week for 6 weeks at either 30% or 40% body-weight support (El Semary & Daker 2019). They found that people in the 40% group had superior improvements in walking speed (89.36% vs. 23.84%, p = 0.001), step length (17.23% vs. 0.89%, p = 0.001), stride length (51.81% vs. 13.66% p = 0.001), and in cadence (16.07% vs. 4.69%, p = 0.009).

Partially because SCI is known as a 'low-frequency' condition, it can be difficult to get enough participants into one study to test its effects on people with different levels of injury. In a prospective controlled trial, Grasmücke et al. (2017) tested BWSTT using the HAL exoskeleton in four different subgroups of people with SCI: incomplete paraplegia, incomplete tetraplegia, complete paraplegia, and complete tetraplegia (though all participants needed to have some residual motor function of the hip and knee extensor and flexor muscle groups to trigger and control the exoskeleton). After 12 weeks of 5 times per week BWSTT, all participants' walking ability increased, as evidenced by improvements in walking speed (mean 47% faster 10MWT), in walking endurance (mean 50% greater distance in 6MWT), and 43% of participants were less dependent on walking aids than before starting training. Surprisingly, there were no significant differences in walking outcomes between all subgroups of completeness or SCI level of injury.

Other prospective controlled trials using HAL found that, although people with all SCI types and classifications can benefit from walking training, that those with incomplete injuries at lower levels and with lower AIS classifications of severity tend to improve more. Okawara et al. (2020) classified participants into 'low' and 'high' walking groups, and there were significant differences

between participants in the high/low groups at enrollment; the low group had more people with cervical level injuries and people classified as AIS B. In the high group, there was a significant improvement in 10MWT time (134.0 to 88.3 s, $p = 0.01$), speed (0.26 to 0.34 s/m, $p < 0.01$) and number of steps (44.8 to 36.5 steps, $p = 0.05$) (this decrease in number of steps indicates an extension of step length). Additionally, no participants in the low group in this study were able to complete the 10MWT at any time point. Buehner et al. (2012) showed that people with AIS C improved significantly after walking training in LEMS, but participants in AIS D significantly improved in LEMS, 6MWT and 10MWT. Harkema et al. (2012) also found that people with AIS D walked significantly further than those with AIS C.

A standard protocol for locomotor training has been developed for people with SCI by the NeuroRecovery Network (NRN) designed to be applied to people who have nonprogressive SCI above the 11th thoracic level with an AIS grade of C or D (Morrison et al. 2012). The standardized locomotor training occurs 3-5 times per week, addressing three components – step/stand retraining (using body-weight support and manual facilitation with physical therapists), overground walking training (evaluating the transfer of step/stand training to level ground walking, improvement in posture and walking skills), and community integration (instruction helping the patient perform daily activities in home and community environment). It is recommended to continue with the program as long as progress is being made in any of the three components. The NRN protocol may be a useful starting point for anyone with SCI when beginning walking training in rehabilitation.

Conclusions

There is level 1 evidence (from 2 RCTs: Piira et al. 2019a; Piira et al. 2019b) that BWSTT with manual assistance or Lokomat® training does not improve walking or LEMS more than usual care in patients with chronic and motor incomplete SCI.

There is level 1 evidence (from 1 RCT: Field-Fote & Roach 2011) that different strategies for implementing body weight support gait retraining (i.e., including BWSTT with various assists and FES-assisted overland training) all yield improved ambulatory outcomes and strength in people with chronic, incomplete SCI, except for robotic-assisted treadmill training, which showed little change in walking speed. It is recommended that therapists choose a body weight support gait retraining strategy based on available resources (Field-Fote & Roach 2011).

There is level 1 evidence (from 1 RCT: Alexeeva et al. 2011) that different locomotor interventions (structured rehab program individualized for each participant; BWS ambulation on a fixed track; and BWS ambulation on a treadmill) provide significant improvements in maximal walking speed and muscle strength, regardless of training method, in patients with chronic and incomplete SCI.

There is level 1 evidence (from 1 RCT: Labruyère & van Hedel 2014) that four weeks of a strength training program provides larger improvements in 10MWT at maximal speed compared to a RAGT with Lokomat in patients with incomplete and chronic SCI.

There is level 2 evidence (from 6 prospective controlled/cohort trials: Buehner et al. 2012; Behrman et al. 2012; Grasmücke et al. 2017; Lorenz et al. 2012; Okawara et al. 2020; Sawada et

al. 2021) and level 4 evidence (from 3 pre-test/post-test studies: Harkema et al. 2012; Jansen et al. 2017b; Winchester et al. 2009) that BWSTT (with different approaches) is effective for improving ambulatory function in people with chronic and incomplete SCI.

Key Points

Body weight supported gait training strategies can improve gait outcomes in patients with chronic and incomplete SCI, but there is no limited evidence that one strategy is better than another (i.e., overground, treadmill training, robotic-assisted treadmill training, exoskeleton assisted walking; with/without functional electrical stimulation).

Clinical judgment on the walking training strategy based on the safety of the patient should be employed.

Walking training programs are beneficial in improving lower limb muscle strength in patients with chronic SCI, with some evidence favoring robotic-assisted treadmill training (Lokomat) in comparison with regular overground walking training.

5.3 Robot-Aided Gait Training with End-Effector Devices

In recent years, various types of robotic devices have been developed for motor rehabilitation (Choi et al. 2019). Generally, these robotic devices are divided into two categories based on the driving principle: exoskeleton and end-effector type robots (Choi et al. 2019). Exoskeleton robots move in parallel to the skeleton of the patient, so that no additional degrees-of-freedom or ROM are needed and each single joint is guided along a preprogrammed trajectory (Venenan et al. 2007; Molteni et al. 2019). End-effector type robots place patient's feet on footplates, generating movements from the most distal segment of the extremity in trajectories that simulate the stance and swing phases of walking (Hesse et al. 2010; Molteni et al. 2019).

Table 9. Robot-Aided Gait Training with End-Effector Devices

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Shin et al. 2023 South Korea RCT PEDro = 4	**Population:** 29 patients with incomplete SCI: • RAGT group (n = 16): Median (IQR) age: 52 (32, 65) years 9 male, 7 female	1. Within-group comparison after the intervention: After 20 sessions of the intervention, all clinical outcome measures significantly improved in both groups.

Level 2 N = 29	Traumatic (n = 14), non-traumatic (n = 2) Level: Tetraplegia (n = 14), paraplegia (n = 2) AIS C (n = 2), AIS D (n = 14) Median (IQR) time since injury: 54 (37, 92.2) days • Conventional therapy group (n = 13): Median (IQR) age: 60 (55, 64) years 12 male, 1 female Traumatic (n = 11), non-traumatic (n = 2) Level: Tetraplegia (n = 10), paraplegia (n = 2) AIS C (n = 4), AIS D (n = 9) Median (IQR) time since injury: 44 (33, 94) days **Treatment:** Participants were randomly assigned to either the RAGT or the conventional therapy group: • The RAGT group underwent 30 minutes of RAGT with the Morning Walk® and 1 hour of conventional therapy five times per week for 4 weeks (20 sessions in total). Cadence, step length and BWS were adjusted according to the individual's performance during RAGT sessions. Participants received also conventional therapy, which consisted of 30 minutes of ergometer training and 30 minutes of sitting and standing balance training, sit-to-stand training, OGT if possible, and strengthening exercises. • The conventional therapy group received 1.5 hours of conventional therapy (30 minutes of ergometer training and 1 hour of sitting and standing balance training, sit-to-stand training, OGT if possible, and strengthening exercises) five times per week for 4 weeks (20 sessions in total). **Outcome Measures:** 10MWT, 6MWT, WISCI II, LEMS, BBS, and SCIM-III mobility category were assessed within	2. Between-group comparison after the intervention: Only WISCI II improved significantly in the RAGT group compared to the CT group (p = 0.028).

	48 hours before the initial intervention session and after the final intervention session.	
Shin et al. 2021 Korea Prospective controlled trial Level 2 N = 13	**Population:** 13 participants with SCI; 8 males and 5 females; median (range) age 52 (19-85) years; tetraplegia (n = 11) and paraplegia (n = 2); AIS C (n = 1) and AIS D (n = 12); and median (range) time since injury 48 (19-139) days. Participants were sub-grouped according to the initial proprioception status: • Normal group (n = 6): Participants with grade 2 of proprioception of the ankle and knee. • Abnormal group (n = 7): Participants with grade 0 or 1 of proprioception of the ankle and knee. **Treatment:** Participants received RAGT with Morning Walk® with visual feedback (through a VR screen), so the participants could have the experience of walking through a park or the forest according to the gait speed. RAGT were performed for 30 min in the ground-level (starting with a cadence of 30 steps/min, a step length of 30 cm, and 20% BWS; and an estimated progression for each participant). In addition, one hour of conventional physiotherapy (consisting of strengthening exercises) were performed 5 times per week for 4 weeks. **Outcomes measures:** 10MWT, 6MWT, LEMS, proprioception (proprioception of the ISNCSCI at the ankle and knee), BBS, and WISCI II were assessed within 48 h before and after the intervention.	1. After the intervention, the patient with paraplegia AIS C improved to AIS D, and the proprioception of the ankle and knee and BBS had significantly improved (p = 0.027 and 0.001, respectively). 2. After the intervention 10MWT, 6MWT, LEMS, and WISCI II significantly improved ($p < 0.003$). 3. Based on the subgroup analysis of the initial proprioception status: a. The normal group showed a significant improvement on the 10MWT, 6MWT and WISCI II ($p \leq 0.028$); however, LEMS did not show a significant improvement ($p = 0.068$). b. In the abnormal group 10MWT, 6MWT, LEMS, and WISCI II, were significantly improved ($p \leq 0.028$). c. In the between-group comparisons, only the WISCI II showed a statistically significant difference ($p = 0.037$); with an improvement favoring the normal group.
Calabrò et al. 2021 Italy Pre – post Level 4 N = 15	**Population:** 15 patients with subacute (i.e., up to 18 months) SCI; 9 males and 6 females: mean (± SD) age 42 ± 14 years; level of injury C5 (n = 2), C6 (n = 3), C7 (n = 1), T1 (n = 1), T4 (n = 1), T6 (n = 1), T7 (n = 3), and T10 (n = 3); AIS C (n = 8) and AIS	1. None of the enrolled patients reported any side effects. 2. None of the patients achieved a complete recovery of walking function at T0, but they showed a significant improvement in the

	D (n = 7); and mean (± SD) time from injury 7 ± 4 months. **Treatment:** All participants continued all other rehab activities regularly during the study participation. Patients were given a daily session of the end-effector G-EO System device (an [non-treadmill] end-effector made of two footplates with three degrees of freedom on which the harness secured patient stand), 6 days per week, for two months. The RAGT consisted of a block of floor walking in a passive and active assisted mode for 30 min, 5 min of rest, and 20 min of going up/downstairs in a passive and active assisted mode. Participants performed the training at their maximum tolerable velocity and the BWS was set initially at 80% and was progressively reduced by 10% every week, down to 10% or the maximum tolerable BWS. **Outcome Measures:** Motor scores of the AIS; WISCI II; 10MWT; and gait analysis during an active-assisted gait training session once the patient became confident with the device were assessed at baseline, right after (T_0), and 3 (T_3) and 6 (T_6) months after the end of the rehabilitation training.	walking outcome measures up to T3: a. 10MWT (p = 0.004; 80% of patients achieved the MCID, p = 0.01). b. Motor AIS (p < 0.001; 93% of patients achieved the MCID, p = 0.004). c. WISCI II (p = 0.004; all patients achieved the MCID, p = 0.009). 3. All patients retained some improvements up to T6 limited to WISCI II, and Beck Depression Inventory.
Choi et al. 2019 Korea Pre-post Level 4 N = 189 (40 SCI)	**Population:** 189 patients with various neurologic disorders (mean age: 53.2 years; 123 males, 66 females): • SCI (n = 40): 23 male, 27 female Mean (SD) age: 61.8 (16.5) years Tetraplegia (n = 18), paraplegia (n = 22) AIS C-D • Brain lesions (n = 110) • Parkinson's disease (n = 8) • Peripheral neuropathies (n = 9) • Pediatric patients (n = 22) **Treatment:** Each participant performed 30 minutes of RAGT, with the end-effector device Morning Walk®, five times a week, for a total of 24 sessions. **Outcome Measures:** Medical Research Council scales of the lower extremities	1. Of the 189 patients, 22 (11.6%) failed to complete the RAGT, and the remaining 167 (88.4%) completed the training. 2. No serious events, such as episodes of neurological deterioration, falling, fractures, or skin lesions, occurred during any session in patients that either completed or failed to complete the training. 3. In the comparison between the pre- and post-training motor and ambulatory functions, patients with brain lesions, spinal cord injuries, and peripheral neuropathies showed statistically significant improvement in both the Medical Research Council scales and FAC.

	and FAC were recorded pre- and post-RAGT. Feasibility measures were also assessed.	
Hesse et al. 2004 Germany Pre-post N = 4	**Population:** 4 patients with SCI: 3 male, 1 female AIS C (n = 1), AIS D (n = 3) Tetraplegia (n = 1), paraplegia (n = 2), cauda syndrome (n = 1) Time since injury: More than 3 months post-injury **Treatment:** Participants performed 25 min of LT with an end-effector device (electromechanical gait trainer plus FES) daily for five weeks in addition to regular therapy. **Outcome Measures:** Gait analysis, 6MWT, and 10MWT	1. The patients tolerated the program well, and therapists rated the program less strenuous compared to manually assisted treadmill training. 2. Gait ability improved in all four patients; three patients could walk independently on the floor with the help of technical aids, and one required the help of one therapist after therapy; gait speed and endurance more than doubled, and the gastrocnemius activity increased in the patients with a central paresis.

Discussion

Overall, end-effectors seemingly allow achievement of greater gait recovery as compared to grounded exoskeletons in stroke populations (Mehrholz & Pohl 2012; Schröder et al. 2019); however, there are fewer studies in SCI populations. Specifically, there are two studies which assessed the effects of walking training with an end-effector device in walking and lower limb strength outcomes in patients with acute SCI. The RCT by Shin et al. (2023) included 29 participants with incomplete (AIS C-D) and acute SCI. Participants in the intervention group performed RAGT with an end-effector device for four weeks, five times per week, 30 minutes each session (Shin et al. 2023). Additionally, participants performed conventional training, which consisted of 30 minutes of ergometer training and 30 minutes of sitting and standing balance training, sit-to-stand training, OGT if possible, and strengthening exercises (Shin et al. 2023). Participants assigned to the control group received the same conventional training with same dosage (30 minutes of ergometer and 1 h of the rest of the training) (Shin et al. 2023). After four weeks of training both groups showed significant improvements in walking endurance (6MWT), walking speed (10MWT), walking ability (WISCI II), lower limb strength (LEMS), balance (BBS), and functional independence (SCIM-III mobility subscore); however, walking ability significantly improved more in the RAGT group than in the control group (Shin et al. 2023).

In a prospective controlled trial, Shin et al. (2021) assessed if 30 min of RAGT with the end-effector device plus one hour of conventional physiotherapy, five times per week, had effects on walking outcomes in 13 patients with acute tetraplegia (n = 11) or paraplegia (n = 2) (mean time since injury 48 [19-139] days). After four weeks of intervention, gait speed (10MWT), gait endurance (6MWT), muscle strength (LEMS) and walking ability (WISCI II) showed significant improvements; and one patient with paraplegia AIS C improved to AIS D (Shin et al. 2021). They also did a stratified analysis dividing groups by their proprioception levels of the knee and ankle; the participants who had at least grade 2 proprioceptive abilities in their knees and ankles improved significantly more in functional walking than those without (p = 0.037).

Lastly, the pre-post study (feasibility) by Choi et al. (2019) assessed patients with different neurologic disorders, including SCI (n = 40, AIS C-D). After 24 sessions of RAGT (30 min, five times per week, for four weeks) the subgroup of participants with SCI showed significant improvements in lower extremity strength (Medical Research Council scale) and ambulation ability (functional ambulation category [FAC]) (Choi et al. 2019). Although no serious adverse events occurred during sessions; 11.6% of the total sample failed to complete the RAGT (Choi et al. 2019). The reasons included decreased cooperation, musculoskeletal pain, saddle seat discomfort, excessive body-weight support, joint spasticity or restricted joint motion, urinary incontinence from an indwelling urinary catheter, and fatigue (Choi et al. 2019). These three studies used the end-effector device called Morning Walk® for RAGT, which is an end-effector type robot and the first gait training robot using a saddle for weight support (Shin et al. 2021) (Figure 2).

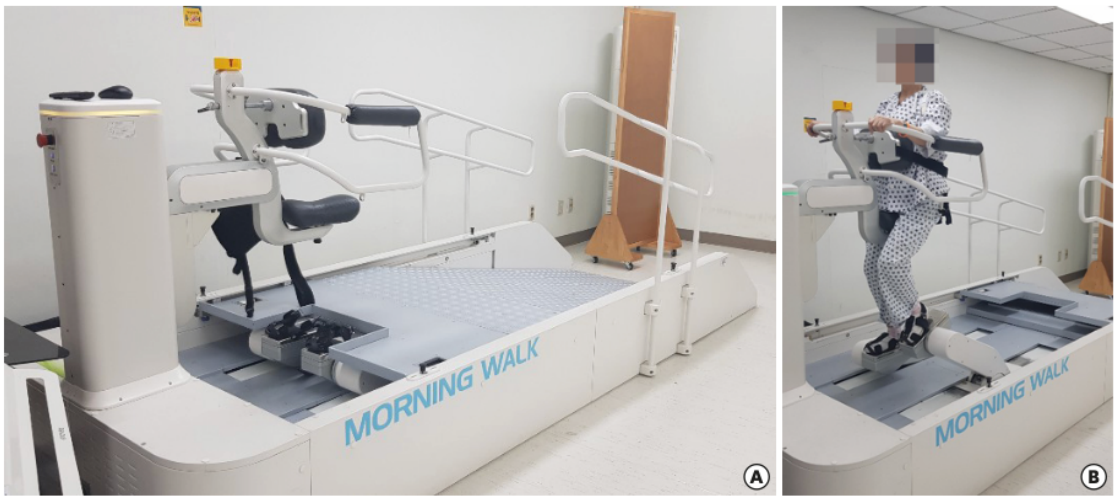


Figure 2. The Morning Walk® device. From (Choi et al. 2019). Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0).

To date, the pre-post study of Calabrò et al. (2021) was the only study where patients with SCI were provided with RAGT by means of the G-EO System device, which is a (non-treadmill) end-effector device made of two footplates with three degrees of freedom on which the harness secured the patient's stand (Calabrò et al. 2021) (Figure 3). Fifteen patients with subacute and incomplete SCI continued all other rehab activities regularly and were provided with a daily session of the end-effector G-EO System device, six days per week, for two months (Calabrò et al. 2021). It was found that patients achieved a clinically significant improvement in gait velocity (10MWT), sensory and motor functions of ASIA scale, disability burden (SCIM-III), functional ambulation (WISCI II), and quality of life (SF-36) up to six months post-treatment (Calabrò et al. 2021).

FIGURE 1 | The G-EO system used in the Robot-Assisted Stair-Climbing Training (Written informed consent was obtained from the individual pictured, for the publication of this image).

Figure 3. The G-EO System device. From (Gandolfi et al. 2019). Creative Commons Attribution License (CC BY).

Conclusions

There is level 2 evidence (from 1 RCT: Shin et al. 2023) that RAGT with an end-effector device (Morning Walk®) plus conventional physical therapy performed five times per week for four weeks provides significantly higher improvements in walking ability (WISCI II) than conventional physical therapy alone for people with acute and incomplete SCI.

There is level 2 evidence (from 1 prospective controlled trial: Shin et al. 2021) that RAGT (with Morning Walk®) with visual feedback and conventional physiotherapy provides improvements in gait speed (10MWT), gait endurance (6MWT), muscle strength (LEMS) and walking ability (WISCI II) in patients with acute (mean time since injury 48 days) motor incomplete SCI. The participants with higher proprioceptive abilities in their knees and ankles improved significantly more in functional walking than those without.

There is level 4 evidence (from 1 pre-post study: Choi et al. 2019) that RAGT (with Morning Walk®), performed five times a week, for a total of 24 sessions, provides significant improvements in a subgroup of participants (n = 40) with incomplete SCI.

There is level 4 evidence (from 1 pre-post study: Calabrò et al. 2021) that a 2-month program of daily sessions of RAGT with the end-effector device using the G-EO System, added to all other regular rehab activities, provides a significant improvement in motor AIS, gait velocity (10MWT) and walking ability (WISCI II) at the end of the intervention, and these improvements are retained up to six months of follow-up in patients with incomplete and subacute SCI.

Key Points

The use of an end-effector device for Robot-Aided Gait Training, in addition to regular rehab activities could provide improvements in walking function (6MWT, 10MWT, WISCI II) and lower limb strength in patients with incomplete, and acute or chronic SCI.

Further high-quality studies need to be performed to confirm these promising effects in comparison with other established bodyweight supported treadmill training methods.

5.4 Orthoses/Braces

There are several available devices used for bracing the legs in order to support standing and walking function for both complete and incomplete SCI. These range from single-joint bracing (e.g., ankle-foot orthosis [AFO]), which are usually for people with low, incomplete spinal lesions, to whole-leg/long-leg braces that extend from the lower back to the ankle.

Knee ankle-foot orthoses (KAFOs) are also used with complete injuries, and with these braces, you can sit in a wheelchair and get up and down throughout the day without risk of skin issues if they are fitted properly. With these braces, people will walk with a swing through or reciprocal stepping style, depending on the level of their injury. They require substantial upper-body strength to achieve standing. A swing through gait can tiring for the arms, and a reciprocal gait can be slow, so most people will opt for a wheelchair when long distances are required. These can be appropriate for some persons, but there has been poor adherence over the long term, with rates ranging from 32-50% (Yemisci et al. 2022; Frasunska et al. 2020). The most common reasons for discarding orthoses included difficulty in donning and doffing, limited functional improvement, high cost of devices, and wear and tear of orthoses (3%) (Yemisci et al. 2022; Frasunska et al. 2020).

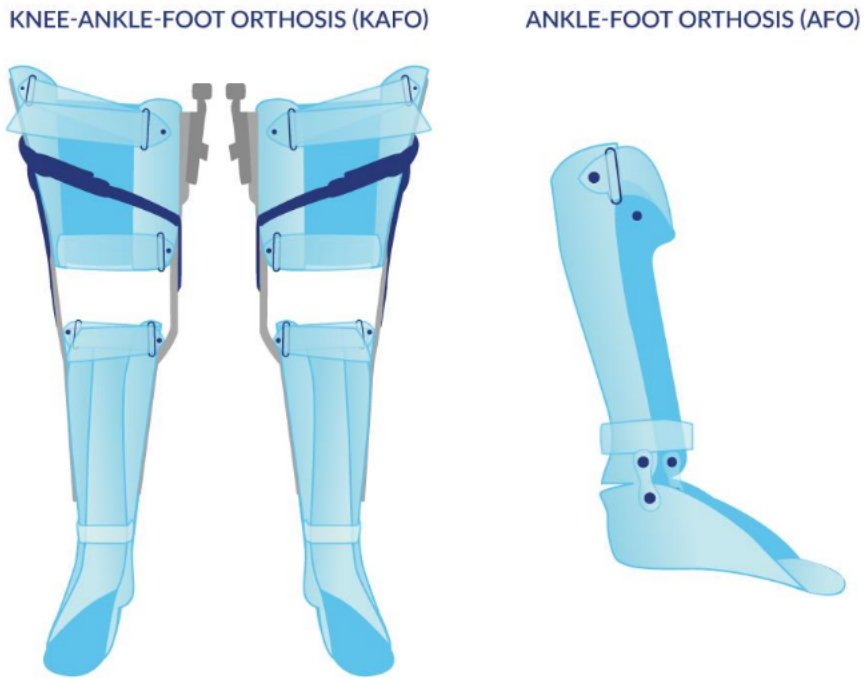


Figure 4. Hinged Ankle-Foot Orthosis (AFO) and a Custom Knee-Ankle-Foot Orthosis (KAFO)

Many styles of AFOs and knee hyperextension braces are used to assist with standing and walking. These can be for joint protection when there is a significant muscle imbalance around a joint, such as a knee hyperextension brace (Swedish knee cage or Ossur knee sleeve, for example). Depending on an individual's strength, tone, and ROM, there are many different AFO's people can use, ranging from a dynamic small brace to assist with toe clearance (e.g., the Dictus) to a more rigid custom AFO to stabilize and hold the entire foot and ankle. The more rigid a brace is, the more it will impede "normal" dynamics around the joint, although this may be clinically necessary to protect the joints and provide a safe, stable base to weight bear on. These braces for the knee and lower leg may require a walking aid like the higher braces, but may be able to be used without an aid.

Braces have been advanced with powered actuators to reduce the effort required to advance the limb. Earlier models used actuators in single joints (e.g., ankle or hip), while newer models control multiple lower extremity motions. Some of the newest models utilize an exoskeleton with battery-powered motors to control multiple degrees of freedom, and the weight of the device is transferred into the ground by the exoskeleton, alleviating the participant from bearing the weight of the device. The technology of these devices appears to be the main focus of research in rehabilitation and assisted walking and ambulation in patients with SCI (Arazpour et al. 2016), hindering the progression in development of the mechanical orthoses, previously cited above.

5.4.1 Ankle-Foot Orthoses (AFOs) in SCI

Table 10. Ankle-Foot Orthoses (AFOs)

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Kim et al. 2004 Canada RCT PEDro = 5 Level 2 N = 19	**Population:** 19 participants with incomplete SCI who had 'dropfoot' but were able to walk independently. **Treatment:** Randomized to conditions of ankle-foot orthosis (AFO), no AFO, FES and FES and AFO. They walked at their self-selected speed along a flat walkway. **Outcome Measures:** Walking speed and 6MWT.	1. Gait speed increased 7.5% from 0.4 m/s (no orthosis) to 0.43 (AFO). 2. 6MWT increased 16% from 138 to 160 m.
Arazpour et al. 2013 Iran RCT PEDro = 4 Level 2 N = 5	**Population:** 5 participants with incomplete SCI (thoracic lesion). **Treatment:** Gait evaluation while walking with 1) no shoe; 2) solid AFO and 3) hinged AFO. **Outcome Measure:** Step length, cadence.	1. Solid AFO improved step length from 28.5 from 26.3 cm and cadence from 52 to 62 steps/min. 2. No significant differences between the no shoe and hinged AFO condition.

Discussion

Because bracing devices are used widely by clinicians, and often seen as simple assistive devices for improving walking function or stability and limiting pain, there are very few studies actually researching the benefits.

Both studies we found (Kim et al. 2004; Arazpour et al. 2013) examined the immediate effects of an AFO after randomizing different brace conditions. Positive effects consisted of increased gait speed, step length, cadence and improved performance on the 6MWT. These are not typical experimental designs for an RCT, as all the conditions were assessed within one single session rather than allowing participants to adapt to different brace conditions over several weeks or sessions. However, it is generally recognized in the clinical field that effects from an AFO are attained immediately, although it is likely that practice over a few sessions may improve a person's confidence, learning and function.

Conclusions

There is level 1 evidence (from 2 RCTs: Arazpour et al. 2013; Kim et al. 2004) that an AFO can enhance walking function in patients with incomplete SCI who have drop-foot.

Key Points

Ankle-foot-orthosis can enhance walking function in patients with incomplete SCI who have drop-foot.

5.4.2 Hip-Knee-Ankle-Foot Orthoses in SCI (HKAFOs/KAFOs)

Intensive ambulatory training with KAFOs for low thoracic SCI requires a large amount of determination and motivation from the patients (Senthilvelkumar et al. 2023). Patients can usually walk short distances, at slow average velocities and greatly increased energy expenditure (Senthilvelkumar et al. 2023). Despite these challenges, walking is beneficial for them due to many physiological and psychological benefits (Senthilvelkumar et al. 2023).

Unlike the other orthotic devices (locked stance-KAFO, walkabout orthoses, reciprocating gait orthosis) for persons with low thoracic SCI, the polypropylene solid AFO with aluminum uprights is a relatively lightweight orthosis, as bilateral KAFOs weigh approximately 3 kgs (6.5 lbs.) (Senthilvelkumar et al. 2023). Though ambulation with knees locked in full extension increases the energy cost, it provides safety as the positive drop lock enables the persons to lock and unlock the knees as needed during standing, walking, and sitting on a chair (Senthilvelkumar et al. 2023). Additionally, polypropylene KAFO can be worn underneath clothes and is cosmetically more acceptable than other devices (Senthilvelkumar et al. 2023).

Few people use orthotic walking as the primary mode of walking (Senthilvelkumar et al. 2023) as there are challenges such as the functional use of hands, fear of falls, difficulty negotiating steps and uneven terrain, difficulty donning and doffing orthosis, the appearance, and bulkiness of the orthoses, as well as the need for substantial energy expenditure (3–9 times that of those without SCI), which leads to early fatigue (Senthilvelkumar et al. 2023). Because the legs are paralyzed, the primary contributors to walking are the upper extremity and trunk muscles, so selective strengthening of the trunk and upper extremity muscles improves gait performance and postpones fatigue and shoulder pain (Baniasad et al. 2018; Senthilvelkumar et al. 2023). Under these circumstances, patients who wish to ambulate with KAFOs should be given precise information regarding the advantages and disadvantages of orthotic ambulation rather than an adulated impression (Senthilvelkumar et al. 2023).

Table 11. Hip-Knee-Ankle-Foot Orthoses (HKAFOs/KAFOs)

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Seyyedzadeh et al. 2021 Iran Prospective controlled trial Level 2 N = 3	**Population:** 3 participants with SCI; 2 males and one female; mean (± SD) age 29.7 (± 3.8) years; level of injury T8 (n = 1) and T10 (n = 2); and AIS C (n = 3). **Treatment:** Two different medial linkage mechanisms while wearing a KAFO were used: • KAFO equipped with a sliding mechanism. • KAFO equipped with a medial linkage mechanism associated with reciprocating gait motion. Each participant underwent 2 weeks of gait training after the initial fitting of each KAFO, with three 2-hour sessions per week. The training program included trunk, upper-limb and lower-limb stretching, and a period of training that focused on standing and walking. Two weeks of orthotic gait training was considered for each KAFO separately. **Outcome Measures:** 10MWT and 6MWT were assessed after each intervention.	1. Use of the KAFO with medial linkage mechanism associated with reciprocating gait motion improved the speed of walking (0.03 ± 0.002 m/s with sliding mechanism vs. 0.043 ± 0.008 m/s with medial linkage mechanism associated with reciprocating gait motion) and distance walked (9.25 ± 1.03 m with sliding mechanism vs. 11.08 ± 1.5 m with medial linkage mechanism associated with reciprocating gait motion) when compared with the use of the KAFO with the sliding mechanism.
Senthilvelkumar et al. 2023 India Case series Level 4 N = 430	**Population:** 430 patients with motor complete low thoracic SCI admitted for a comprehensive rehabilitation program and completed a minimum of 6 weeks inpatient rehabilitation program; 383 males and 47 females; mean (± SD) age 32.3 (± 11.1) years; AIS A (n = 395) and AIS B (n = 35); injury level T9 (n = 41), T10 (n = 125), T11 (n = 90), and T12 (n = 174); and mean (± SD) time from the injury to the onset of rehabilitation 15.4 (± 34 months).	1. WISCI II: 260 (60.5%) patients achieved WISCI II level 12, and 105 (24.2%) achieved WISCI II level 9 at the time of discharge. 2. Speed and distance walking: a. People with WISCI level 12 (n = 234; missing data = 26) were able to walk with a mean speed of 0.297 (± 0.097) m/s and covered a mean distance of 376 (± 179.7) m. b. People with WISCI level 9 (n = 80; missing data = 25) were able to walk with a mean speed of 8.2

	Treatment: Patients were trained to be wheelchair independent and considered for orthotic walking training. The orthotic walking training consisted of a progressive training program with the aim of walking independently using KAFOs and elbow crutches. Training sessions lasted two hours per day and six days per week for 12 weeks. **Outcome measures:** WISCI II, walking speed and endurance were assessed at the time of discharge.	(± 5.8) m/min and covered a mean distance of 215.5 (± 104.6) m at the time of discharge. 3. Multivariate logistic regression revealed that people with male gender, time since injury less than 6 months, single neurological level of injury of T10, T11, and T12, negative Beevor's sign, and length of stay more than 12 weeks also increased the chance of achieving orthotic walking after LT-SCI. 4. Multivariate analysis revealed that age (< 30 years), single neurological level of injury of T10 & below, and etiology of the SCI were the factors that predicted the achievement of WISCI II level 12. Age less than 30 years and the single neurological level of injury of T12 increased the chance of achieving WISCI II level 12 by 10 times.

Discussion

Exploring the maximum walking potential of people with SCI through restorative or compensatory gait training programs is common. One of the reasons why is that most of the barriers to community reintegration are related to the wheelchair inaccessibility of homes, public buildings, and transportation (Senthilvelkumar et al. 2023).

A large case series by Senthilvelkumar et al. (2023) included 430 patients with motor complete (AIS A and B) and low thoracic SCI who were trained to walk independently using KAFOs and elbow crutches for two hours per day, six days a week. After 12 weeks of training, 84.9% (n = 365) of people achieved walking using orthoses and walking aids either with a walker (WISCI II level 9, n = 105) or elbow crutches (WISCI II level 12, n = 260) (Senthilvelkumar et al. 2023). Additionally, younger adults (<30 years) with traumatic SCI and an injury level of T10 and below could perform better than others with orthotic gait training (Senthilvelkumar et al. 2023). This method of walking requires high energy and the risk of falls is high, so the selection of the ideal candidate is crucial (Senthilvelkumar et al. 2023).

Literature suggests that a walking speed of 0.59 m/s (35.4 m/min) is essential for independent and safe community walking following SCI (van Silfhout et al. 2017). Participants in Senthilvelkumar et al. (2023) showed an average speed of 0.297 m/s (only half of the expected walking speed for successful community walking). However, these values were taken at the time of discharge, and walking velocity generally improves over time.

Various designs of sliding medial linkages have been used within KAFOs to assist standing and walking in patients with SCI, including the Moorong (sliding-type medial hip joint) and the Primewalk (sliding-type medial hip joint) (Seyyedzadeh et al. 2021). A new type of KAFO with a

medial linkage mechanism has been developed by Bani et al. (2015). This type of mechanism incorporates two gears that enable the extension of one limb to provide flexion to the contralateral limb and vice versa; it is also sensitive to pelvic motion, enabling the user to activate hip flexion and extension (Seyyedzadeh et al. 2021). In a prospective controlled trial, three patients with low thoracic and incomplete SCI underwent two weeks of gait training (trunk, upper-limb and lower-limb stretching, standing and walking) with these two types of KAFO. Using the KAFO with the medial linkage mechanism, as compared to the SM, was associated with reciprocating gait motion showed improvements in walking speed (10MWT), walking distance (6MWT), and reduced the physiological cost index, but not donning nor doffing (Seyyedzadeh et al. 2021). These results should be taken with caution as the sample size was small, and neither statistical analyses nor the order of interventions were mentioned.

Conclusions

There is level 4 evidence (from 1 case series: Senthilvelkumar et al. 2023) that patients with motor complete low thoracic SCI using KAFOs and elbow crutches could achieve walking (although not at speeds sufficient for community ambulation).

Key Points

Knee-Ankle-Foot Orthoses can enable walking with elbow crutches or a walker in people with motor complete and low thoracic SCI, but caution should be exercised (i.e., assessing whether walking speed is quick enough to safely walk in the community.

5.4.3 Wearable Powered Exoskeletons (WPEs) in SCI

Wearable powered exoskeletons (WPEs) could be defined as computer-guided systems using motorized orthoses to facilitate autonomous overground movement in people with disabilities (Rodriguez-Tapia et al. 2022). WPE or robotic orthoses are other terms that are used interchangeably for these robotic devices, which are wearable and operate in the proximity of the joints of patients (Jamwal et al. 2022). Activation of these systems can be triggered by patients' voluntary movements or by a computer algorithm, depending on the patients' capabilities and the exoskeleton characteristics (Rodriguez-Tapia et al. 2022).

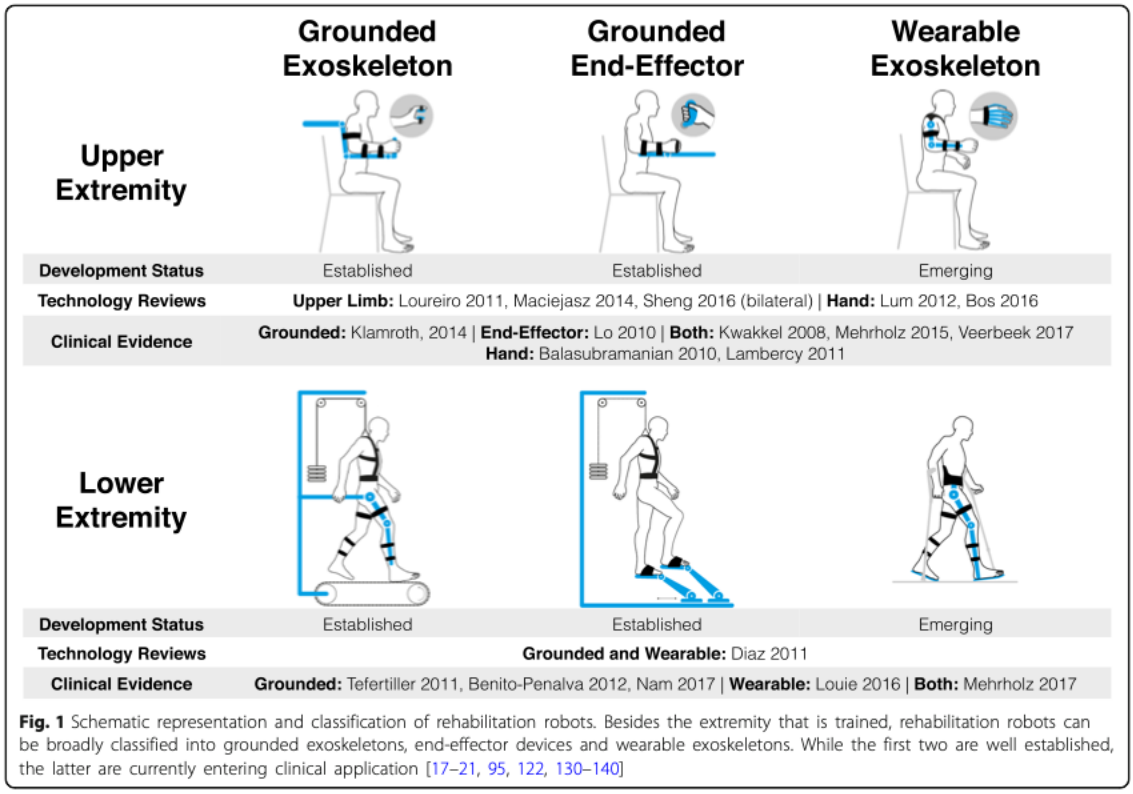


Fig. 1 Schematic representation and classification of rehabilitation robots. Besides the extremity that is trained, rehabilitation robots can be broadly classified into grounded exoskeletons, end-effector devices and wearable exoskeletons. While the first two are well established, the latter are currently entering clinical application [17–21, 95, 122, 130–140]

Figure 5. Schematic representation and classification of rehabilitation robots. In (Gassert & Dietz 2018). Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/)

WPE differs from other RAGT systems because it offers new possibilities and key advantages in gait rehabilitation (Heinemann et al. 2020; Rodriguez-Tapia et al. 2022):

1. WPE allows self-balancing, overground, and gait training, with or without upper limb assistance.
2. Assistance during gait can be triggered voluntarily by the participant through muscle contraction and body movements.
3. Gait training, through task-specific rehabilitation, can be performed in more ecological environments, promoting a more human-like gait pattern (including activation of trunk muscles during overground or treadmill training).
4. Some WPE are not limited to a laboratory or clinic setting, and users can wear them in community and home settings, providing opportunities to practice walking outside of a clinical environment.
5. WPE enable walking with a lower energetic cost compared to other systems.

In a systematic review, Rodríguez-Fernández et al. (2021) identified 25 wearable lower-limb powered exoskeletons for overground training that have been tested for use with people who have gait disorders due to neuromuscular impairments (e.g., SCI, stroke, and other pathologies).

Only six of these have Food and Drug Administration (FDA) approval, are commercially available and regulated for use in the USA (i.e., Ekso, HAL, Indego, REX, ReWalk and SMA) (Rodríguez-Fernández et al. 2021; Onate et al. 2024).

Figure 6. Different exoskeleton models. In (Rodríguez-Fernández et al. 2021). With Creative Commons Attribution 4.0 International License.

Table 12. Wearable Powered Exoskeletons (WPEs)

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Xiang et al. 2021 China RCT (pilot) PEDro = 8 Level 1 N = 18	**Population:** 18 patients with SCI; 15 males and 3 females; mean age 38.2 years; AIS A (n = 12), AIS B (n = 2), and AIS C (n = 4); level of injury T4-T10 (n = 9) and T11-below (n = 9); and median duration of injury 2 months. **Treatment:** The participants were divided into EAW with the AIDER (EAW) group (n = 9) or conventional group (n = 9). Intensity, duration, and frequency were similar in both groups (40–60% HR_{max}, 50–60 min/session, 4 days/week, 4 weeks): • EAW group: Training session included sitting, standing, walking, climbing stairs and slope with the AIDER (AssIstive DEvice for paRalyzed patient) powered robotic exoskeleton. • Conventional group: Consisted in strength training using dumbbell, aerobic exercise, such as walking training with brace. **Outcome Measures:** 6MWT, LEMS and ASIA scores were assessed pre and post intervention.	1. There were no AEs. 2. Of the 10 participants who completed the final 6MWT, 2 were in the conventional group. The outcomes of distance recording as medians (IQR) were 17.3 (11.9) m and 0 (16.0) m for EAW and conventional group, respectively. Nonetheless, EAW training produced no statistical improvements in distance (p = 0.079) than conventional group. 3. For LEMS, there was no statistical difference between two groups (p = 0.777). Additionally, neither group showed improvement in LEMS.
Gil-Agudo et al. 2023 Spain RCT PEDro = 7 Level 1 N = 21	**Population:** 21 participants with incomplete (AIS C or D) SCI, with enough strength in the upper limbs necessary to handle a walker or crutches and the capacity to tolerate standing. 15 males, 6 females Mean age: 46,4 years old Level of injury: C2-C8 (n = 1), T1-T6 (n = 5), T7-L1 (n = 9), and L2-L4 (n = 6) AIS C (n = 12), AIS D (n = 9) Mean time since injury: 5.2 months **Treatment:** Participants were randomly distributed into the two study groups:	1. No major AEs were reported. Participants in the intervention group reported 1.8 cm (SD 1.0) for pain and 3.8 (SD 1.7) for fatigue using the visual analogue scale. 2. Statistically significant differences were observed for the WISCI-II for both the “group” factor (F = 16.75, p < 0.001) and “group-time” interactions (F = 8.87; p < 0.01). A post-hoc analysis revealed a statistically significant increase of 3.54 points (SD 2.65, p < 0.0001) after intervention for the

	• Exoskeleton gait training (intervention group) (n = 11): The IG training protocol consisted of 15 robotic ambulatory gait training sessions (three sessions per week for 5 consecutive weeks), each session lasting 30 min. The HANK exoskeleton was used. • Traditional gait training (control group) (n = 10): The CG rehabilitation program was comprised of 15 sessions, 30 min long, of a traditional gait training program (analytical mobilization, strengthening exercises for the lower limbs and gait re-education), distributed similarly as in the intervention group. **Outcome Measures:** LEMS, 10MWT, TUG test, WISCI II, and SCIM-III were measured at baseline and end of training period (post-intervention).	intervention group but not in the control group (0.7 points, SD 1.49, p = 0.285). 3. No statistical differences were observed between groups for the remaining variables.
Rodríguez-Fernández et al. 2022 Spain RCT Crossover PEDro = 7 Level 1 N = 10	**Population:** 10 participants with chronic motor-complete SCI; 9 males and one female; mean (± SD) age 44.10 ± 5.93 years; level of injury T4 (n = 3), T6 (n = 1), T8 (n = 2), T10 (n = 1), T11 (n = 2), and T12 (n = 1); AIS A (n = 8) and AIS B (n = 2); and mean time since injury 10.5 years. **Treatment:** Participants were randomly assigned to one of two groups, depending on the device used for the training program: • KAFO. • Knee-powered bilateral lower limb exoskeleton (i.e., the ABLE Exoskeleton). The training program consisted of 10 sessions (2 sessions per week, for 5 weeks) of 90-min duration: 8 OGT sessions (sessions 1 to 4 and 6 to 9) plus 2 evaluation sessions (sessions 5 and 10). Participants spent a minimum of 30 min per training session doing sit-to-stand and stand-to-sit transitions, and standing and walking exercises using one of the two devices and the aid of a walker. There was a 2-week resting period between the final evaluation session and	1. No serious AEs were reported during the study. 2. The average level of assistance provided by the therapist to the participants was slightly higher for the ABLE group compared to the KAFO group (ns). 3. No significant differences were found between the two groups for 6MWT and 10MWT. 4. Spatiotemporal parameters and gait kinematics: Walking with the ABLE Exoskeleton improved gait kinematics compared to the KAFOs, providing a more physiological gait pattern with less compensatory movements (38% reduction of circumduction, 25% increase of step length, 29% improvement in weight shifting). 5. Linear regression analysis between the outcome metrics of the standardized clinical tests and the level of injury revealed significant, strong correlations for the KAFO group. In contrast, correlations for the ABLE group were low to mild and not statistically significant.

	the first training session with the crossed-over device. **Outcome Measures:** 6MWT; 10MWT; and gait kinematics and spatiotemporal parameters (during 6MWT) were assessed at session 10.	
Shackleton et al. 2024 South Africa RCT PEDro = 6 Level 1 N = 16	**Population:** 16 participants with chronic and incomplete tetraplegia; reliant upon a wheelchair as the primary mode of mobility; and sufficient anthropometrics and ROM to achieve a normal, reciprocal gait pattern within the Ekso GT™. • Robotic locomotor training group (n = 8): Mean (SD) age: 40.5 (11.2) years 8M, 0F Injury level: C4-C7 AIS C (n = 4) and AIS D (n = 4) Mean (SD) time since injury: 13.8 (8.2) years. • ABT group (n = 8): Mean (SD) age: 38.4 (14.3) years 7M, 1F Injury level: C4-C7 AIS C (n = 5) and AIS D (n = 3) Mean (SD) time since injury: 7.3 (6.4) years. **Treatment:** The exercise intervention consisted of 24 weeks of supervised robotic locomotor training and ABT. Both interventions consisted of three sessions per week, 60-min each. Participants were randomized into one of the following groups: • Robotic locomotor training involved solely walking in an Ekso® GT Variable Assist Model exoskeleton. Intensity levels were determined by the attending therapist and ranged from standing and walking time of 10 to 50 min and between 50 and 1800 steps taken. • ABT consisted of a combination of resistance (20-30 min), cardiovascular (20-30 min), and flexibility training in various positions. Gait retraining, without a treadmill or robotic assistance, was also performed in the ABT group.	1. Participants had an average adherence of 93.9 ± 6.2% (67 out of 72 sessions) with no statistical difference between groups. 2. Strength capacity: a. There were no significant differences between groups for LEMS (p = 0.86; ES = 0.05). Only the robotic locomotor training group showed a significant increase in LEMS from pre (16.00 ± 11.00) to post intervention (19.00 ± 11.00) (p < 0.05). b. There were no significant group differences for back (p = 0.77; ES = 0.14) or abdominal muscle strength (p = 0.80; ES = 0.13). However, both groups had a significant change in abdominal strength from pre- to post intervention (p = 0.02), with a mean increase of 7.04 [0.00; 22.35] Nm and 9.84 [0.00; 22.01] Nm for the robotic locomotor training and ABT group, respectively. 3. Walking capacity: a. There were no significant between-group differences over time for distance walked during the SCI-FAI test (p = 0.47; ES = 0.53). Only the robotic locomotor training group had a significant improvement in distance walked over time (p = 0.02), with an increase of 0.97 [0.00; 6.88] m. b. Six (n = 4 ABT; n = 2 robotic locomotor training) of the 16 participants were non-ambulatory from baseline and continued to be so for the

	Outcome Measures: LEMS, isometric dynamometry of abdominal flexion and back extension, and SCI-FAI were measured at pre, 6 weeks, 12 weeks, and post (24 weeks).	length of the intervention. Two participants in the robotic locomotor training group who were non-ambulatory at baseline, both managed to achieve an improved distance of 2.44 m and 0.82 m by week 24. c. SCI-FAI device score and technique score remained unchanged for both interventions over time.
Tsai et al. 2024 USA RCT PEDro = 6 Level 1 N = 28	**Population:** 28 participants with acute SCI and with enough hand function to partially manage a walking aid. • Acute inpatient rehabilitation with incorporated EAW group (n = 16): 10M, 6F Mean (SD) age: 45.8 (18.3) years. Level of injury: Cervical (n = 7), thoracic (n = 5), and lumbar (n = 4). AIS A (n = 3), B (n = 4) and C (n = 9). Etiology: Traumatic (n = 13) and non-traumatic (n = 3). • Standard acute inpatient rehabilitation group (n = 12): 9M, 3F Mean (SD) age: 46.8 (18.3) years. Level of injury: Cervical (n = 5), thoracic (n = 4), and lumbar (n = 3). AIS A (n = 4), B (n = 2) and C (n = 6). Etiology: Traumatic (n = 9) and non-traumatic (n = 3). **Treatment:** Both groups received 15 hours of acute inpatient rehabilitation therapy per week, which included physical therapy and occupational therapy for bed mobility, seated and standing balance, strength, gait, transfers, and wheelchair mobility training to improve participants' independence in ADLs. Additionally, participants were randomly allocated into one of the following groups: • The acute inpatient rehabilitation with incorporated EAW group (n = 16) received EAW training for overground walking utilizing a powered exoskeleton (EksoGT) as	1. There was a significant main effect of time in the SCIM total score [F(1, 26) = 117.78, p < 0.01]. Participants had significantly higher SCIM total scores at discharge compared with the scores at admission. There was also a significant treatment group-by-time interaction effect in the SCIM total score [F(1, 26) = 5.59, p = 0.03]. The pattern of improvement in the SCIM total score between admission and discharge was significantly different between the acute inpatient rehabilitation with incorporated EAW and Standard acute inpatient rehabilitation groups, which was in favor of the acute inpatient rehabilitation with incorporated EAW group. Changes in the SCIM total scores between admission and discharge were approximately 13 points (95% CI [1.7, 24.1]) higher in the acute inpatient rehabilitation with incorporated EAW group compared with the Standard acute inpatient rehabilitation group. 2. There were significant effects of time in SCIM mobility score (F(1, 26) = 111.75, p < 0.01) and LEMS (F(1, 26) = 33.29, p < 0.01). Participants had significantly higher SCIM mobility scores and LEMS at discharge compared with the

	part of a minimum of their 15 hours per week of acute inpatient rehabilitation therapies, and aimed to provide two to three 1-hour sessions per week. • The Standard acute inpatient rehabilitation group (n = 12) received the same amount of acute inpatient rehabilitation therapies incorporating walking with the use of parallel bars, a treadmill with an overhead lift, and ceiling track, or a body-weight support device on wheels. Both groups also had the same discharge criteria. Participants would be discharged from acute inpatient rehabilitation when they had achieved the functional mobility and performance of ADLs goals set by the clinicians or when their progress in reaching those goals had reached a plateau. **Outcome Measures:** SCIM-III and LEMS were measured at admission and at discharge from acute inpatient rehabilitation.	scores at admission. There were significant treatment group by time interaction effects in the LEMS [F(1, 26) = 5.82, p = 0.02]. The patterns of improvement in LEMS from admission to discharge were significantly different between the acute inpatient rehabilitation with incorporated EAW and Standard acute inpatient rehabilitation groups, which were in favor of the acute inpatient rehabilitation with incorporated EAW group. Changes in LEMS between admission and discharge were approximately 9 points higher in the acute inpatient rehabilitation with incorporated EAW group compared to the Standard acute inpatient rehabilitation group.
Edwards et al. 2022 USA RCT PEDro = 5 Level 2 N = 25	**Population:** 25 patients with chronic motor incomplete SCI, with self-selected gait speed of <0.44 m/s, the ability to take at least one step, and be able to fit into the Ekso device; 18 males and 12 females; mean age 47.2 years; AIS C (n = 9) and AIS D (n = 21); level of injury C1-T10; and mean time since injury 6.8 years. *45 participants were enrolled, of which 33 were randomized to the main study and 12 enrolled as run-in participants. Of the 33 randomized participants, 25 completed the assessments and training related to the primary endpoint analysis. **Treatment:** Over 12 weeks, participants were randomly assigned to one of three study arms: • Ekso Robotic Intervention (n = 9): Participants performed a 45 min session (standing/up and walking) in the Ekso device, 3 times per week; and if possible, overground training without BWS.	1. There were 3 serious AEs (urinary tract infections unrelated to the device [n = 2]) and one participant in the active group admitted to a hospital with lower extremity numbness and a urinary tract infection). 2. From the total sample of 45 participants*, AEs that were deemed “possibly” or “probably” related to the device or training include the following: 12 (8 Ekso, 4 Active) upper and lower extremity musculoskeletal issues; 4 (3 Ekso, 1 Active) neurological issues; 6 (5 Ekso, 1 Active) skin issues; and 1 (Ekso) visceral issue. 3. Self-selected gait speed following the 12-week intervention increased in the Ekso group by 51% (mean, SD; 0.18 ± 0.23 m/s) Active Control by 32% (0.07 ± 0.11 m/s) and Passive Control 14% (0.03 ± 0.03 m/s), within

	• Active Control (n = 10): Each session comprising 45 min of BWSTT, and if possible, OGT without BWS. • Passive Control (n = 6): Participants continued with daily activities as normal. **Outcome Measures:** Gait speed (10MWT); endurance (6MWT); functional mobility (WISCI II); need of assistance and devices, and safety (AEs and serious AEs). All outcomes were assessed at baseline, at midpoint (6 weeks), at the end of the intervention (12 weeks), and at 12 weeks post-intervention.	group and between group comparisons (ns). 4. The proportion of participants with improvement in clinical ambulation category from home to community speed post-intervention was greatest in the Ekso group (>1/2 Ekso, 1/3 Active Control, 0 Passive Control, p < 0.05). 5. The median distance covered in the 6MWT following the 12-week intervention was 538.0 feet (Quartile 268.0–687.3) for the Ekso Group, 346.6 feet (Quartile 219.5–711.5) for the Active Control, and 320.0 feet (Quartile 148.8–466.6) for the Passive Control representing improvements of 34%, 28%, and 18%, respectively (ns). 6. Most participants in both the Ekso group and the Active Control group showed no change in type of assistive device used outside the clinic throughout the duration of the protocol; with no changes observed in the Passive Control group.
Tarnacka et al. 2023 Poland RCT PEDro = 5 Level 2 N = 105	**Population:** 105 participants with SCI • Control group (n = 33): 28 males, 5 females Median age: 36.5 years AIS A (n = 14), AIS B (n = 4), AIS C (n = 11), AIS D (n = 4) Level of injury: Cervical (n = 7), thoracic (n = 17), and lumbar (n = 9) Median time since injury: 13 months • Experimental group (n = 72): 58 males, 14 females Median age: 36.5 years AIS A (n = 27), AIS B (n = 7), AIS C (n = 13), AIS D (n = 25) Level of injury: Cervical (n = 17), thoracic (n = 32), and lumbar (n = 23) Median time since injury: 13 months **Treatment:** The therapeutic program consisted of two phases: first, 3 weeks, then, after a 1-week break, 3 weeks in the second phase. The program was conducted six days per week.	1. There were no significant differences between groups for SCIM-III scores. 2. Patients with incomplete SCI assigned to the experimental group achieved significant improvements in motor score [2.58 (SE 1.21, p < 0.05)] and WISCI II [3.07 (SE 1.02, p < 0.01])] scores in comparison with patients assigned to the control group. 3. Both the Lokomat group and the Dynamic parapodium group improved on their SCIM-III and AIS motor scores significantly, though the Lokomat group's score difference was slightly greater in X and Y. 4.

	Participants were allocated into two groups: • The control group received conventional physiotherapy and 30 min dynamic parapodium training. • The experimental group received 30 min sessions of RAGT with exoskeleton EKSO-GT or Lokomat Pro with the general exercise program and ground gait training. *The dynamic parapodium is a piece of individualized uprighting equipment (a combination of thoracolumbosacral orthosis and HKAFO device of the dynamic type) that allows the patient to stand and walk by swinging the trunk. All participants from the Lokomat group with incomplete SCI started with 60% BWS and an initial treadmill speed of 1.5 km/h; patients with complete SCI started with 100-90% BWS. Patients with a thoracic level of injury were mostly enrolled in the EKSO-GT group, and with a cervical level, in the Lokomat group. **Outcome Measures:** The AIS Motor Score, SCIM-III, WISCI II, and Barthel Index were conducted before the start of the therapy and after 7 weeks of therapy.	
Hong et al. 2020 USA RCT PEDro = 5 Level 2 N = 50	**Population:** 50 participants with chronic (> 6 months) SCI who were non-ambulatory; 38 males and 12 females; mean (± SD) age 38.7 (± 14.2) years; AIS A/B (n = 31) and AIS C/D (19); and mean (± SD) time since injury 4.69 (± 5.18) years. **Treatment:** Eligible participants were randomized within site to one of two groups for 12 weeks (3 months): • Group 1 received EAW first for 12 weeks then crossover to usual activity for a second 12 weeks. • Group 2 received usual activity first for 12 weeks then crossover to EAW for 12 weeks of training. Participants were divided by four neurological deficit sub-groups: motor complete tetraplegia (n = 4); motor incomplete tetraplegia (n = 10); motor	1. There were four “possibly study-related” severe AEs and there were 49 total study-related AEs which included 39 skin abrasions/bruising, eight musculoskeletal/edema, and two falls. All study-related skin abrasions and musculoskeletal AEs were resolved, and participants continued in study. There were two falls during EAW, but no injuries occurred. 2. There were no order effects for Group 1 (immediate) vs. Group 2 (delayed therapy) for total steps. The number of steps taken per session increased overall sessions for both devices, but participants who used the Ekso took more total overall steps than those who used the ReWalk.

	complete paraplegia (n = 27); and motor incomplete paraplegia (n = 9). • The EAW arm consisted of EAW training, three sessions per week (4–6 h/week) for 36 sessions. Two powered exoskeleton devices were used depending individual characteristics of each participant, namely the ReWalk™ and the Ekso™. Most participants with injury level of T3 or lower used the ReWalk (n = 28) and participants with injury level higher than T3 used the Ekso (n = 22). • The usual activity arm consisted of the identification of usual activities for each participant and encouragement to continue with these activities throughout the 12-week usual activity arm. **Outcome Measures:** 10MWT and 6MWT were performed at 12, 24, and 36 sessions.	3. Participants who used the Rewalk had significantly better performance during the 10MWT and 6MWT than participants using the Ekso at session 36 ($p < 0.0001$). 4. There were significant improvements in the performance of the 10MWT and 6MWT from session 12 to session 36 ($p < 0.0001$); but there were no significant differences between sub-groups in terms of improvements from 12 to 36 sessions on the 10MWT ($p = 0.067$), and 6MWT ($p = 0.339$).
Guanziroli et al. 2019 Italy Prospective controlled trial Level 2 N = 15	**Population:** 15 participants with chronic (< 6 months post-injury) and motor-complete SCI, and with a regular use of a reciprocal gait orthoses or therapeutic standing frame; 11 males and 4 females; mean (± SD) age 39.33 (± 10.31) years; injury level T4 to L1; AIS A-B; and mean (± SD) time since injury 5.47 (± 4.68) years. **Treatment:** Participants performed 60-min sessions 3 times a week for at least 8 weeks with a wearable lower limb powered exoskeleton (ReWalk). The training included sit-stand transfers, stand-sit transfers, stepping skills; and once acquired these underlying skills, the main focus of the training was to improve walking performance with step triggering, coordinating step timing and foot clearance, integrating safe and effective stopping and a full self-control using the wrist pad controller. Participants were divided into two groups: • Group 1 (n = 5): Participants used the first generation of ReWalk software control. • Group 2 (n = 10): Participants used the second generation software control	1. Patients required an average of 21.77 ± 4.68 training sessions to achieve independent walking with ReWalk. 2. Group 2 covered more distance in 6 min (+124.52%) ($p < 0.01$) and required less time (-70.34%) ($p = 0.03$) to perform 10MWT and to STS-time (-38.25%) ($p = 0.08$) if compared to group 1. 3. Group 1 showed a correlation between weight, height, neurological lesion level and the level of performance reached by the participants; instead, group 2, showed correlation only between neurological lesion level and performance. 4. Patients of group 2 with lower lesion level, covered longer distance if compared to those with higher lesion, while patients of group 1 with lower distance covered, were characterized by higher weight and height characteristics.

	of the same exoskeleton (which that allowed a better movement pattern based on healthy kinematics and kinetics profiles) with no change in hardware. **Outcome Measures:** 6MWT, 10MWT, and sit to stand time (which measures the time needed to pass from sitting to standing and start to walk) were assessed at the end of the training period while wearing the exoskeleton.	
Tamburella et al. 2020b Italy Prospective controlled trial Level 2 N = 8	**Population:** 8 participants with incomplete SCI and the ability to walk overground (with aids if necessary); 6 males and 2 females; mean age 53.5 years; injury level C6 (n = 1), C7 (n = 2), T5 (n = 1), T10 (n = 2), and T11 (n = 1); AIS D (n = 8); and mean (± SD) time since injury 18.3 (± 13.5) months for experimental group and 21.6 (± 11.1) months for control group. **Treatment:** All participants performed 10 sessions of 40-min gait training 3 times per week with the main goal of improving comfortable gait speed. Each training session was composed by few min of preparation (performing ankle or knee movements), followed by a specific walking training. Participants were divided into two groups: • Experimental group (n = 4, prospective enrollment): Participants used the NeuroMuscular Controller-controlled Achilles ankle exoskeleton (developed to assists plantar/dorsiflexion during walking). • Control group (n = 4, case-control matched): Participants didn't use the Achilles exoskeleton. **Outcome Measures:** Motion outcome measures (spatiotemporal parameters [speed, step length and width, gait cycle time and stance phase percentage] and ground reaction forces) were assessed by using four force plates; clinical outcome measures (6MWT*, 6-min gait speed, fatigue, muscle force [assessed by MMT of hip, knee and ankle joints] were assessed at baseline and at the end of the training in free walking conditions.	1. After the intervention, no statistical differences were found for any analyzed variables between groups. 2. Comparing after training vs. baseline data: a. Significant improvements in spatiotemporal parameters (gait speed, gait cycle time, and step length) were found only for the experimental group. b. Very minor changes in ground reaction forces and MMT were found for both groups. c. At baseline, experimental participants were unable to complete the 6MWT without the support of the Achilles and was easily completed with the Achilles at the end of training; meanwhile only two participants in the control group showed improvements in 6MWT. d. For MMT and BBS, there was no statistically significant modifications in both groups.

	*6MWT was assessed with and without Achilles for the experimental group, and only in free walking condition for control group.	
Tsai et al. 2020 USA Case control Level 3 N = 30	**Population:** 30 patients with acute or subacute SCI (< 6 months post injury) and eligible for LT; 24 males and 6 females; mean age 49.4 years; AIS A (n = 3), AIS B (n = 3), AIS C (n = 13), and AIS D (n = 11); incomplete tetraplegia (n = 12), complete paraplegia (n = 3), and incomplete paraplegia (n = 15); level of injury cervical (n = 12), thoracic (n = 14), and lumbar (n = 4); and mean time since injury 19.3 days. **Treatment:** All participants received a minimum of 15 hours of standard of care acute inpatient rehabilitation therapy per week. Two groups were compared: • Intervention group (n = 10) (prospective): Participants received EAW training for overground walking using a powered exoskeleton (EksoGT). • Control group (n = 20) (retrospective): Participants were matched controls and did not receive any EAW training. *The participants in the intervention group had significantly longer days of inpatient stay than the control group [39.9 ± 11.4 d vs. 30.9. ± 12.9 d, P < .05]). **Outcome Measures:** LEMS was assessed at baseline and at discharge. For the intervention group only, the number of EAW sessions performed, AEs, total steps, and total up and walk times in each EAW session were recorded as well.	1. A minor skin abrasion was the only AE recorded. 2. Changes from admission to discharge LEMS (14.3±10.1) were significantly greater in the intervention group compared with the control group (4.6±6.1) (P<.01). After adjusting for the days of inpatient stay, a significant difference was found between the groups, with the intervention group having a better change score when compared with the control group (P = .02). 3. There was an average of 4.2 ± 1.8 sessions of EAW training for each participant. 4. Participants using the exoskeleton could stand up and walk for about 30 min with 450 steps during each session. 5. There is a positive correlation trend between the number of EAW sessions and maximum walking time in the device (ρ = 0.56, large effect size, P = .09).
Arnold et al. 2024 USA Case series Level 4 N = 18	**Population:** 18 participants with SCI; who had completed a minimum of one overground exoskeleton gait training session during both inpatient and outpatient therapy Mean (SD) age: 37.4 (15) years 15M, 3F Paraplegia (n = 9) and tetraplegia (n = 9) ASIA A (n = 5), B (n = 4), C (n = 7), and D (n = 2)	1. The average number of overground exoskeleton gait training sessions across inpatient and outpatient settings was approximately 19 for both motor complete and motor incomplete SCI groups spanning over an average of 17 to 18 weeks. 2. Patients demonstrated improved overground exoskeleton gait

	Treatment: A typical overground exoskeleton gait training session in both inpatient rehabilitation and outpatient therapy settings was 45 minutes during which the participant completed standing and walking tasks in the exoskeleton device (Ekso GT). **Outcome Measures:** WISCI II was collected during both inpatient and outpatient admissions.	training session tolerance on device metrics including "walk" time (motor complete, 7:51 ± 4:42 to 24:50 ± 9:35 minutes; motor incomplete, 12:16 ± 6:01 to 20:01 ± 08:05 minutes), "up" time (motor complete, 16:03 ± 7:41 to 29:49 ± 12:44 minutes; motor incomplete, 16:38 ± 4:51 to 23:06 ± 08:50 minutes), and step count (motor complete, 340 ± 295.9 to 840.2 ± 379.4; motor incomplete, 372.3 ± 225.2 to 713.2 ± 272). 3. Across therapy settings, patients with motor complete SCI experienced improvement in WISCI II scores from 0 ± 0 at inpatient admission to 3 ± 4.6 by outpatient discharge, whereas the motor incomplete group demonstrated a change of 0.2 ± 0.4 to 9.0 ± 6.4.
Kerdraon et al. 2021 France & USA Pre – post Level 4 N = 11	**Population:** 12 participants with chronic complete (AIS A) SCI and able to wear the Atalante exoskeleton; 10 males and 2 females; mean age (± SD) 22.9 (± 9.3); injury level T5 (n = 2), T6 (n = 4), T8 (n = 1), T10 (n = 2), T11 (n = 1), and T12 (n = 2); and mean (± SD) time since injury 88 (± 63.2) months. **Treatment:** Participants received 12 one-hour training sessions for 3 weeks. Patients walked on floor and wore a harness connected to a mobile suspension system (without weight bearing) to prevent from falling, while using the Atalante exoskeleton. **Outcome Measures:** The ability to walk 10 m, without human or material assistance; 10MWT; the ability to sit down without human assistance, with intrinsic perturbations such as arm and upper body movements; the ability to turn 180° in less than 3min (U-turn); and the ergonomics of Atalante exoskeleton were assessed at the 6th and at the 12th session.	1. The only treatment-related AEs were skin redness (n = 5) and ischial skin abrasion (n = 1) with a complete resolution. 2. Walking parameters: Seven out of 11 patients passed the 10MWT unassisted at the 12th session (average speed was 0.13 m/s ± 0.01), representing 63.6% of success. The remaining four patients required human assistance. No relationship was observed with age, gender, height, weight or level of injury. 3. Postural parameters: All patients succeeded in standing up, sitting down and standing up for two min at the 6th and 12th session. At the 6th session, all the patients passed the U-turn test with some assistance, whereas during the 12th session two patients performed the U-turn without any help.
Kim et al. 2021	**Population:** 10 non-ambulatory patients with SCI with sufficient postural stability	1. There were not severe AEs, but there were several minor events

Korea Pre – post Level 4 N = 10	to sit independently, ability to transfer from wheelchair to bed independently, and sufficient bilateral upper extremity strength to manage crutches, among others; 7 males and 3 females; mean age 48.1 years; AIS A (n = 7), AIS B (n = 1), and AIS C (n = 2); level of injury C6 (n = 1), T1 (n = 1), T4 (n = 1), T8 (n =1), T10 (n = 4), T11 (n = 1), and L1 (n = 1); and mean time since injury 5.7 years. **Treatment:** The program was performed 3 times per week, over 10 weeks. Each training session consisted of standing up from sitting on a chair, walking across a flat floor, and sitting down on a chair with the exoskeleton H-MEX for 60 min. **Outcome Measures:** 6MWT and Korean version of FES-I (KFES-I) were assessed at pre-training and post-training. *6MWT were also assessed at mid-training (15 sessions).	(two skin abrasions and one near fall). 2. 6MWT: a. Statistically significant improvement between the pre- and mid- training assessment, and between the mid-training and post-training assessment (P < 0.014) were reported. b. After training, the mean distance achieved (49.13 ± 15.22 m) was significantly enhanced compared with baseline (20.65 ± 5.55; P = 0.005). 3. The mean score in the KFES-I questionnaire was reduced post-training (36.00 ± 9.09) compared to pre-training (37.80 ± 8.40), but this result was not statistically significant (P = 0.475).
Park et al. 2021 Korea Pre – post Level 4 N = 10	**Population:** 10 nonambulatory participants with SCI; 7 males and 3 females; mean (± SD) age 48 (± 8.7) years; AIS A (n = 7), AIS B (n = 1), and AIS C (n = 2); injury level C6 (n = 1), T1 (n = 1), T4 (n = 1), T8 (n = 1), T10 (n = 4), T11 (n = 1), and L1 (n = 1); and mean (± SD) time since injury 5.7 (± 4.8) years. **Treatment:** The training program was the same as described above in Kim et al. (2021). **Outcome Measures:** 6MWT was assessed at pre-training (baseline), at mid-training (15 sessions), and post-training (after 30 sessions).	1. In the 6MWT, the participants walked a significantly further distance at mid-training (37.5 ± 10.5 m) than at pre-training (20.7 ± 5.5 m) (p = 0.005) and covered more distance at post-training (49.1 ± 15.2 m) than at pre- and mid-training (p = 0.05 and p = 0.014, respectively).
Xiang et al. 2020 China Pre – post Level 4 N = 28	**Population:** 28 participants with SCI; 20 males and 8 females, mean (± SD) age 41.3 (± 11.8) year; AIS A (n = 22) and AIS B (n = 6); level of injury beyond T11 (n = 17) and at T11 or lower (n = 11); and median (± IQR) duration of injury 4.0 (± 10.4) years. **Treatment:** Along with the usual basic rehabilitation therapies, participants performed a gait training protocol (sitting, standing, transitioning between the two, and walking) for 30 min/session,	1. There were several AEs, (i.e., urinary tract infection [n = 2]; upper respiratory tract infection [n = 2]; conjunctivitis [n = 1]; femoral [n = 1] and foot [n = 1] fracture; skin integrity event [n = 1]; and diabetes [n = 1]). 2. Walking parameters: a. 6MWT was improved in week 2 (16.2 ± 5.3 m) compared with baseline (0 m).

	one session/day, 5 days/week for 2 weeks using the new powered lower limb robotic exoskeleton (AIDER). **Outcome Measures:** Safety indicators, 6MWT, 10MWT, Hoffer walking ability grade, LEMS, and WISCI II were assessed. Walking parameters were assessed at baseline (with the usual orthosis if they had one), at the mid-term of the training with the robotic exoskeleton and crutches (week 1), and at the end of the training with those (week 2).	b. 10MWT at week 1 and week 2 were 0.039 ± 0.016 m/s and 0.045 ± 0.016 m/s in the exoskeleton, respectively with a mean. c. Participants with higher injuries (T6–T11) demonstrated greater improvements in gait speed and walking distance than those with lower injuries. The same pattern was shown in participants with AIS-A compared to those with AIS-B injuries. d. Participants showed an improvement in WISCI II and in the Hoffer walking ability grades. 3. There was no change in the LEMS after the program.
Swank et al. 2020 USA Case-control Level 3 N = 59 patients with SCI	**Population:** 155 patients who had completed inpatient rehabilitation due to stroke (n = 96) or SCI (n = 59). The patients with SCI were 19 males and 12 females, had an average age of 48.2 years; 66.1% were tetraplegic; and 64.4% had cervical level injuries. **Treatment:** Patients were retrospectively (based on medical records) divided into two groups: • Overground robotic exoskeleton gait training group (n = 31 SCI and 44 stroke): Patient who completed a minimum of one overground robotic exoskeleton gait training session. • Usual care group (n = 28 SCI and 52 stroke): Matched controls who participated in a minimum of one session of usual care gait training interventions. **Outcome Measures:** FIM motor and WISCI II (for patients with SCI) were assessed at baseline and at discharge. *Only patients with SCI will be assessed here. ** To describe outcomes between patients receiving overground robotic exoskeleton gait training plus usual care and patients receiving usual care only, patients who completed a minimum of 5 overground robotic exoskeleton gait	1. Dosage: a. The average overground robotic exoskeleton gait training session count was 6.3 ± 3.8 (range = 1–17). b. Within the standard 45-min therapy session, the average overall overground robotic exoskeleton gait training session time increased from about 15 min (session 1) to 30 min (sessions 13, 14, and 17) and the time spent 'walking' nearly matched the total 'up' time. c. Patients in the overground robotic exoskeleton gait training group averaged 9.5 more min per day than the usual care group (16.3 ± 8.1 vs. 6.8 ± 6.5 min, P < 0.0001). 2. Functional outcomes: a. Overground robotic exoskeleton gait training 5+ and usual care groups both showed improvements in WISCI II and FIM motor at baseline compared with at discharge; but without significative differences between groups.

	training sessions were included (SCI, n = 18, 58%).	
Khan et al. 2019 Canada Pre-post Level 4 N = 12	**Population:** 12 participants with chronic, non-progressive SCI, using the wheelchair as the primary mode of mobility and able to use forearm crutches; mean (± SD) age 37.5 (± 13.7) years; level of injury C6 (n = 2), C7 (n = 1), T3 (n = 2), T4 (n = 2), T6 (n = 1), T7 (n = 2), T9 (n = 1), T10 (n = 1); AIS A (n = 6), AIS B (n = 2), AIS C (n = 3) and AIS D (n = 1); and mean (± SD) time since injury 7.7 (± 8.1) years. *Uninjured (i.e., control) participants were also recruited for comparison of some physiological measures. **Treatment:** Participants used the ReWalk 2.0 (exoskeleton) for training different activities (such as donning and doffing, sit-to-stand, stand-to-sit, balancing in standing and walking) 4 days per week during 12 weeks of training. **Outcome Measures:** Walking (10MWT during continuous walking in the ReWalk, 6MWT); manual muscle strength (LEMS); was measured on a force platform) were taken before, during, immediately after, and at follow-up (2–3 months after training).	1. AEs and technical issues included two falls (without no injuries sustained by the participants because the trainer could control the fall); skin abrasions which some time away necessary to improve the healing; and some minor injuries in the trainer when he was trying to control the participant's falls. 2. Three participants were able to perform 10MWT, 6MWT without the ReWalk, using their preferred walking aid. All three walked further (but p > 0.05) in the 6MWT and at a lower effort (less physiological cost index) with the ReWalk compared to without the ReWalk. 3. All participants required some assistance with donning and doffing the device; however, many walking tasks were possible for most of the participants without assistance. 4. Two out of three participants with motor incomplete injuries showed improvements in LEMS.
McIntosh et al. 2019 Canada Pre – post Level 4 N = 11	**Population:** 11 participants with SCI and with the ability to use the Ekso GT exoskeleton; 8 males and 3 females; mean age 41 years; AIS A (n = 5), AIS C n = 5), and AIS D (n = 1); level of injury C6 (n = 2), T5 (n = 1), T6 (n = 1), T7 (n = 3), T10 (n = 1),T12 (n = 1), L1 (n = 1), and L2 (n = 1); and mean time since injury 9.5 weeks. *Six participants completed all 25 training sessions. **Treatment:** The training regime consisted of 25 one-hour walking sessions with the Ekso GT exoskeleton, 3 times per week. Participants progressed through the various walk modes of the device with progressions individually determined.	1. There were 3 AEs (skin integrity issues [n = 2] and a fall without resulting in injury [n = 1]). Mean visual analogue scale pain scores were low and consistent with mild pain (0-30 mm). 2. As participants progressed through the training sessions, up time in the exoskeleton, the proportion of time spent walking, and the number of steps taken increased. 3. On the 6MWT, participants consistently covered more distance (117.1 ± 11.7 m) in session 25 compared to session 2 (47.6 ± 6.6 m).

	Outcome Measures: Up time, walk time, number of steps, and AEs (falls, pain and skin integrity) were collected each session; and 6MWT and 10MWT were collected at sessions 2, 13 and 25.	4. On the 10MWT, all participants showed consistently improved gait speed, traveling on average 3.2 times faster during their last training session (0.40 ± 0.04 m/s) in comparison to session 2 (0.12 ± 0.01 m/s). 5. Participants with AIS C demonstrated greater improvements in gait speed than those with AIS A (0.44 ± 0.05 m/s vs. 0.33 ± 0.09 m/s, respectively) as well as improved distance covered on the 6MWT (128.1 ± 17.3 m vs. 102.7 ± 13.1 m, respectively).
Tefertiller et al. 2018 USA Pre-post Level 4 N = 32	**Population:** 32 non-ambulatory participants with SCI; 27 males and 5 females; mean age 37 years; injury level T4-L2; and AIS A (n = 21), AIS B (n = 5), and AIS C (n = 6). Time since injury not stated. **Treatment:** The participants completed 24 training sessions at a frequency of 3 times per week for 8 weeks. Throughout the trial, participants were asked to perform various gait-related tasks while wearing the Indego exoskeleton. **Outcome Measures:** 10MWT (indoor and outdoor assessments); 6MWT; and 600-meter walk test were assessed. The 10MWT and 6MWT were completed midway (session 11, 12, or 13) and during the final walking sessions (session 24 or 25) utilizing the device and an appropriate assistive device. The 600-meter walk test was completed once during the trial on indoor surfaces between the midway and final assessments.	1. A combined total of 66 AEs were reported: a. Eleven of these AEs were directly device related and were reported on six participants. The majority (9/11) of the device-related AEs were skin redness, small abrasions, mild joint edema, or mild bruising on the lower legs and hips that were resolved with improved padding and pressure relief. b. Sixty-four of 66 AEs were minor and were not device-related. c. Two events were categorized as moderate (right greater trochanteric blister due to pressure and friction while walking in the device, and ankle sprain while walking in the device), without interruption in training for either participant. 2. 10MWT: Final indoor and outdoor walking speeds among all participants significantly ($p < 0.05$) improved to 0.37 m/s (± 0.08 and ± 0.09, respectively). 3. 6MWT: For all participants, average distance completed during the initial 6MWT was 92.0 m and an average distance of 107.5 m (± 28.3) was completed during the final evaluation period.

		4. The average time it took all participants to walk 600 m was 35 min 24 s (± 13.44 s).
Baunsgaard et al. (2018a; 2018b) Denmark, Germany, the Netherlands, Norway, Spain, Sweden and Switzerland. Pre-post Level 4 N = 52	**Population:** 52 participants with SCI; 36 males and 16 females; mean age 47.0 years; injury level C5–L2; AIS A-B-C (n = 33) and AIS D (n = 19); and time since injury were subgrouped (recently injured [TSI ≤ 1 year], n = 25; chronically injured [TSI > 1 year], n = 27). **Treatment:** The training protocol consisted of gait training three times per week for eight weeks, as an "add on" to existing training. Two exoskeletons were used, the Ekso (n = 8) and the Ekso GT (n = 44). **Outcome Measures:** Total up time (time standing plus time walking), walk time (time in walk motion) and number of steps, recorded by the device during the training session, alongside the walk-mode and the assistive device used. LEMS and SCIM-III mobility subscore were assessed at baseline, at end of the training period (TS24) and at a follow-up session 4 weeks after the last training session. Participants who had or acquired gait function during the training period performed 10MWT, and WISCI II at baseline, midway (TS12), at end (TS24) and at follow-up.	1. All training characteristics (up time, walk time and steps) increased significantly from TS1 to TS24 ($P < 0.001$), including all sub-groups: recently and chronically injured, paraplegia and tetraplegia, and incomplete and complete injury ($P < 0.001$). 2. In the recently injured group, five participants (20%) had gait function at baseline which increased to 14 (56%) at TS24, ($P = 0.004$) and to 15 participants (60%) at follow-up ($P = 1.00$). In the chronically injured group, 11 participants (41%) had gait function at baseline which increased to 12 (44%) at TS24 and at follow-up. 3. The recently injured participants significantly improved 10MWT, LEMS, and mobility subscore of SCIM-III but not WISCI II from baseline to TS24. The chronically injured participants did not significantly improve 10MWT, WISCI II, mobility subscore of SCIM-III or LEMS from baseline to TS24. These changes were retained at follow-up in both groups.
Gagnon et al. 2018 Canada Pre-post Level 4 N = 13	**Population:** 14 participants with a motor complete SCI who use a wheelchair as their primary mode of mobility; 9 males and 5 females; mean (± SD) age 38.7 (± 10.9) years; injury level C6 (n = 1), T3 (n = 1), T4 (n = 2), T6 (n = 6), T8 (n = 1), T9 (n = 1), and T10 (n = 2); AIS A (n = 13) and AIS B (n = 1); and mean (± SD) time since injury 7.4 (± 7.8) years. **Treatment:** Participants began a six-week progressive LT program that encompassed a total of 18 training sessions (three sessions/week; 60 min/session) with the EKSO GT robotic exoskeleton. Depending on the level of	1. Five participants reported training-related pain or stiffness in the upper extremities during the program, six participants experienced orthostatic hypotension with systolic blood pressure drops of ≥ 20 mmHg during a training session, and one participant sustained bilateral calcaneal fractures and stopped the program. 2. On average, during the LT program, the standing time, the walking time, and the number of steps taken per session were 49.7 ±

	each participant's proficiency, on the participant's tolerance, and on the activities planned for the session (e.g., instructions and basic training to initiate sit-stand transfers, walking and turning with forearm crutches), the workload was periodically adjusted using walking distance, duration, and speed parameter progressions. **Outcome Measures:** After each session, all training parameters and other relevant information (e.g., total standing time, total walking time, and total number of steps) were recorded. Also, the performance when walking with the exoskeleton at self-selected comfortable walking speed measured using the 10MWT was assessed at the start (within the first 5 sessions) and at the end of the program.	12.7 min, 33.4 ± 12.5 min, and 1190 ± 561 steps, respectively; and were progressed by 45.3%, 102.1%, and 248.7%, respectively, between the start and the end of the program. 3. Walking speed increased significantly ($p \leq 0.0001$; + 66.8%) between the start (0.15 ± 0.02 m/s) and end (0.25 ± 0.05 m/s) of the training program.
Hartigan et al. 2015 USA Pre-Post Level 4 N = 16	**Population**: 16 participants - 13 males and 3 females; SCI ranging from C5 complete to L1 incomplete; age range= 18-51 years. **Treatment**: To assess how quickly each participant could achieve proficiency in walking, each participant was trained in the system (Indego exoskeleton) for 5 sessions, each session lasting approximately 1.5 hours. Following these 5 sessions, each participant performed a 10MWT and a 6MWT. **Outcome Measures:** 10MWT, 6MWT, donning and doffing times, ability to walk on various surfaces.	1. At the end of 5 sessions (1.5 hours per session), average walking speed was 0.22 m/s for persons with C5-6 motor complete tetraplegia, 0.26 m/s for T1-8 motor complete paraplegia, and 0.45 m/s for T9-L1 paraplegia. 2. Distances covered in 6 min averaged 64 m for those with C5-6, 74 m for T1-8, and 121 m for T9-L1. 3. Additionally, all participants were able to walk on both indoor and outdoor surfaces.
Yang et al. 2015 USA Post Test Level 4 N = 12	**Population**: 12 participants - 10 males and 2 females; 9 AIS A, 2 AIS B and 1 AIS C; Level of injury between C8 to T11; age range= 31 to 75. **Treatment**: Twelve participants with SCI ≥1.5 years who were wheelchair users participated. They wore a powered exoskeleton (ReWalk) with crutches to complete 10-meter (10MWT) and 6MWT walk tests. Level of assistance was defined as modified independence, supervision, minimal assistance, and moderate assistance. Best effort EAW	1. 7 of 12 participants ambulated ≥0.40 m/s. 5 participants walked with modified independence, 3 with supervision, 3 with minimal assistance, and 1 with moderate assistance. Significant inverse relationships were noted between level of assistance and EAW velocity for both 6MWT and 10MWT. 2. There were 13 episodes of mild skin abrasions. Modified independence and supervision groups ambulated

	velocity, level of assistance, and observational gait analysis were recorded. **Outcome Measures:** 10MWT, 6MWT, level of assistance, degree of hip flexion, degree of knee flexion, step time.	with 2-point alternating crutch pattern, whereas the minimal assistance and moderate assistance groups favored 3-point crutch gait.
Esquenazi et al. 2012 USA Pre-post Level 4 N = 12	**Population:** 12 participants with chronic SCI (8M 4F); 18-55 yrs old; all motor-complete cervical and thoracic; >6 months post-injury. **Treatment:** All participants had gait training using the ReWalk powered exoskeleton; participants were trained for up to 24 sessions of 60-90 min duration over approximately 8 weeks. **Outcome Measures:** 6MWT; 10MWT; gait laboratory evaluation; dynamic electromyogram; survey containing questions about comfort and confidence using the ReWalk; assessment of spasticity and pain; physical examination; Short Form-36 v2 Health Survey Questionnaire.	1. By completion of the trial, all participants had walked under their own control without human assistance while using the ReWalk for at least 50-100m continuously and for a period of at least 5-10 min. 2. Excluding 2 participants with considerably reduced walking abilities, average distances and average walking speed significantly improved. Average walking speed was 0.25m/s (0.03-0.45m/s). (No significance testing done). 3. Three participants reported their overall spasticity improved after training. 4. All participants had strong positive comments regarding the emotional/psychosocial benefits of the use of ReWalk. 5. At the 12-month follow-up, general health status as measured by study clinicians did not change.

Discussion

The majority of the systematic reviews and meta-analyses testing WPE in people with SCI have shown improvements in walking speed, walking distance, and/or lower limb strength (Duddy et al. 2021; Moriarty et al. 2024; Shackleton et al. 2019; Tamburella et al. 2022; Zhang et al. 2022; Rodriguez-Tapia et al. 2022).

EXO vs. Physical Therapy (Usual Care)

Studies that we found comparing exoskeleton to conventional physical therapy or 'usual care' showed that both types of training improved walking outcomes in people with SCI. However, only a few higher-quality studies performed between-group analyses that show if one method is better than the other at helping people with SCI to regain walking ability.

Shackleton et al. (2024) compared the effects of robotic locomotor training to activity-based therapy (ABT) in people with SCI; they found that after 24 weeks, participants in both groups improved their functional walking (SCI-FAI) and lower extremity strength (LEMS), however,

neither group significantly outperformed the other (Shackleton et al. 2024). Xiang et al. (2021) compared exoskeleton walking training versus strength training and aerobic exercise at similar intensities. After 4 weeks of training, patients in both groups improved similarly on walking distance (6MWT), but neither group showed improvements in LEMS (Xiang et al. 2021). However, Tsai et al. (2020) found that people who used a powered exoskeleton (EksoGT) had statistically significant improvements compared to patients who did not receive any walking training with exoskeleton during the acute inpatient rehabilitation.

EXO vs. OGT/BWSTT

Gil-Agudo et al. (2023) compared the effects of robotic locomotor training versus traditional gait training on walking to determine which method is superior at developing walking ability and lower limb strength in people with SCI. After 5 weeks, the exoskeleton group developed significantly more functional walking ability (e.g., higher WISCI-II scores) than the traditional gait training group. Both groups walked significantly further at the end of training (6MWT – Exo: +68 meters; OGT: +48 meters), but neither walked significantly further than each other. Both groups improved slightly LEMS and in walking speed (-.2m/s and -.1m/s) (Gil-Agudo et al. 2023).

Edwards et al. (2022) compared Ekso robot gait training to an active control group, who engaged in BWSTT, and a passive control group, who received no additional activities (i.e., usual PT). After 12 weeks, the proportion of participants with improvement in clinical ambulation category from home to community speed was greatest in the Ekso group (>1/2 Ekso, 1/3 Active Control, 0 Passive Control, $p < 0.05$). Self-selected gait speed following the 12-week intervention increased in the Ekso group by 51% (mean, SD; 0.18 ± 0.23 m/s) Active Control by 32% (0.07 ± 0.11 m/s) and Passive Control 14% (0.03 ± 0.03 m/s; all differences ns). The median distance covered in the 6MWT following the 12-week intervention was 538.0 feet for the Ekso Group, 346.6 feet for the Active Control, and 320.0 feet for the Passive Control (ns) (Edwards et al. 2022).

We found one network meta-analysis of RCTs and non-RCTs comparing BWSTT (i.e., Lokomat) to EAW on walking outcomes (Zhang et al. 2022). They found that of the studies aiming to develop walking speed (i.e., 10MWT) it was mostly likely for EAW to rank first (89%) and for Lokomat to rank second (47%), whereas in studies measuring functional walking (i.e., WISCI-II scores) it was mostly like for Lokomat to rank first (73%) and EAW to rank second (63%) (Zhang et al. 2022).

Which Type of Exoskeleton is Best?

There are few if any studies comparing one exoskeleton to another, likely due to the high cost of this type of walking technology. Currently, exoskeletons can be subdivided into assistive devices used in the community, such as the Indego Personal and Rewalk exoskeletons, or devices designed for rehabilitation with a therapeutic intent, such as the EksoNR and Indego Therapy exoskeletons (Yip et al. 2022). For patients with tetraplegia, the US FDA has approved three devices: Ekso® (allowed only for C7–T3 AIS D patients), Indego® (C7 or below) and Hal® (C4–L5 AIS C or D) (Rodriguez-Tapia et al. 2022). These three exoskeletons can be used after SCI if upper limb strength is enough to allow the use of assistive devices, such as crutches or

walkers (Rodriguez-Tapia et al. 2022). Other self-balancing WPE, like Atalante® or Rex®, allow ambulation without upper limb help or the use of an assistive device (Postol et al. 2021; Rodriguez-Tapia et al. 2022).

Who for? How Much? How long?

van Dijsseldonk et al. (2021) studied the validity of some parameters as predictors of performance related to the use of the ReWalk device in people with chronic SCI. Factors such as an active lifestyle, younger age at the time of the injury, a lower lesion level, and a low body mass index were found to be factors significantly correlated to the achievement of required motor tasks during training (i.e., maintenance of upright position and walking) (van Dijsseldonk et al. 2021). However, according to the meta-regression analysis by Zhang et al. (2022), it was shown that age, time after injury, and the AIS score had no impact on the outcomes of patients undergoing wearable EAW and Lokomat training.

Regarding training dosage, Shackleton et al. (2019) showed that the most common intervention length was 8 weeks and typically, training was conducted three times per week for 60 min per session; however, there is still some degree of variability in training dosage according to other systematic reviews (Fang et al. 2020; Rodriguez-Tapia et al. 2022; Shackleton et al. 2019; Tamburella et al. 2022).

Limitations

There is understandable interest around the use of exoskeleton technologies for regaining the ability to stand and ambulate (Fritz et al. 2019). There are several limitations to exoskeleton use as a rehabilitation therapy tool and as a personal mobility device, such as device safety, set-up requirements, slow speeds for community ambulation, level and completeness of injury, body composition and weight, ROM required for use, high cost, and limited accessibility and availability for gait rehabilitation (Heinemann et al. 2020; Gorgey 2018; Herrera-Valenzuela et al. 2023).

Regarding safety, one systematic review by Duddy et al. (2021) reported that powered exoskeleton devices seem to be safe to use with patients with neurological impairments, with no serious AEs occurring. Conversely, two systematic reviews on exoskeleton trials in people with SCI documented an AE rate of 25-30%, with the most frequent AEs being skin lesions; less frequently occurring AEs were extreme fatigue, falls, bone fractures or muscle strains (Rodriguez-Tapia et al. 2022; Tamburella et al. 2022). Bass et al. (2022) developed an algorithm based on bone mineral density aimed at minimizing fracture risk for people with SCI engaging in exoskeleton walking training available here. Possible AEs should always be considered prior to exoskeleton walking training and appropriate caution should always be exercised.

There are multiple limitations to the research conducted to date on exoskeletons and people with SCI. Most studies established improvement in walking outcomes whether exoskeleton training or more conventional PT was employed; it would be most helpful to know whether the benefits deriving from the use of exoskeletons are greater or lesser than conventional physical therapy (Duddy et al. 2021; Shackleton et al. 2019; Tamburella et al. 2022). This could be established with additional RCTs, larger sample sizes, and clearer emphasis on between-group analyses.

Conclusions

There is level 1 evidence (from 1 RCT: Xiang et al. 2021) that walking training with an exoskeleton (AIDER exoskeleton) provides a similar benefit in gait endurance (6MWT) as strength and aerobic exercise training in patients with acute SCI.

There is level 1 evidence (from 1 RCT: Gil-Agudo et al. 2023) that robotic locomotor training (using the HANK exoskeleton) compared with traditional gait training for five weeks provides significant improvements in walking ability (WISCI II); but not in walking distance (6MWT), walking speed (10MWT), lower limb strength (LEMS), or functional independence (SCIM-III) in participants with acute and incomplete SCI.

There is level 1 evidence (from 1 RCT: Shackleton et al. 2024) that a 24-week program of walking training using an exoskeleton (EksoGT) compared to ABT provides similar benefits in LEMS and functional walking (SCI-FAI) in people with chronic incomplete SCI.

There is level 2 evidence (from 1 RCT: Edwards et al. 2022) that walking training with an exoskeleton (Ekso exoskeleton) compared to BWSTT and usual PT in people with chronic motor incomplete SCI provides significant benefits in functional ambulation (WISCI-II scores), but all groups had similar improvements in gait speed (10MWT) and walking distance (6MWT).

There is level 3 evidence (from 1 case control study: Tsai et al. 2020) that OWT with an exoskeleton (EksoGT) in comparison with usual care (not receiving any walking training with an exoskeleton), provides a significant improvement in LEMS in patients with acute or subacute (mean time since injury = 19.3 days) SCI during inpatient rehabilitation.

Key Points

Wearable exoskeleton-assisted gait training can enable safe walking and improvements in gait and strength outcomes in patients with SCI.

There is no consensus regarding training regimens and exoskeleton models used.

There is insufficient evidence regarding whether wearable exoskeleton-assisted training provides better walking function compared with other approaches (such as Robot-Aided Gait Training with Lokomat or Knee-Ankle-Foot Orthoses) in people with SCI.

6 Neuromodulation

Neuroplasticity refers to the capacity of the nervous system to modify its structural and functional organization, adjusting itself to changing demands and environment; neuromodulation can be defined as the induction of neuroplastic changes via local application of electrical, magnetic, acoustic, optic, tactile, or pharmacological stimuli (De Ridder et al. 2016). The SCIRE YouTube channel demonstrates neuromodulation in a number of ways, including

chemically (intrathecal baclofen), via electrical stimuli (FES and epidural stimulation), and magnetic fields (transcranial magnetic stimulation [TMS]). Neuromodulation can be applied to three main areas of the body: the brain, the spinal cord, and the peripheral nerves, through invasive and/or non-invasive approaches.

In recent years, the combination of rehabilitative training with neuromodulation of the brain or the spinal cord has been investigated as a means to enhance the excitability of motor circuits and to increase training efficacy, promoting motor recovery (Hofer & Schwab 2019). There is promising therapeutic potential using neuromodulation for movement, sensation, bowel, bladder, and sexual function in people with SCI (Perrouin-Verbe & Van Kerrebroeck 2024). Over the last few years, translation of stimulation-enhanced activity-based rehabilitation from the pre-clinical to a clinical setting has yielded improvements in motor functionality (Hofer & Schwab 2019).

6.1 Functional Electrical Stimulation (FES) and Walking

The idea of compensating for paralyzed function using ES was first tested in the 1960s when FES of the common peroneal nerve was effective in assisting foot clearance during the swing phase of walking (Liberson et al. 1961). Approaches that focus on swing phase activity are more suitable for people with less severe disabilities and adequate balance to support their stance leg during gait. There are also more complex systems that involve several channels of stimulation that support proper extension as well as foot clearance during swing (e.g., Sigmedics 2000). These are more suitable for patients who require assistance in standing as well as gait, such as those with neurologically complete SCI. FES systems such as the Parastep or ALT-2 provide stimulation of thigh extensor muscles (quadriceps, gluteal muscles) to support extension and standing, as well as stimulation of the common peroneal nerve to assist with swing phase movements. FES may also be combined with bracing to counter trunk and hip instability (Solomonow et al. 1997). FES to assist with foot clearance during swing (drop-foot) has been studied more extensively in the stroke population (e.g., Bosch et al. 2014) but they may provide some assistance for people with incomplete SCI who present with hemiparesis similar to stroke.

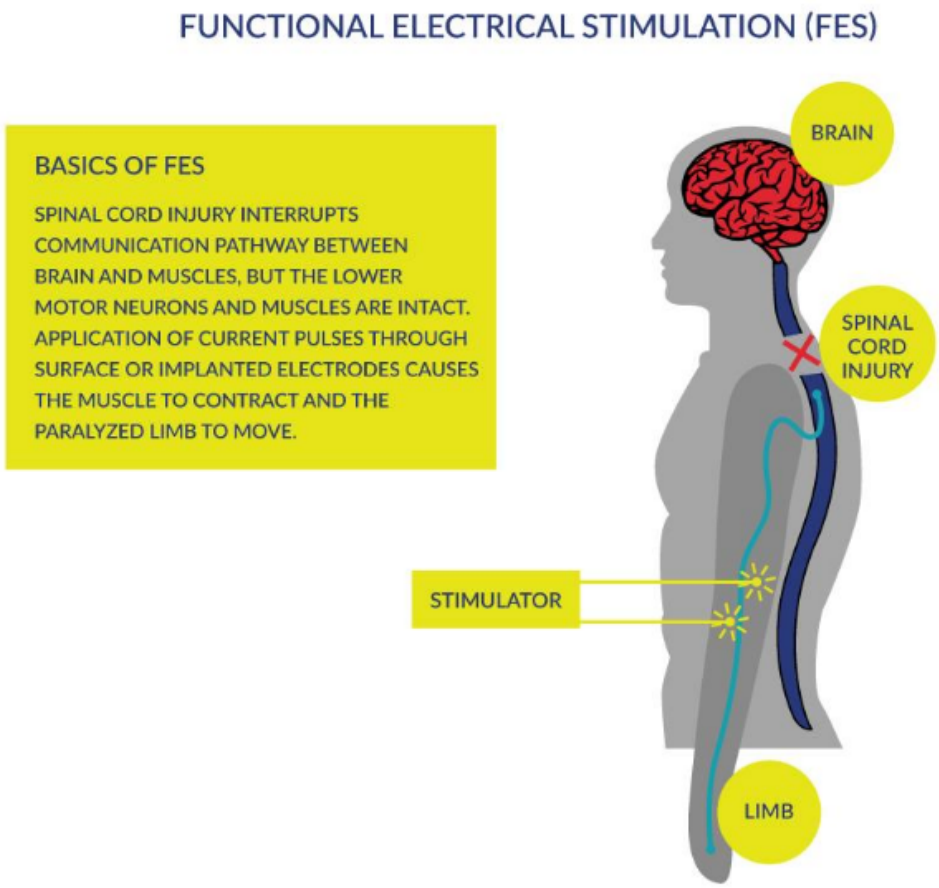


Figure 7. Basics of Functional Electrical Stimulation (FES)

With improvements in electronics technology, FES systems have become smaller and more practical for everyday use. In addition, some patients have opted for implanted FES systems that may be inserted without surgery. Percutaneous electrodes, which are inserted through the skin with a hypodermic needle, offer one possibility to circumvent complications with surface electrodes, as well as offering more precise delivery of stimulation and greater muscle selectivity, including access to deeper muscles like the hip flexors (Kobetic et al. 1997; Marsolais & Kobetic 1986). However, there may be complications due to infection or irritation at the site of insertion, and electrode movement or breakage (Agarwal et al. 2003). Thus, preliminary reports of the use of such innovative FES technology are promising, but further study is warranted to determine the long-term stability, efficacy, and complications of such implanted systems.

6.1.1 Functional Electrical Stimulation (FES) to Improve Walking

Table 13. FES to Improve Locomotor Function

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Galea et al. 2018 Australia RCT PEDro = 7 Level 1 N = 116	**Population:** 116 participants who had sustained a SCI above the level T12; 98 males and 18 females; mean age 41.45 years; level of injury C2-C8 (n = 62), T1-T6 (n = 31), and T7-T12 (n = 23); AIS A (n = 57), AIS B (n = 17), AIS C (n = 12), and AIS D (n = 30); and mean time since injury 4.7 years. **Treatment:** The intervention consisted of 36 sessions over 12 weeks. Participants were randomly assigned to: • Full-body exercise program (n = 60: Participants in received a triad of interventions comprising LT (BWSTT for 30 min), FES-assisted cycling (for 10-60 min), and trunk and upper and lower extremity exercise. • Upper body exercise program (n = 56): Participants received a circuit-based exercise program for the upper body, incorporating resistance and aerobic training. **Outcome Measures:** Spinal Cord Injury–Falls Concern Scale (SCI-FCS), 6MWT, and 10MWT were assessed at baseline, 12 weeks, and 24 weeks after randomization.	1. There were no statistically significant between-group differences for 6MWT, 10MWT and SCI-FCS after 12 weeks of training or at 6 months follow-up. 2. There was neither consistent trend toward improvement nor deterioration of walking performance on the 10MWT or the 6MWT. 3. AEs: 31 serious AEs (16 full-body exercise, 15 upper body exercise) and 719 AEs (404 full-body exercise, 309 upper body exercise) were recorded over the 6-month trial period. a. One serious AE in full-body exercise (bilateral medial femoral condyle and tibial plateau subchondral insufficiency fractures) was considered to be definitely related to the intervention. b. Another serious AE in full-body exercise (severe worsening back pain) was considered probably related to the intervention. 4. In upper body exercise, one serious AE (pain and loss of strength in upper limbs) was considered possibly related to the intervention.
Gurcay et al. 2022 Turkey Pre – post	**Population:** 15 participants with SCI, able to stand up and walk with long leg braces or assistive devices and with stable neurological status; 9 males and 6	1. No AEs were recorded during the intervention period. 2. In gait analysis, temporal spatial parameters including gait

Level 4 N = 15	females; mean (± SD) age 32.4 (± 10.0) years; injury level T1 (n = 4), T8 (n = 1), T10 (n = 4), T11 (n = 1), T12 (n = 1), L1 (n = 2), L2 (n = 1), and L5 (n = 1); AIS A (n = 4), AIS B (n = 4), AIS C (n = 5), and AIS D (n = 2); and mean (± SD) time since injury 65.9 (± 55.9) months. **Treatment:** The program was applied 30 min (5-min warm-up, a 20-min training of FES lower extremity cycling, and a 5-min cool-down) regularly at a frequency of 3 sessions per week, for 6 weeks. **Outcome Measures:** 6MWT; 20-meter walk test (20-MWT); and thigh circumference were conducted at baseline (T0) and after the 6-week (T1) FES-cycling program.	distance (p = 0.001) and step length (p = 0.001) increased at T1 due to the intervention. 3. The required time for 20MWT (T1; p = 0.011) and the number of rests needed was reduced (T1; p = 0.007). Cadence increased but reached no significant level (p > 0.05).
Duffell et al. 2019 UK Pre – post Level 4 N = 11	**Population:** 11 participants with incomplete SCI who were using a wheelchair for at least 2 hours per day; 10 males and one female; mean age 56.5 years; injury level C1 (n = 2), C3 (n = 1), C4 (n = 1), T2 (n = 3), T3 (n = 1), T5 (n = 1), T7 (n = 1), and T12 (n = 1); AIS C (n = 7) and AIS D (n = 3); and median time since injury 1 year and 1 month. **Treatment:** Participants trained three 1-h sessions per week over 4 weeks on the iCycle (which is a FES ergometer) with biofeedback through a VR game (in which the speed of the avatar depends on the actual crankshaft torque while motion is maintained by a motor) to encourage voluntary drive during pedaling. **Outcome Measures:** Voluntary motor function (assessed using ISNCSCI motor scores); Oxford scale motor power grading (carried out for knee extension/flexion and ankle plantarflexion/dorsiflexion); WISCI II; and 10MWT were assessed pre- and post-training, and 4 weeks after completing training.	1. All 11 participants completed the training sessions, with no reported serious AEs. Only two participants noticed skin redness at the end of a session. 2. Only two of the participants included in the trial were ambulatory, therefore WISCI II scores and the 10MWT could only be completed for these participants. a. Participant #7 showed no change in either measure. b. Participant #15 demonstrated an improvement in WISCI II score of 5 points at end of training compared with baseline, and 10MWT time improved from 82 s at baseline to 41 s at end of training.
Kuhn et al. 2014 Germany Pre-post	**Population**: 30 participants; average age 44 ± 15.5y; motor complete and incomplete spinal cord injuries in the cervical, lumbar, and thoracic regions;	1. For the 5 patients with partial walking ability at the start of the study, the mean 6MWT distance significantly increased from

Level 4 N = 30	AIS A = 10, B = 3, C = 15, D = 2; 0-122 months post injury. **Treatment**: During the 4-week study period, all patients received eight 20min FES interventions at the beginning and end of each week. At every intervention, circumferential measurement and spasticity testing before and after FES cycling (pretest/post-test) were performed. Ultrasound, walking tests, and MMT were only performed at the beginning of week 1 (T1) and at the end of week 4. **Outcome Measures:** Circumferential measurement, muscular ultrasound measurement, spasticity measured by Modified Ashworth Score, Walking (6MWT).	62.3±135.3 to 94.3±167.1 m throughout the study (P = 0.03).
Ladouceur & Barbeau 2000a Canada Pre-post Level 4 N = 14 (enrolled) N = 10 (analyzed)	**Population:** 14 participants; age 25-49 yrs; all participants had an incomplete SCI; C3-L1 lesion level; 1.8-19.1 yrs post-injury. **Treatment:** Surface FES: bilateral or unilateral common peroneal nerve, home use as much as possible ~1 year (26 and 56 weeks), 2 participants also had bilateral quadriceps. **Outcome Measures**: Temporal gait measures.	1. Training with FES-assisted walking during the first year increased walking speed by 0.10 m/s (P = 0.007). However, FES-assisted walking had only minor effects (P > 0.05) on the rest of the spatiotemporal parameters (stride length, stride frequency, stance duration, and swing duration).
Ladouceur & Barbeau 2000b Canada Pre-post Level 4 N = 14 (recruited) N = 10 (completed)	**Population:** 14 participants; age 25-49 yrs; all participants had an incomplete SCI; C3-L1 lesion level; 1.8-19.1 yrs post-injury. **Treatment:** Surface FES: bilateral or unilateral common peroneal nerve, 2 participants also had bilateral quadriceps, home use as much as possible ~1 year. **Outcome Measures**: Temporal gait measures.	1. 7/14 participants showed improvement based on type of ambulatory device. 2. 13/14 participants improved gait speed with FES. 3. Training/carryover effect after long-term use: increase evident even when FES off in 12/14 participants.
Wieler et al. 1999 Canada Pre-post Level 4 N = 31	**Population:** 31 males and females; mean (SD) age 36(2) yrs; all participants had an incomplete SCI; mean (SD) 6 (1) yrs post-injury. **Treatment:** Surface FES: common peroneal nerve; some participants also received FES to hamstrings, quadriceps,	1. There was a significant improvement in gait speed in participants when treated with FES (p<.01) but that improvement in gait speed persisted even when participants walked without

	gluteus medius, duration of FES ranged from 3 months to over 3 years. Each participant was tested at the start and end of the study both with and without FES. **Outcome Measures:** walking speed, stride length, cycle time.	FES (p<.01). 2. The slowest quintile of participants increased their walking speed by 70% while the fastest quintile of participants increased their walking speed by 20%. 3. The initial gait speed at the start of study was significantly faster when patients used FES than when no FES was used (p<.05).
Klose et al. 1997 USA Pre-post Level 4 N = 16	**Population:** Mean (SD) age 28.4 (6.6) years; all participants had complete SCI; T4-T11 lesion level; 0.7-9.0 yrs post-injury. **Treatment:** Surface FES: Parastep: 6 channels (bilateral common peroneal nerve, quadriceps, glutei); 3X/week, 32 sessions (once participants had sufficient strength to stand). **Outcome Measures**: walking distance and speed (with FES).	1. Most participants improved endurance and gait speed. Longest distance walked with FES was between 12 to 1707 m (mean: 334 m; SD 402 m). 2. There were significant differences in distance travelled (p<.001) and gait speed (p<.001) over the 11 weeks.
Granat et al. 1993 Scotland Pre-post Level 4 N = 6	**Population**: 6 males and females; age 20-40 yrs; all participants had diagnosis of Frankel C and D; C3-L1 lesion level; 2 to 18 yrs post-injury. **Treatment**: Surface FES-assisted LT: quadriceps, hip abductors, hamstrings, erector spinae, common peroneal nerve, home program >30 min, 5X/week, 3 months. **Outcome Measures:** MMT, MVC, upright motor control, walking speed, stride length, cadence.	1. Significant mean increase in stride length, but not speed or cadence. 2. 3 to 4 participants had significant individual increases in gait speed, stride length and cadence.
Stein et al. 1993 Canada Pre-post Level 4 N = 10	**Population:** 10 males and females; age 20-44 yrs; all participants had an incomplete SCI; C2-T10 lesion level; 2.5-10 years post-injury. **Treatment:** Surface, percutaneous, or implanted FES of common peroneal nerve, and sometimes quadriceps, glutei, and psoas. **Outcome Measures:** Speed, gait parameters.	1. All participants improved gait speed when FES was on (mean change was 4 m/min). 2. Participants with more severe SCI were the most receptive towards the FES treatment.

Discussion

To date, there are few randomized controlled or blinded assessments of the training effects of FES to improve mobility after SCI. Furthermore, only six of the studies reviewed here (Duffell et al. 2019; Granat et al. 1993; Gurcay et al. 2022; Kuhn et al. 2014; Klose et al. 1997) report specific usage parameters for FES during gait rehabilitation, whereby FES was applied for at least 20 min, 2 to 5 times/week for up to 4.5 months. In the remainder of the studies, participants were provided with FES systems to use at home "as much as possible" or "as desired" over the course of the study (Ladouceur & Barbeau 2000a; 2000b; Wieler et al. 1999; Stein et al. 1993). Results from the nine pre-post studies included here show that almost all the participants showed improvements in gait parameters (walking speed or distance) when FES was used (Gurcay et al. 2022; Kuhn et al. 2014; Ladouceur & Barbeau 2000a; 2000b; Wieler et al. 1999; Klose et al. 1997; Granat et al. 1993; Stein et al. 1993). This is not surprising, given that the FES could compensate for weakened or paralyzed muscle function during gait.

Of greater interest is the finding of carryover effects after FES training. Several investigators have also reported a carryover effect after FES training such that improvements in functional ambulation (e.g., overground walking speed and distance, step length) persisted even when the stimulator was turned off (Ladouceur & Barbeau 2000b; Wieler et al. 1999). This suggests that neuroplastic changes may have taken place in response to regular use of FES during walking. Indeed, it has been shown in people without disabilities that the combination of treadmill walking and FES led to an acute increase in corticospinal excitability that persists even after the cessation of FES (Thompson & Stein 2004). The use of FES and weight-bearing also helps to maintain the subtalar and midfoot joint mobility needed for walking (Bittar & Cliquet 2010).

Despite the positive findings of FES usage in multiple pre-post studies, the one RCT that we found in people with SCI was less conclusive. In comparing a 12-week full body exercise program that included FES cycling versus an upper body exercise program, there were no differences between groups in 6MWT, 10MWT, or improvements in falls concerns (Galea et al. 2018). The authors stated that the heterogeneity of their sample, which included participants with a range of injury levels and severity, may have contributed to these results (Galea et al. 2018).

Although laboratory studies advocate the efficacy of FES systems for improving ambulatory function in patients with SCI, the effectiveness of any technology is only as good as its acceptance by the intended users. Some have reported difficulties with finding the proper stimulation site or technical difficulties with the leads, switches, or electrodes (Wieler et al. 1999). There have also been reports of musculoskeletal complications such as ankle sprain, calcaneum fracture, back pain, or falls with FES use (Brissot et al. 2000; Gallien et al. 1995). Some of these complications may have been associated with the commencement of upright exercise (gait) after a period of being non-ambulatory. Anecdotal reports found in several studies suggest that most participants mainly use FES indoors or at home, for short-distance walking, to prevent complications due to prolonged immobilization, and to enhance physical fitness rather than functional community ambulation (Brissot et al. 2000; Gallien et al. 1995; Klose et al. 1997).

The functional benefits derived from FES are also quite variable. For instance, Stein et al. (1993) reported that most participants showed a modest improvement in gait speed (average: 0.07 m/s), which was more significant for people with more severe disabilities. Higher-functioning participants felt that this small benefit in gait speed did not warrant the daily use of FES. In contrast, Ladouceur and Barbeau (2000b) reported that there was a tendency for the participants with initially faster gait speed to have greater absolute improvements. Thus, outcomes from FES-use also seem to be quite variable in terms of walking speed or distance (Ladouceur & Barbeau 2000b; Stein et al. 1993; Klose et al. 1997).

Conclusions

There is level 1 evidence (from 1 RCT: Galea et al. 2018) that a multimodal exercise training program (comprising BWSTT, FES cycling, and trunk and upper and lower limb exercises) does not provide better neurological or walking improvements than an upper body exercise program in patients with chronic SCI.

There is level 4 evidence (from 8 pre-post studies: Gurcay et al. 2022; Kuhn et al. 2014; Ladouceur and Barbeau 2000a; 2000b; Wieler et al. 1999; Klose et al. 1997; Granat et al. 1993; Stein et al. 1993) that FES-assisted walking or cycling can enhance walking speed and distance in people with complete and incomplete SCI.

There is level 4 evidence from two independent laboratories (Ladouceur & Barbeau 2000a, 2000b; Wieler et al. 1999) that the regular use of FES in gait training or activities of daily living leads to persistent improvement in walking function that is observed even when the stimulator is not in use.

Key Points

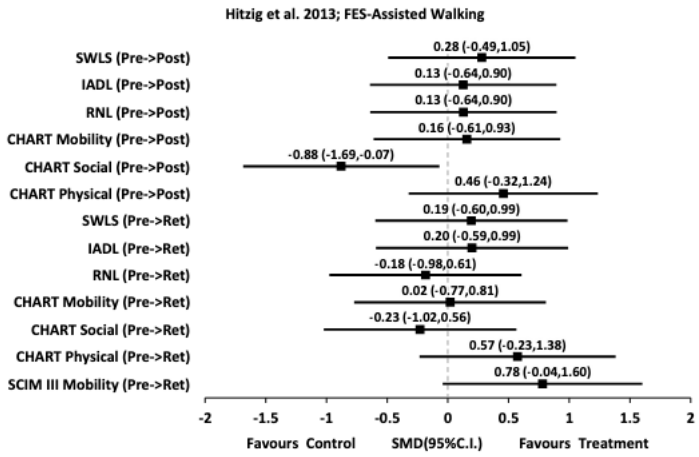
Functional electrical stimulation (FES)-assisted walking or cycling can enable walking or enhance walking speed in incomplete SCI or complete SCI.

Regular use of FES in gait training or activities of daily living can lead to improvement in walking even when the stimulator is not in use.

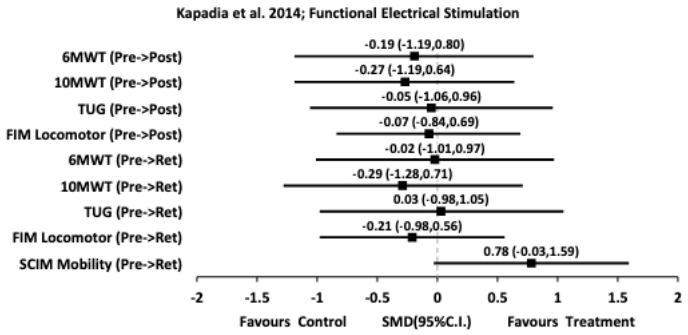
6.1.2 Functional Electrical Stimulation (FES) With Gait Training to Improve Locomotor Function

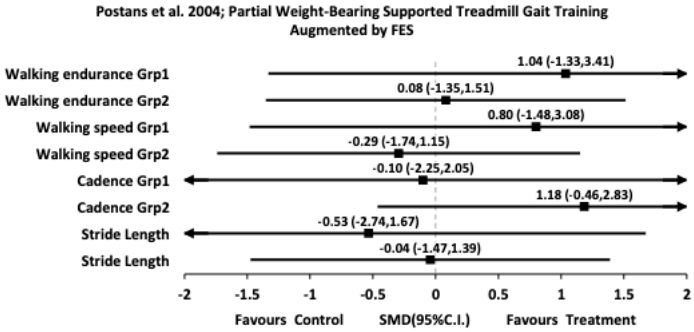
Table 14. FES with Gait Training to Improve Locomotor Function

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Field-Fote & Roach 2011 USA RCT PEDro = 8 Level 1 N = 64	**Population:** Patients with chronic SCI at least 1-year post-injury, mean ages between 38 and 45 of each group; TM group (14 males, 3 females), TS group (14 males, 4 females), OG group (11 males, 4 females), LR group (12 males, 2 females). **Treatment:** Training 5 days/week for 12 weeks with: treadmill-based training with manual assistance (TM), treadmill-based training with stimulation (TS), overground training with stimulation (OG), or treadmill-based training with robotic assistance (LR). **Outcome Measures:** Walking speed (over 10m), distance walked in 2 min, LEMS.	1. There was a significant time effect of training on walking speed: walking speed significantly increased for the OG group (0.19(0.21) to 0.28(0.28) m/s; Effect Size=0.43), TS group (0.18(0.18) to 0.23(0.18) m/s; ER=0.28). 2. There was a significant effect of training on walking distance: walking distance significantly increased for the OG group (24.0(35.3) to 38.3(46.1) m; ES=0.40) and the TS group (20.6(23.1) to 24.4(24.3) m; ES=0.16), but not for the TM (22.1(21.4) to 23.0(21.1) m; ES=0.04) or the LR group (16.8(11.3) to 17.9(11.9); ES = 0.11). 3. There was a significant time x group interaction, with the increase in the OG group's walking distance being significantly greater than the TS, TM and LR groups. 4. Effect sizes for speed and distance were largest with OG (d=0.43 and d=0.40, respectively). Effect sizes for speed were the same for TM and TS (d=0.28); there was no effect for LR. The effect size for distance was greater with TS (d=0.16) than with TM or LR, for which there was no effect.
Hitzig et al. 2013	**Population:** 34 participants with SCI. For the FES group (n=17, 14M 3F); mean (SD)	1. The FES group had a significant increase in SCIM mobility

<table>
<tr><td rowspan="2">Canada
Parallel-group RCT
PEDro = 7
Level 1
N = 34</td><td>age= 56.6(14); DOI = 8.75 (9.7); 6 AIS C, 11 AIS D. For the control group (n=17, 12M 5F); mean (SD) age=54.1(16.5); DOI= 10.3 (11.1); 7 AIS C, 10 AIS D.
Treatment: Participants were randomized to intervention (FES) or control group. The FES group received FES stimulation while ambulating on a BWS treadmill. Control group exercise program consisted of 20-25 min of resistance and 20-25 min of aerobic training.
Outcome Measures: SCIM; SWLS; IADL; Craig Handicap Assessment Report Technique; RNL.</td><td>subscores (mean (SD)= 17.27 (7.2) to 21.33 (7.6)) compared to the exercise group (mean (SD) = 19.9 (17.1) to 17.36 (5.5)) from baseline to 1-yr follow-up.
2. No significant between-group differences were detected for other outcomes.
3. Both FES and control group reported positive gains in wellbeing from trial participation.</td></tr>
<tr><td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- to post-intervention data and pre-intervention to retention/follow-up data.
 
</td></tr>
<tr><td>Kressler et al. 2013
USA
Single-blind RCT
PEDro = 7
Level 1
N = 62</td><td>Population: 62 participants with SCI; AIS C or D; injury at T10 or higher.
Treatment: Participants trained 5 days/wk for 12 wks. Groups were treadmill-based LT with manual assistance, transcutaneous electrical nerve stimulation (TENS), and a driven gait orthosis and overground LT with ES.
Outcome Measures: Oxygen uptake, walking velocity and economy, substrate utilization during participant-selected “slow”, “moderate” and “maximal” walking speeds.</td><td>1. All groups increased velocity but to varying degrees: Driven gait orthosis = 0.01(0.18) Ln[m/s]; treadmill-based LT with manual assistance = 0.07(0.29) Ln[m/s]; TENS = 0.33(0.45) Ln[m/s]; overground LT = 0.52(0.61) Ln[m/s].
2. Only the TENS and overground LT groups had significant improvement over driven gait orthosis LT. Overground LT was also significantly higher than treadmill-based LT with manual assistance (p=.015).</td></tr>
</table>

		3. Changes in walking economy were only significant for TENS (0.26(0.33) Ln[L/m], p=.014) and overground LT (0.44(0.62) Ln[L/m], p=.025).
Nooijen et al. 2009 USA RCT PEDro = 7 Level 1 N = 51	**Population:** All participants had motor-incomplete spinal cord injuries and were at least 1-year post injury; Group 1: mean age = 38.15; T11-C3; Group 2: mean age = 39.47; T9-C4; Group 3: mean age = 41.64; T6-C4; Group 4: mean age = 44.33; L2-C6. **Treatment**: 12-week training period. All BWSTT: Group 1 = treadmill with manual assistance; Group 2 = treadmill with peroneal nerve stimulation; Group 3 = overground with peroneal nerve simulation; Group 4 = treadmill with assistance from Lokomat. **Outcome Measures**: Cadence, step length, stride length, symmetry index, intralimb coordination, timing of knee extension onset within the hip cycle; all compared to non-disabled controls.	1. BWSLT led to improvements in gait quality regardless of training condition. There were smaller improvements in the Lokomat group, possibly due to less active engagement/more passive movement. 2. Training significantly improved: cadence, step length and stride of both the stronger and weaker legs. After training, participants were also able to take more steps per min. 3. Post hoc analyses revealed overground training plus stimulation had a significantly larger gain than Lokomat group.
Kapadia et al. 2014 Canada RCT PEDro = 5 Level 2 N = 27	**Population**: 27 participants; traumatic (>18 months) and incomplete chronic spinal cord lesions between C2 and T12, AIS C and D. **Treatment**: 45 min of therapy per session, 3 days per week, for 16 weeks (48 sessions in total). Outcome measures were assessed at baseline, 4 months, 6 months, and 12 months post baseline. **Outcome Measures:** Gait Measures- 6MWT, 10MWT, Assistive Device Score, Walking Mobility Scale; Functional Measures- SCIM, FIM; Spasticity Measure- Modified Ashworth Scale, Pendulum Test.	1. SCIM mobility sub-score significantly improved over time for the intervention group (p<.01) but not for the control group (baseline/12 months: 17.27/21.33 vs. 19.09/17.36, respectively). 2. On all other outcome measures the intervention and control groups had similar improvements. 3. Walking speed and endurance during ambulation all improved upon completion of therapy and the majority of participants retained these gains at long-term follow-ups.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- to post-intervention data and pre-intervention to retention/follow-up data.	

		
Field-Fote et al. 2005 USA RCT PEDro = 4 Level 2 N = 27	**Population:** 27 males and females; age 21-64 yrs; all participants had an incomplete SCI; C3-T10 lesion level; >1 yr post-injury. **Treatment:** Randomized to 4 gait training strategies, 45-50 min, 5x/wk, 12 wks: 1) manual BWSTT (n=7); 2) BWSTT + FES (common peroneal nerve) (n=7); 3) BWS overground + FES (n=7); 4) BWS Lokomat (robotic gait device) (n=6). **Outcome Measures**: Walking speed over 6 m (short bout) and 24.4 m (long-bout).	1. Overall, training was associated with a 55% increase [range = -59% to +417%] in short-bout walking speed and a 37% increase [range = -38% to +203%] in long-bout speed. 2. There were no significant differences between groups (i.e., types of locomotor training), however, post-hoc t-tests reveal that there were differences in pre- to post-training short-bout walking speed in both the TS group (P=.02) and in the OG group (P=.008), while differences were not observed in the TM or the LR groups. 3. Tendency for initially slower walkers (<0.1m/s) to show greater improvement (106%) compared to initially faster walkers (17%).
Postans et al. 2004 Scotland RCT w/crossover PEDro = 3 Level 2 N initial = 14 N final = 10	**Population:** 14 males and females; ages 19-57 yrs; all participants had an incomplete SCI; C4-T9 lesion level; mean 12.2±5.9 weeks post-injury. **Treatment:** Crossover design: Intervention - Partial weight-bearing supported treadmill gait training augmented by FES for up to 25 min a day, 5 days a week for 4 weeks; Control - 4-week period of standard physiotherapy. Patients were randomly assigned to either an AB (4 weeks control then 4 weeks intervention) or BA	1. Between the intervention and control periods for the BA group, there was a significant difference in walking endurance (in meters; Mean: 60.10, CL: 9.2 to 110.9, P=.030) as well as for walking speed (in m/s; Mean: 0.22, CL: 0.05 to 0.37, P= .019). 2. Between the intervention and control periods for the AB group, there was a significant difference in walking endurance (in meters; Mean: 72.20, CL: 39.8

	(4 weeks intervention then 4 weeks control) group. **Outcome Measures:** Overground and treadmill walking endurance and speed.	to 104.6, P=.003) as well as for walking speed (in m/s; Mean: 0.23, CL: 0.13 to 0.33, P=.004).
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data.  *Cross-over study, where participants acted as their own controls. Grp1: control-intervention. Grp 2: intervention-control **Overground measurements only ***SMD 95%CI calculated from 95%CI of changes in mean outcome values	
Triolo et al. 2012 USA Longitudinal Level 2 N = 15	**Population:** 15 participants with thoracic or low cervical level SCI (14M 1F); 10 AIS A, 4 AIS B, 1 AIS C; Mean (SD) DOI: 72.6(71.87) months. **Treatment:** Participants received the 8-channel neuroprosthesis and completed rehabilitation with the device. This study follows the patients from discharge to follow-up ranging from 6-19 months after discharge (with exception of one participant at 56 months). **Outcome Measures:** Neuroprosthesis usage, maximum standing time, BWS, knee strength, knee fatigue index, BWS, electrode stability, and component survivability.	1. Levels of maximum standing time, BWS, knee strength, and knee fatigue index were not statistically different from discharge to follow-up. 2. Neuroprosthesis usage was consistent with participants choosing to use the system on approximately half of the days during each monitoring period. Although the number of hours using the neuroprosthesis remained constant, participants shifted their usage to more functional standing vs. more maintenance exercise, suggesting that the participants incorporated the neuroprosthesis into their lives. 3. Safety and reliability of the system were demonstrated by electrode stability and a higher component stability rate (>90%).
Crosbie et al. 2009 Australia Pre-post	**Population:** 4 males with complete (ASIA A) SCI; age 38-62 years; level of injury: thoracic (T4, n = 2; T7, n = 1; T10-11, n = 1); 2-13 years post injury.	1. All participants increased ambulation capacity with training, but while the first three participants tripled or quadrupled their walking

Level 4 N = 4	**Treatment:** Each participant prepared for ambulation training using at least eight weeks of FES-induced semi-recumbent cycling. The program consisted of 18 interval training sessions, conducted three times per week for six weeks. Each session involved treadmill walking for a target duration at a speed as great as could be tolerated, followed by a similar duration seated recovery, repeated until muscle fatigue precluded further walking. Participants progressed from an initial duration of 2 min, repeated three times, up to a maximum of 5 min repeated up to seven times over the course of gait training. Participants ambulated on a treadmill, using a wheeled walking frame for balance only, while wearing a protective overhead chest harness designed to prevent a fall, but offering no BWS. Ambulation was produced through stimulation applied via surface electrodes placed over the motor points of the primary bilateral antigravity muscles (quadriceps femoris and gluteus maximus), and via stimulation of the common peroneal nerve to elicit a flexor withdrawal reflex. The gait cycle consisted of contralateral flexion and extension activation. The stimulator applied biphasic pulses at a frequency of 25 Hz, at a pulse width of 150 ms and an initial current intensity of 140 mA (pulse peak, constant current). **Outcome Measures:** Participants walking continuously to onset of muscle fatigue (as indicated by knee buckle after stimulation had reached a maximum level) before and after the training program.	distance, participant D's distance increase was more modest. 2. Walking duration increased in a similar fashion to distance traveled; however, the increased walking speed attained over the course of the training meant that the increase in walking duration was between 40% and 200%.
Hesse et al. 2004 Germany Pre-post Level 4 N = 4	**Population:** 3 males; age 45-62 yrs; all participants had a diagnosis of AIS C or AIS D; C5-T8 lesion level; 8-18 months post-injury. **Treatment:** Electromechanical gait trainer + FES to quadriceps and hamstrings: 20-25 min, 5x/wk, 5 wks.	1. Gait ability improved in all patients; 3 could walk independently over ground with aids. Overall gait speed and endurance more than doubled. 2. Study made no reports of

	Outcome Measures: Gait velocity and endurance.	significance levels or testing of results.
Field-Fote & Tepavac 2002 USA Pre-post Level 4 N = 14	**Population**: 14 males and females; age 18-50 yrs; all participants had a diagnosis of AIS C; C4-T7 lesion level. **Treatment:** BWSTT + common peroneal nerve FES: <90 min, 3x/wk, 12 wks. **Outcome Measures:** Over ground gait speed.	1. All participants showed an increase in walking speed. 2. Participants with slower walking speeds showed greater improvement. 3. Study made no mention of significance levels or testing of results.
Field-Fote 2001 USA Pre-post Level 4 N = 19	**Population:** 19 males and females; mean age 31.7±9.4 yrs; all participants had a diagnosis of AIS C either paraplegia or tetraplegia. **Treatment:** BWSTT + common peroneal nerve FES: <90 min, 3x/wk, 12 wks. **Outcome Measures:** LEMS, Gait speed.	1. Significant increase in walking speed (initial 0.12 ± 0.8m/s; final 0.21 ± 0.15m/s, p = .0008, median change of 77%). 2. LEMS had median increases of 3 points in both the FES-assisted leg and the non-stimulated leg. 3. Increase in AIS lower limb motor scores in 15 of 19 incomplete SCI (AIS C).

Discussion

Findings from four RCTs (Hitzig et al. 2013; Field-Fote & Roach 2011; Field-Fote et al. 2005; Kapadia et al. 2014) and three pretest/posttest studies (Hesse et al. 2004; Field-Fote & Tepavac 2002; Field-Fote 2001) demonstrated favorable outcomes when BWSTT was combined with FES in people with chronic, incomplete SCI. Hitzig et al. (2013) and Kapadia et al. (2014) studied the effects of FES stimulation while ambulating on a BWS treadmill and found a significant increase in SCIM mobility scores from baseline to 1-year follow-up compared to the control group. However, it should be noted that both studies compared BSWT training plus stimulation versus aerobic/resistance training. So, it is not possible to tell whether the walking training or the stimulation was the more important contributor to increased mobility scores, just that the combination of BWST and stimulation or better than more standard rehabilitation.

The Kressler et al. (2013) study provides evidence for increased benefit of ES over manual assistance and braces (driven gait orthosis). In this study, the transcutaneous electrical stimulation group and the overground LT with electrical stimulation group had significantly higher walking speeds, while the treadmill-training with manual assistance group and driven gait orthosis group had nonsignificant improvements in walking speed.

Conclusions

There is level 1 evidence (from 2 RCTs: Field-Fote & Roach 2011; Field-Fote et al. 2005) and level 4 evidence (from 2 pre-post studies: Field-Fote & Tepavac 2002; Field-Fote 2001) for an

overall enhancement of short-distance functional ambulation, as measured by overground gait speed over 6 m, and walking distance when BWSTT was combined with FES of the common peroneal nerve.

There is level 1 evidence (from 1 RCT: Kressler et al. 2013) for increased benefit of ES over manual assistance and braces (driven gait orthosis).

There is level 1 evidence (from 2 RCTs: Hitzig et al. 2013; Kapadia et al. 2014) for a significant increase in SCIM mobility scores when participants undergo BWSTT combined with FES versus more standard rehabilitation (e.g., aerobic/resistance training).

There is level 4 evidence (from one small pretest/posttest study: Hesse et al. 2004) suggesting that BWSTT combined with FES to the quadriceps and hamstring muscles enhances functional ambulation.

There is level 4 evidence (from 1 pre-post study: Crosbie et al. 2009) that a 6-week program consisting of interval treadmill walking (without body-weight support) training sessions combined with FES to the quadriceps femoris, gluteus maximus improves walking function (walking and distance) in people with complete (ASIA A) and chronic SCI.

There is level 4 evidence (from one case series study: Triolo et al. 2012) that an 8-channel neuroprosthesis system is safe and reliable, but its use with rehabilitation training shows no statistically significant difference in walking outcomes.

Key Points

Body weight supported treadmill training combined with functional electrical stimulation can lead to an overall enhancement of walking speed, as well as indicating improvements in walking function.

Results currently suggest that applying stimulation when performing walking training is superior to training without stimulation.

6.2 Transcranial Direct Current Stimulation (tDCS)

Transcranial direct current stimulation (tDCS) is increasingly used in rehabilitation research as a neuromodulatory approach to influence the excitability of cortical and cerebellar networks (Evans et al. 2022). The aim is often to “prime” neural circuits to increase corticospinal activation and to augment effects of MST (Evans et al. 2022). The majority of the studies published on the combination of tDCS and motor rehabilitation is related to upper limb, and studies examining the effects of tDCS on lower limb motor learning in persons with motor-incomplete SCI are still sparse (Kumru et al. 2016b).

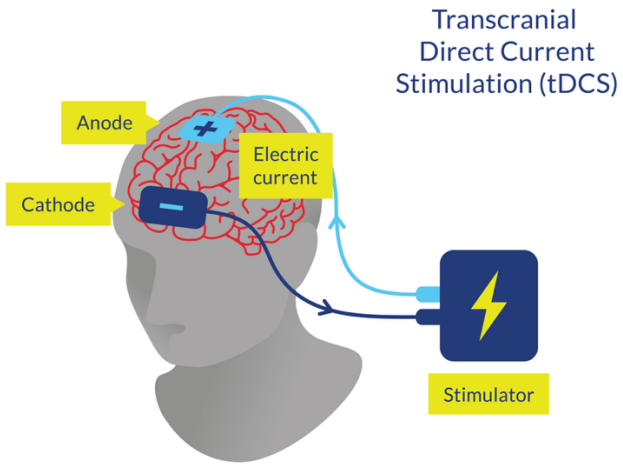


Figure 8. Transcranial Direct Current Stimulation (tDCS)

Table 15. Transcranial Direct Current Stimulation (tDCS)

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Overground Training in Combination With tDCS		
Evans et al. 2022 USA RCT PEDro = 10 Level 1 N = 26	**Population:** 25 participants with chronic motor-incomplete SCI; 18 males and 7 females; mean age 48.6 years; level of injury C4 (n = 9), C5 (n = 7), C6 (n = 2), C7 (n = 4), T6 (n = 1), and T8 (n = 2); AIS C (n = 2) and AIS D (n = 23); and mean time since injury 85.85 months. **Treatment:** Participants were randomly allocated to one of two groups: • MST+tDCS$_{sham}$ group (n = 14). • MST+tDCS group (n = 11). Interventions were carried out during 3 consecutive days and consisted of: • Motor Skill Training (MST): Each of the six motor task activities was performed in	1. AEs included cases of mild-to-moderate headache following tDCS and delayed onset muscle soreness following MST. 2. Analyses revealed a significant effect of the MST circuit, with improvements in walking speed, cadence, bilateral stride length, stronger limb trailing limb angle, weaker limb intralimb coordination, BBS, and FES-I observed in both groups. 3. No differences in outcomes were observed between groups.

	consecutive order and repeated four times as a circuit. Participants were asked to complete as many repetitions as possible in 60 s with the intent to maintain a moderate exercise intensity (40–60% HRR). The MST activities were intended to promote rapid volitional activation and deactivation of lower extremity muscles. • tDCS was delivered via two electrodes for 20 min, which was delivered concurrently with MST. **Outcome Measures:** Overground walking speed (10MWT); spatiotemporal gait characteristics (cadence and stride length), peak trailing limb angle and intralimb coordination (this kinematic data was obtained during each 10MWT using a 3D inertial measurement unit motion capture system). Outcomes were assessed at baseline on Day-1 and 24-h post-intervention on Day-5. To examine within-day (online) and between-day (offline) effects of intervention on outcome measures associated with walking, a subset of selected outcomes was assessed pre- (D2pre, D3pre, D4pre) and post-intervention (D2post, D3post, D4post) on each intervention day.	
Evans & Field-Fote 2022 USA RCT PEDro = 10 Level 1 N = 26	**Population:** 25 participants with chronic motor-incomplete SCI; 18 males and 7 females; mean age 48.6 years; level of injury C3-C8 (n = 22) and T1-T10 (n =3); AIS C (n = 2) and AIS D (n = 23); and mean time since injury 85.85 months. **Treatment:** Participants were randomly allocated to one of two groups: • MST + $tDCS_{sham}$ group (n = 14). • MST + tDCS group (n = 11).	1. AEs included cases of mild-to-moderate headache following tDCS, and delayed onset muscle soreness and skin irritation following MST. 2. There was a significant effect of TIME on walking speed, $p < 0.001$; but without GROUP nor TIME × GROUP interaction. 3. There was a significant effect of TIME on walking distance, $p < 0.001$, but without GROUP nor TIME x Group interaction.

	Intervention protocol was the same as Evans et al. (2022). **Outcome Measures:** Overground walking speed (10MWT); total walking distance (measured by 2MWT); and spatiotemporal gait characteristics (cadence, stride length, step length, and step symmetry index) were assessed at baseline (day 1) and 24 hours after the last day of intervention (day 5).	4. There was a significant effect of TIME on cadence, $p < 0.001$, stronger limb stride length, $p < 0.001$, and weaker limb stride length, $p < 0.001$; but without effects of GROUP or TIME × GROUP interaction. Additionally, no changes in symmetry index were observed.
Klamruen et al. 2024 Thailand RCT PEDro = 8 Level 1 N = 34	**Population:** 34 participants with SCI and the ability to walk at least 15 m independently (with or without a walking device): • Anodal Group (n=17): Mean (SD) age: 41.88 (13.50) years; 13M, 4F; etiology: Traumatic (n=13) and non-traumatic (n=4); ASIA: ASIA C (n=7) and ASIA D (n=10); level of injury: Tetraplegia (n=8) and paraplegia (n=9); and median (IQR Q1-Q3) time since injury: 17.0 (8.0-22.50) months. • Sham Group (n=17): Mean (SD) age: 48.41 (13.36) years; 12M, 5F; Etiology: Traumatic (n=12) and non-traumatic (n=5); ASIA: ASIA C (n=5) and ASIA D (n=12); Level of injury: Tetraplegia (n=9) and paraplegia (n=8); and Median (IQR Q1-Q3) time since injury: 12.0 (12.0-16.0) months. **Treatment:** Participants were randomly assigned into one of the following two groups: • Anodal Group (n=17): Anodal tDCS was administered over the vertex (lower-limb motor area) at an intensity of 2 mA for 20 min while sitting. • Sham Group (n=17): Participants received the delivered current only for the first 30 seconds before it was automatically terminated, and the electrodes remained on	1. No serious AEs of tDCS were observed. The anodal group reported itching (42% of participants) and tingling (44% of participants) sensations only during the stimulation period. The sham group reported itching sensations a moment after starting stimulation, which disappeared after a few (1-2) minutes of stimulation. 2. 10MWT: a. For fast speed, within-group differences were shown for the anodal (P < .001) and sham (P = .001) groups. The mean (95% CI) between-group differences in change scores favored the anodal group at POST (0.10 m/s (0.02 to 0.17), P = .006), 1M (0.11 m/s (0.03 to 0.19), P=.002), and 2M (0.11 m/s (0.03 to 0.20), P = .001). b. For self-selected speed, the median (95% CI) between-group differences in change scores favored the anodal group at POST (0.10 m/s, (0.06 to 0.14), P < .001) and 2M (0.09 m/s, 95% CI (0.01 to 0.19), P = .049). 3. Stride length, stride duration, and cadence: a. For stride length, the median (95% CI) between-group differences in change scores favored the anodal group at POST (0.07 m, (0.01 to 0.14), P = .041). b. For stride duration, changes over time in the anodal (P = .005) and

	the participant's head for 20 minutes. After tDCS, all participants underwent OGT at a moderate intensity (RPE level of 5). The total gait training time was 40 minutes. The intervention program was administered for 5 consecutive days. **Outcome Measures:** 10MWT (at self-selected and fast speeds); spatiotemporal gait parameters using the inertial wireless sensor device (the BTS G-WALK) attached to the fifth lumbar spinous process with a belt for assessing cadence, stride length, and stride duration; TUG test, FTSTS test; and WHOQOL-BREF were assessed at pre-intervention (PRE), immediately post the 5 sessions on the same day (POST), at 1-month follow-up (1M), and at 2-month follow-up (2M).	sham (P = .030) groups were shown; however, no between-group differences were found for all time points. c. For cadence, changes over time in the anodal (P = .020) and sham (P = .004) groups were shown; however, no between-group differences were found for all time points. 4. For FTSTS test, changes over time in the anodal (P = .002) and sham (P = .040) groups were shown; however, no between-group differences were found for all time points. 5. Subgroup analysis: a. The subgroup analysis of time since injury showed that in participants with post-injury >12 months, the anodal group had greater improvements in fast speed, self-selected speed, and stride length than the sham group. For fast speed, the median (95% CI) between-group differences in change scores favored the anodal group at POST (0.06 m/s, (0.01 to 0.25), P=.043), 1M (0.13 m/s, (0.01 to 0.24), P = .028), and 2M (0.13 m/s, (0.01 to 0.24), P = .028). For self-selected speed, the median differences (95% CI) favored the anodal group at POST (0.10 m/s, (0.04 to 0.15), P = .001) and 2M (0.12 m/s, (0.01 to 0.25), P = .043). For stride length, the median (95% CI) between-group differences in change scores favored the anodal group at POST (0.08 m (0.02 to 0.20), P = .006). However, in participants with post-injury <12 months, the median (95% CI) between-group differences in self-selected speed favored the anodal group only at POST (0.10 m/s, (0.04 to 0.18), P = .004).

		b. The subgroup analysis by injury level showed that in participants with tetraplegia, the anodal group showed greater improvements in fast and self-selected speed than the sham group. For fast speed, the median (95% CI) between-group differences in change scores favored the anodal group at POST (0.14 m/s (0.03 to 0.26), P = .006), 1M (0.16 m/s (0.04 to 0.29), P = .011), and 2M (0.14 m/s (0.05 to 0.25), P = .036). For self-selected speed, the median differences (95% CI) favored the anodal group at POST (0.15 m/s (0.04 to 0.18), P = .002) and 2M (0.13 m/s (0.01 to 0.31), P = .027). However, in participants with paraplegia, the median (95% CI) between-group differences in self-selected speed favored the anodal group only at POST (0.08 m/s (0.05 to 0.12), P < .001). No significant between-group differences were observed for the other outcome measures.
BWSTT in Combination With tDCS in Patients With Acute – Subacute SCI		
Kumru et al. 2016b Spain RCT PEDro = 8 Level 1 N = 24	**Population:** 24 patients with incomplete motor SCI who were candidates for Lokomat®; 16 males and 8 females; mean age 51.3 years; AIS C (n = 20) and AIS D (n = 4); level of injury C1 (n = 1), C3 (n = 2), C4 (n = 8), C5 (n = 1); C7 (n = 2), C8 (n = 1), T3 (n = 3), T4 (n = 1), T5 (n = 1), T6 (n = 1), T10 (n = 1), T11 (n = 1), and T12 (n = 1); and mean time since injury 4.1 months. **Treatment:** All participants received standard care (5 h of therapy a day, 5 days per week) for SCI rehabilitation. Participants also received 20-min tDCS sessions (5 days per week for 4 weeks) during the Lokomat gait rehabilitation session; and they were randomly divided into:	1. All patients tolerated the study without complications. 2. At baseline, two of the 12 patients with SCI could perform 10MWT and five patients during follow-up period in both groups. 3. Gait velocity, cadence, step length, and WISCI II were not different between anodal vs. sham tDCS group neither after four weeks of tDCS, nor during follow-up (p > 0.1 for all comparison). 4. LEMS was 20.5 ± 9.2 at baseline and improved to 23.9 ± 9.0 after last anodal tDCS (p < 0.03) and in sham tDCS it was 18.7 ± 10.3 at baseline and also improved to 22.8 ± 11.4 after last session (p < 0.03).

	• Anodal tDCS (n = 12): The anode was placed over the leg motor cortex (vertex) and the cathode over the non-dominant supraorbital area. • Sham tDCS (n = 12). Lokomat® gait training sessions were performed 5 days per week, 30 min per day for 8 weeks. **Outcome Measures:** LEMS, 10MWT (time, step length and cadence), and WISCI II were assessed at baseline, after 4 weeks of training (at the last session of tDCS), and after 8 weeks of training (follow-up 4 weeks after cessation of tDCS).	However, after four weeks of tDCS changes score were not significant between groups (3.4 ± 4.4 for anodal tDCS; 4.1 ± 3.2 for sham) (p = 0.68).
BWSTT in Combination with tDCS in Patients With Chronic SCI		
Simis et al. 2021 Brazil RCT PEDro = 9 Level 1 N = 43	**Population:** 43 participants with incomplete SCI; 33 males and 10 females; median (IQR) age 38 (28-45) years; injury level paraplegic (n = 28) and tetraplegic (n = 15); AIS C (n = 20) and AIS D (n = 23); and median (IQR) time since injury 16 (6.5-23.5) months. **Treatment:** Participants were randomly allocated to receive 30 sessions of active (n = 21) or sham (n = 22) tDCS immediately before RAGT with Lokomat. All participants received 20-min tDCS sessions; 30-min sessions of Lokomat training; and their normal rehabilitation program. • During RAGT sessions, the participant body weight, guidance force and training speed were progressively incremented depending on each participant. • tDCS was performed using a monophasic current device with the anode placed over the primary motor cortex region and the cathode placed over the supraorbital	1. All the participants tolerated tDCS sessions, without unexpected AEs. One participant did not tolerate Lokomat training due to pain related to the straps of the BWS mechanism and was excluded from the study. 2. At post-treatment, there was a statistically significant difference in the percentage of participants that improved in WISCI II (33% in the sham group vs. 70% in the active group) (p = 0.046); and in the follow-up, there was also statistically significant difference in the changes for the two groups (p = 0.046). 3. Regardless of intervention group, statistical improvement existed between baseline and the other periods as measured by 10MWT and 6MWT. 4. Regarding the improvement in the 10MWT, and 6MWT, there was no statistical difference between groups for the tested periods.

	region, contralateral to the anode. **Outcome Measures:** WISCI II; BBS; 10MWT; 6MWT; and Lower Extremity Isokinetic Dynamometry were assessed before the beginning of the intervention (baseline), after 15 sessions (intermediate), after 30 sessions (post-treatment) and three months after treatment (follow-up).	
Raithatha et al. 2016 USA RCT PEDro = 9 Level 1 N = 15	**Population:** 15 participants with traumatic SCI; 10 males and 5 females; mean (range) age 47.5 (24 – 67) years; level of injury C4 (n = 1), C5 (n = 1), C5-C6 (n = 1), C6 (n = 5), C8 (n = 1), T2 (n = 1), T6 (n = 2), T12 (n = 1), and L1 (n = 2); AIS B (n = 1), AIS C (n = 11) and AIS D (n = 3); and mean (range) time since injury 7.9 (1 – 39) years. **Treatment:** All participants attended to 36 sessions (3/week for 12 weeks) of tDCS immediately before LT with a robot-assisted gait orthosis (LT-RGO). They were randomly allocated into 2 groups: • Active anodal tDCS paired with LT-RGO (active group, n = 9). • Sham tDCS paired with LT-RGO (control group, n = 6). tDCS*:* Each participant in the active tDCS group received 20 min of tDCS. *LT-RGO:* The Lokomat was used with a novel approach to LT-RGO (with progressively decreased treadmill speed and guidance force in order to minimize momentum and thereby avoid eliciting passive movement). **Outcome Measures:** Muscle strength (assessed by MMT) of hips (flexion, extension, abduction, adduction, internal and external rotation), knees (flexion, extension), ankles (dorsiflexion, plantarflexion), great toes (flexion, extension), and toes (flexion, extension); 10MWT; 6MWT; were assessed at baseline, post-intervention, and 1-month follow-up timepoints.	1. There were no AEs during the intervention period. 2. Within-group changes from baseline to post- intervention indicated overall improvement on all outcome measures for both groups. Statistically significant improvement was evident on MMT (both lower extremities) in the active tDCS group and for the left lower extremity in the sham tDCS group. Within-group changes from baseline to 1-month follow-up indicated significant improvement on MMT (both lower extremities), 10MWT, and 6MWT only for the active tDCS group. 3. Between-groups comparison of changes from baseline to post-intervention revealed that the active group improved significantly more than the sham group on MMT (right lower extremity). However, the sham tDCS group improved significantly more than the active tDCS group on 6MWT. Between-groups comparison of changes from baseline to 1-month follow-up revealed significantly greater improvements in MMT (right lower extremity) for the active tDCS group.

Discussion

Two high-quality studies (Evans et al. 2022; Evans & Field-Fote 2022) found that locomotor-related MST, with and without tDCS, provided significant increases in overground walking speed (10MWT), walking distance (2MWT), cadence, and bilateral stride length, but the addition of tDCS was not associated with greater improvements compared with the sham application. Another high-quality RCT (Klamruen et al. 2024) found that both anodal tDCS and sham tDCS groups showed similar significant improvements in gait kinematics (stride length, stride duration, and cadence), lower extremity strength (FTSTS test), and self-selected speed (10MWT); however, higher improvements were observed in the experimental group for walking speed (10MWT) (Klamruen et al. 2024). Similarly, other studies, such as the RCT by Nijhawan and Kataria (2024), had shown similar significant improvements in LEMS after an active or sham tDCS application for five sessions per week over two weeks (plus conventional rehabilitation) in participants with chronic SCI.

The combination of gait training with tDCS in patients with neurological disorders has been systematically reviewed by Hernández de Paz et al. (2019), but only two reports included patients with SCI (Kumru et al. 2016b; Raithatha et al. 2016), while the others studied patients with stroke or Parkinson's disease. Three high-quality studies assessed the effects of the combination of tDCS and BWSTT in patients with motor-incomplete SCI, one of them in an acute–subacute phase (Kumru et al. 2016b), and two in a chronic phase (Simis et al. 2021; Raithatha et al. 2016). Kumru et al. (2016b) included patients with a mean time since injury of 4.1 months who received standard care for SCI rehabilitation and 20-min tDCS sessions during BWSTT with Lokomat, 5 days per week, 30 min per day. Patients were randomly allocated to the anodal tDCS or sham application of tDCS group (Kumru et al. 2016b). After 4 weeks of intervention and 4 weeks of follow-up, both groups significantly improved in lower extremity motor strength (LEMS) and gait function (10MWT and WISCI II), but without significant differences between the tDCS and the sham application (Kumru et al. 2016b). In the RCT of Simis et al. (2021), patients with chronic SCI, participants received 20 min of active or sham tDCS immediately before BWSTT with Lokomat for 30 min. After 30 sessions, there was a statistically significant difference in the percentage of participants that improved in WISCI II (33% in the sham group vs. 70% in the active group) and in the follow-up; however, other outcome measures related to walking (10MWT and 6MWT) improved significantly across participants, without statistical differences between groups after 30 sessions or after 3 months of follow-up (Simis et al. 2021). Similarly, Simis et al. (2020) aimed to investigate electroencephalography beta oscillations in the sensorimotor area as a novel biomarker for gait function and response to the same treatment as Simis et al. (2021). The results suggested that beta oscillations could be used as a diagnostic, predictive, and surrogate biomarker in SCI for gait function (Simis et al. 2020). These findings have great rehabilitative potential for patients with SCI, as they can help design therapy based on consistent predictors of positive responses to gait training and tDCS (Simis et al. 2020). Moreover, it can support the decision about the number of sessions and the adequate moment of discharge based on a surrogate outcome, making therapy more cost-effective (Simis et al. 2020). Lastly, the study of Raithatha et al. (2016) was the very first to evaluate the effects of combining tDCS with LT to facilitate gait recovery for people with incomplete and chronic SCI. Patients were randomly allocated into two

groups: 20 min of tDCS (active or sham) immediately before LT with Lokomat (Raithatha et al. 2016). While both groups showed improvement in motor function after 12 weeks of intervention and at long-term follow-up, the active tDCS group showed more improvement in MMT than the sham tDCS group (Raithatha et al. 2016). Walking outcomes (6MWT and 10MWT) results were contradictory, as within-group changes from baseline to 1-month follow-up indicated significant improvement on 10MWT and 6MWT only for the active tDCS group, while between-group comparison of changes from baseline to post-intervention revealed that the sham tDCS group improved significantly more than the active tDCS group on 6MWT (Raithatha et al. 2016).

It should be noted that tDCS seems to be a feasible and safe intervention. Studies of Klamruen et al. (2024), Kumru et al. (2016b), Raithatha et al. (2016), and Simis et al. (2021) stated that all patients tolerated the intervention with no complications; and only Evans et al. (2022) and Evans and Field-Fote (2022) found that four participants in the active tDCS group (n = 14) had mild-to-moderate poststimulation headache related to the tDCS intervention (but it was not stated if the AE occurred in the active or the sham group).

Conclusions

There is level 1 evidence (from 2 RCTs: Evans et al. 2022; Evans & Field-Fote 2022) that a brief intensive MST involving a circuit of ballistic, cyclic locomotor-related skill activities improved overground walking speed (10MWT), walking distance (2MWT), cadence, and bilateral stride length; however, concurrent application of tDCS did not further enhance the effects of MST in patients with motor-incomplete SCI.

There is level 1 evidence (from 1 RCT: Klamruen et al. 2024) that anodal or sham tDCS in a sitting position prior to OGT at moderate intensity for five days provide similar improvements in gait kinematics (stride length, stride duration, and cadence), lower extremity strength (FTSTS test), and self-selected speed (10MWT); but higher improvements in walking speed (10MWT) for the anodal tDCS, in patients with incomplete and chronic SCI.

There is level 1 evidence (from 1 RCT: Kumru et al. 2016b) that 4 weeks of BWSTT with Lokomat and standard care improved lower extremity motor strength (LEMS) and gait function (10MWT and WISCI II); however, concurrent application of tDCS did not further enhance the effects of BWSTT in patients with motor-incomplete and acute SCI.

There is level 1 evidence (from 2 RCTs: Simis et al. 2021; Raithatha et al. 2016) that the application of tDCS immediately before BWSTT with Lokomat significantly improved more the walking ability (WISCI II) and lower extremity motor function (MMT), and similarly the walking speed (10MWT) and walking distance (6MWT) compared to the same intervention but with a sham stimulation in patients with motor-incomplete and chronic SCI.

Key Points

Concurrent application of transcranial direct current stimulation (tDCS) does not seem to further enhance the effects on walking and strength outcomes of motor skill training, overground gait training, or body weight supported treadmill training in patients with motor-incomplete SCI.

6.3 Repetitive Transcranial Magnetic Stimulation (rTMS) and Paired Corticospinal-Motoneuronal Stimulation (PCMS)

Repetitive transcranial magnetic stimulation (rTMS) has been widely explored as a tool for treating a variety of disorders, including depression (Martin et al. 2003; Couturier et al. 2005), pain (Lima & Fregni 2008), and motor disorders following Parkinson's disease (Elahi et al. 2009) and stroke (Corti et al. 2011). Experimental studies in humans have shown that low-frequency rTMS (<1 Hz) can reduce the excitability of the motor cortex whereas high-frequency rTMS (>1 Hz) causes an increase in motor cortical excitability (Kobayashi & Pascual-Leone 2003). Given the ability for rTMS to modulate cortical excitability, there has been much interest in exploring its potential to facilitate supraspinal connectivity as a means to promote motor recovery and function. The recovery of functional ambulation, following motor-incomplete SCI, has been shown to be associated with enhanced excitability of motor cortical areas (Winchester et al. 2005) and corticospinal connectivity to the lower limb (Thomas & Gorassini 2005).

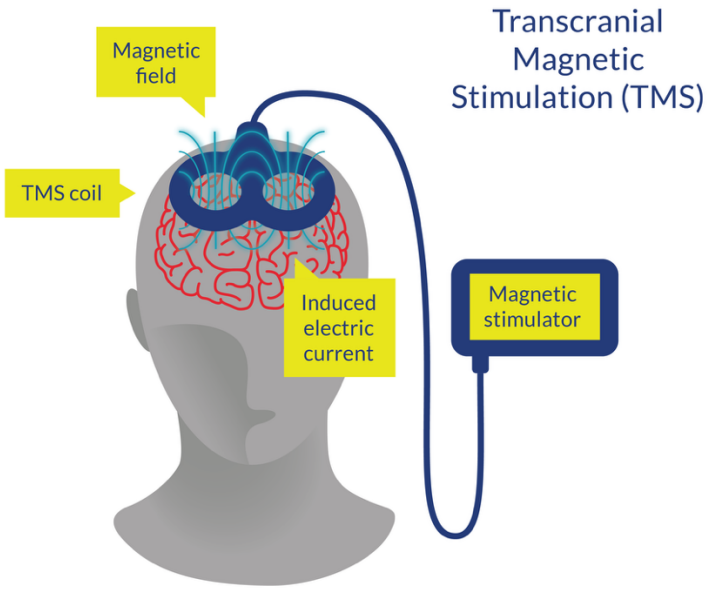


Figure 9. Transcranial Magnetic Stimulation (TMS)

Table 16. Repetitive Transcranial Magnetic Stimulation (rTMS) and Paired Corticospinal-Motoneuronal Stimulation (PCMS)

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Nogueira et al. 2024 Brazil RCT PEDro = 9 Level 1 N = 15	**Population:** 15 participants with chronic and incomplete SCI. • Experimental group: 4M, 3F Mean (SD) age: 38.4 (11.25) years. AIS C (n = 5) and D (n = 2). Mean (SD) time since injury: 6.4 (2.20) years. • Control group: 4M, 3F Mean (SD) age: 33.3 (10.53) years. AIS C (n = 2) and D (n = 6). Mean (SD) time since injury: 6 (4.31) years. **Treatment:** Participants were randomized to the BWSTT/rTMS real (*n* = 7) and BWSTT/rTMS sham groups (*n* = 8). • rTMS protocol: rTMS was applied with participants seated in a comfortable chair, at rest. A rTMS protocol was applied to improve sensorimotor function in incomplete SCI: a total of 1800 pulses (40 pulses, 45 train) delivery at 10 Hz of frequency, through an intensity of 90% resting motor threshold, and intertrain intervals of 28 s. For sham rTMS, participants were exposed to rTMS sounds to mimic the auditory effects of the activity, and the coil, disconnected from the stimulator, was held over Cz for 20 min. • BWSTT protocol: Immediately after the rTMS protocol, participants were forwarded to the BWSTT. The BWSTT was performed on a medical treadmill with a partial body weight-suspension system. The treadmill provided visual feedback on the real-time stride length. Visual feedback was provided through a mirror placed in front of the	1. WISCI II: a. When compared to baseline (median (IQR): 9 (7 to 9)), the median values of WISCI II increased significantly after the 6th (median (IQR): 11 (8.5 to 14.5)) and 12th (median (IQR): 13 (10 to 14.5)) sessions and follow-up (median (IQR): 13 (10 to 14.5)) in the BWSTT/rTMS real group (P = 0.001), but not in the BWSTT/rTMS sham group (P = 0.053) (baseline: median (IQR): 12 (8 to 13)); 6th (median (IQR): 12.5 (8 to 14.5)); 12th (median (IQR): 14 (8 to 16.7)); follow up (median (IQR): 14 (8 to 16.7)). The change in median values after the 6th session was significantly higher in the BWSTT/rTMS real group than in the BWSTT/rTMS sham group (P = 0.028). However, there was no significant difference between the real and sham groups after the 12th session and 30-day follow-up. b. 6th session was higher in the BWSTT/rTMS real (n = 7) (median change (IQR): 3 (1.5 to 3.5)) than in the sham group (n = 8) (median change (IQR): 0 (0 to 0.25), but there was no difference between groups after 12th session

	participant during training to maintain step symmetry and control postural compensation. Each BWSTT session consisted of two series of 7.5 min each (until the 6th session) or 10 min (from the 7th to 12th session), with about 3 min breaks between series. In the first training session, a trained therapist selected the appropriate percentage of BWS and velocity, based on individual motor impairment and exercise tolerance. During BWSTT, two therapists provided manual assistance to the lower limbs. Participants were encouraged to target level in the range of 11–13 (moderate intensity) of RPE. **Outcome Measures:** WISCI II was measured at baseline, after the 6th and 12th sessions, and on follow-up (30 days after the end of intervention). LEMS and SCIM-III were measured at baseline, after the 12th session, and at the 30-day follow-up.	(BWSTT/rTMS real median change (IQR): 4 (2 to 5); BWSSTT/rTMS sham median change (IQR): 0 (0 to 3.25). 2. Compared to baseline, the LEMS increased after 12 sessions in the BWSTT/rTMS real group (P = 0.013), but no significant difference was observed in the sham group (P = 0.200). There was no significant difference between the groups in terms of the median changes at the 12th session and at the 30-day follow-up. 3. The SCIM-III mobility score was increased after 12 sessions in the BWSTT/rTMS real group (P = 0.026), but no significant difference was observed in the sham group (P = 0.444). The change in the median SCIM-III mobility sub-score was significantly higher in the rTMS group than in the sham group at the 30-day follow-up (P = 0.029).
Deng et al. 2024 China RCT PEDro = 7 Level 1 N = 30	**Population:** 30 participants with acute and incomplete SCI. • Sham group (n = 15): 11M, 4F Mean (SD) age: 52.58 (14.02) years. AIS C (n = 10) and AIS D (n = 5) Mean (SD) time since injury: 2.1 (1.1) months. • iTBS group (n = 15): 8M, 7F Mean (SD) age: 47.42 (17.22) years. AIS C (n = 9) and AIS D (n = 6) Mean (SD) time since injury: 1.7 (0.9) months. A total of 10 patients were included who could walk with the aid of a walker, with 5 in the sham group and 5 in the iTBS group.	1. Comparison of Maximum Knee Flexor Strength, Knee Extensor Strength, and LEMS Between the Two Groups: On the 21st day of treatment, the maximum knee flexor strength, the maximum knee extensor strength, and LEMS in the iTBS group were higher than that in the sham group (median [IQR], 20 (14-23) vs. 14 (12-17), z = -2.764, P = 0.006), (median [IQR], 59 (24~64) vs. 33(17~37), z = -2.408, P = 0.016), and (median [IQR], 38 (37-47) vs. 25 (18-26), z = -2.391, P = 0.017), respectively. 2. Comparison of SCIM in the Sham Group and the iTBS Group Before and After Treatment: In intragroup

	Treatment: Patients were randomly assigned to the iTBS group (n = 15) and the sham group (n = 15). • The iTBS group received intermittent theta burst stimulation (iTBS) double-target stimulation (the central cerebral sulcus and the nerve root of the spinal cord injury segment – a form of TMS). iTBS parameter selection: intraplexus stimulation frequency 50 Hz, interplexus stimulation frequency 5 Hz, stimulation intensity 80% - 120% rest motor threshold, stimulation time 2 s, intermittent time 8 s, a total of 600 pulses, total time 192 s, 6 days per week, and the treatment cycle is 21 days. The sequence of treatment was central sulci stimulation first and then stimulation at the nerve root of the spinal cord injury segment. • Patients in the sham group received iTBS dual-target sham stimulation therapy (dummy coils rather than treatment coils). After the iTBS (real or sham) intervention, patients received conventional rehabilitation treatment, including trunk control training, sitting training, balance exercise and gait training, proprioceptive neuromuscular facilitation techniques, related physical factor therapy, occupational therapy, lower limb exoskeleton robot training, and other routine rehabilitation training that lasts for more than 3 hours per day, with a treatment cycle of 21 days. **Outcome Measures:** LEMS, SCIM-III, isokinetic muscle strength assessment (knee flexor strength and knee extensor strength in both lower limbs), patient's gait evaluated by the 3D gait analysis evaluation system (if the patient can walk independently or with a walking frame) were measured before treatment, on the third day of treatment and on the 21st day of treatment.	comparison, SCIM scores in the sham group and the iTBS group on the 21st day of treatment were higher than those before treatment (sham group, $\chi^2 = 29.525$, $P < 0.001$; iTBS group, $\chi^2 = 25.200$, $P < 0.001$). In the comparison between the 2 groups, after 21 days of treatment, SCIM scores in the iTBS group were significantly higher than those in the sham group (median [IQR]; 68(60~91) vs. 46 (30~75), $z = -2.287$, $P = 0.022$). 3. Comparison of Gait Parameters Before and After Treatment Between the Two Groups: a. The results showed that there were no statistically significant differences between the 2 groups in step speed, step frequency, and step length before treatment ($P > 0.05$), and after treatment, these indexes were increased compared with before, with statistical significance ($P < 0.05$). After 21 days of treatment, the step frequency and step length in the iTBS group were significantly higher than that in the sham group (69.00 ± 2.91 vs. 53.00 ± 3.39, $t = -8.000$, $P < 0.001$) and (40.20 ± 1.92 vs. 32.40 ± 2.41, $t = -5.659$, $P < 0.001$), respectively. b. The ground reaction force of the 2 groups were collected and compared using a 3D gait analysis system. The results showed that on the 21st day of treatment, the vertical reaction in the iTBS group was significantly higher

		than that in the sham group (median [IQR]; 78 (75.5~79) vs. 70(65.5~74), z = -2.522, P = 0.012).
Krogh et al. 2022 Denmark RCT PEDro = 7 Level 1 N = 20	**Population:** 20 participants with motor-incomplete SCI and capable of participating in lower limb RT; 15 males and 4 females; mean age 54.45 years; injury level C2 (n = 2), C4 (n = 4), C5 (n = 4), C8 (n = 1), T3 (n = 1), T9 (n = 1), T10 (n = 1), T11 (n = 1), T12 (n = 1), L1 (n = 1), and L2 (n = 2); AIS A (n = 1), AIS C (n = 5), and AIS D (n = 13); and mean time since injury 89.3 days. **Treatment:** All participants received lower limb RT (twice weekly) and lower limb physical therapy (thrice weekly) for 4 weeks; and were randomly assigned to receive active (REAL group) (n = 11) or sham (SHAM group) (n = 9) rTMS with a double-cone coil over bilateral leg motor cortex, daily (Monday–Friday) immediately before training sessions. • Lower limb resistance sessions lasted 60 min and strength exercises, for each major functioning muscle group, were performed (3 x 10 at moderate to vigorous [50–80% 1RM] loading intensity). • Lower limb physical training included stair climbing and mobility exercises, overground training, BWSTT, FES, and stretching/mobilization. Participants were engaged in additional clinical activities as part of their usual care, such as hydrotherapy, occupational therapy, activities of daily living training, and upper extremity RT classes. **Outcome Measures:** MVC, LEMS, and gait function* (10MWT and 6MWT) were assessed the day before the first rTMS session and the day after the last session; except for LEMS assessment, which was performed at admission and within 1 week of discharge. *Gait function was assessed in a sub-group of ambulators (REAL group, n = 8; SHAM group, n = 8).	1. A seizure during stimulation (n = 1 in REAL group) and mild and transitory headaches following their first treatment session (n = 2 in SHAM group) were reported as AEs. Apart from that, only harmless side effects such as drowsiness, twitching facial muscles, and tingling/poking sensations in the scalp were occasionally reported. 2. Total leg (sum of bilateral MVC in both directions), knee flexor, and knee extensor MVC increased more prominently in REAL compared to SHAM, although no clear main effect for real rTMS was found for any MVC outcome measure ($p > 0.15$). 3. LEMS increased significantly ($p = 0.014$) for REAL but not for SHAM at the time of discharge. 4. Both groups demonstrated significant ($p < 0.02$) improvements in 10MWT at POST, with no difference in progression between groups ($p = 0.16$). 5. Both groups improved in the 6MWT at POST with no clear main effects (treatment: $p < 0.76$, treatment x time: $p < 0.90$, time: $p < 0.76$).

Kumru et al. 2016a Spain RCT PEDro = 7 Level 1 N = 31	**Population:** 31 patients with incomplete motor SCI who were candidates for Lokomat®; 24 males and 7 females; mean age 47.55 years; AIS C (n = 26) and AIS D (n = 5); level of injury cervical or thoracic; and mean time since injury 3 months. **Treatment:** All participants received standard care for SCI rehabilitation (5 h of therapy a day, 5 days per week). Participants also received rTMS applied at rest on their back (for 4 weeks) just before the Lokomat® gait training session; and they were randomly divided into: • Real rTMS (n = 15): 2-s duration bursts of 20 Hz (40 pulses/burst) with intertrain intervals of 28 s, for a total of 1800 pulses over 20 min. • Sham rTMS (n = 16). Lokomat® gait training sessions were 30-45 min of duration, 5 days per week, and for 8 weeks **Outcome Measures:** LEMS, 10MWT (time, step length and cadence), and WISCI II were assessed at baseline, after 4 weeks of training (at the last session of rTMS), and after 8 weeks of training (follow-up 4 weeks after cessation of rTMS).	1. Thirty-four participants were included in this study, but 3 of them didn't continue with the study because of repeated urinary tract infections (n = 1) and severe spasticity (n = 2). 2. All participants tolerated well the study. The participants in real rTMS reported only mild undesired effects (slightly uncomfortable twitching of facial muscles or difficulty to speak because of facial muscle contraction during real rTMS [n = 8], and mild headache 1 h after the first rTMS session [n = 1]). 3. After last session and during follow-up period, the number of the participants who could perform 10MWT was higher for real than for sham rTMS, but it did not reach statistical significance (p = 0.09). 4. The gait velocity, cadence, step length, and WISCI II were similar in real vs. sham rTMS group after last stimulation and during follow-up (p > 0.05). 5. The change score in LEMS was significantly higher in real than in sham rTMS after last session (p = 0.001) and during follow-up period (p = 0.02).
Jo & Perez 2020 USA RCT PEDro = 4 Level 2 N = 38	**Population:** 38 participants with chronic SCI; 29 males and 9 females; mean age (± SD) 44.2 (± 14.8) years; injury level C2 (n = 1), C3 (n = 4), C4 (n = 11), C5 (n = 12), C6 (n = 3), T5 (n = 1), T8 (n = 1), T10 (n = 1), L1 (n = 1), L2 (n = 2), and L3 (n = 1); AIS A (n = 12), AIS B (n = 6), AIS C (n = 11), and AIS D (n = 9); and mean time since injury 9.4 years. **Treatment:** 25 participants were randomly assigned to 10 sessions (completed in 2-3 weeks) of exercise combined with paired corticospinal-motor neuronal stimulation (PCMS) (n = 13) or sham-PCMS (n = 12). In an	1. The time to complete the 10MWT decreased significantly on average by 20% after all protocols. 2. The amplitude of corticospinal responses elicited by TMS and the magnitude of MVCs in targeted muscles increased on average by 40–50% after PCMS combined or not with exercise but not after sham-

	additional experiment, 13 participants received PCMS without exercise. During PCMS, 180 pairs of stimuli were timed to have corticospinal volleys evoked by TMS over the primary motor cortex arrive at corticospinal-motor neuronal synapses of upper- or lower-limb muscles (depending on the injury level), 1–2 ms before antidromic potentials were elicited in motor neurons by ES of a peripheral nerve. PCMS and sham-PCMS participants exercised for 45 min immediately after both protocols, which involved: • Upper-limb exercises (n = 31). • Lower-limb exercises (involving OWT and BWSTT, and stair climbing) for 2 participants in the PMCS + exercise group; for 2 participants in the sham + exercise group; and for 3 participants in the PCMS group. **Outcome Measures:** • Motor evoked potentials and MVCs were assessed before and after each intervention. • A subset of participants completed functional tasks (PCMS + exercise: n = 6; sham-PCMS + exercise: n = 8; PCMS: n = 8). In the group receiving lower-limb exercises, 10MWT with BWS was assessed before and after the intervention. A subgroup of participants returned for a 6-month follow-up session to examine the same measurements (PCMS + exercise: n = 5, sham-PCMS + exercise: n = 5).	PCMS combined with exercise: 3. Motor evoked potentials and MVCs increases were preserved 6 months after the intervention in the group receiving exercise with PCMS but not in the group receiving exercise combined with sham-PCMS: 4. Functional outcomes remained increased for 6 months in the PCMS + exercise participants (by 21.6 ± 9.6%, P < 0.05) compared with baseline whereas the increase present after 10 sessions of sham-PCMS + exercise did not persist 6 months later (0.6 ± 10.5%, P = 0.3).
Naro et al. 2022 Italy Case control Level 3 N = 40	**Population:** • 15 participants with incomplete and thoracic SCI (> 6 months since injury) and with spasticity; 6 males and 9 females; mean (± SD) age 38 (± 9); level of injury T3 (n = 3), T4 (n = 1), T5 (n = 3), T6 (n = 1), T7 (n = 1), T8 (n = 2), and T9 (n = 4); AIS C (n = 6) and AIS D (n = 9); and mean (± SD) time since injury 10 (± 4) months.	1. There were no side effects during or after the training. 2. The 10MWT, FIM-L, LEMS, and WISCI II improved in both groups, but the increase was significant higher following RAR + NIBS than RAR − NIBS (p = 0.002, p = 0.02, p = 0.005, and p = 0.002, respectively). 3. The 6MWT test improved in both groups, but without

	• 25 matched-SCI persons with spasticity; 11 males and 14 females; mean (± SD) age 44 (± 14); level of injury T3 (n = 4), T4 (n = 2), T5 (n = 3), T6 (n = 6), T7 (n = 2), T8 (n = 4), T9 (n = 2), T10 (n = 2); AIS C (n = 12) and AIS D (n = 13); and mean (± SD) time since injury 12 (± 3) months. **Treatment:** Participants were divided into: • Robot-assisted rehabilitation (RAR) + non-invasive brain stimulation (NIBS) group (n = 15) (RAR + NIBS). • RAR – NIBS group (n = 25): Matched-SCI persons who previously underwent the same amount or RAR without NIBS. Patients were provided with a daily (six sessions weekly) NIBS session followed by a RAR session, for eight consecutive weeks. • NIBS consisted of a rTMS carried out simultaneously with a transvertebral direct current stimulation (tvDCS). • Patients performed a 40-min session per day of RAR with LokomatPro. The amount of BWS was initially set at 70% of the patient's weight, then progressively decreased, and the gait speed was individually adjusted. Patients underwent conventional physical therapy twice a day and five-times a week using the Bobath principles, occupational therapy, and FES. **Outcome Measures:** 6MWT, 10MWT, WISCI II, FIM-L, and LEMS were assessed at baseline (T0), after (T1), and three months after (T2) the training.	significant differences between groups. 4. There was no significant effect of patients' stratification depending on ASIA on clinical outcome measure changes (all p > 0.1). 5. The significant predictors of recovery were the LEMS, age, and time since injury (all p < 0.0001).
Benito et al. 2012 Spain RCT PEDro = 8 Level 1 N = 17	**Population**: 17 participants - 13 males and 4 females; incomplete SCI; all AIS D; level of injury: C4 – T12; age range= 18 – 60y. **Treatment**: Patients were randomized to active rTMS or sham stimulation. Three patients from the initial group of 10 randomized to sham stimulation entered the active rTMS group after a 3-week washout period. Therefore, a total of 10 patients completed each study condition. Both groups were homogeneous for age, gender, time since injury, etiology, and	1. There was a significant improvement in LEMS in the active group but not in the sham group. 2. The active group also showed significant improvements in the Modified Ashworth Score, 10MWT, cadence, step length, and these improvements were maintained 2 weeks later.

	ASIA scale. Active rTMS consisted of 15 days of daily sessions of 20 trains of 40 pulses at 20 Hz and an intensity of 90% of resting motor threshold. rTMS was applied with a double cone coil to the leg motor area. **Outcome Measures:** LEMS, Modified Ashworth Scale, WISCI II, 10MWT, Step length and cadence (assessed during 10MWT).	3. Following sham stimulation, significant improvement was found only for step length.

Discussion

Few studies have investigated the effects of rTMS on walking-related outcomes in patients with acute, subacute, or chronic SCI (Benito et al. 2012; Deng et al. 2024; Krogh et al. 2022; Kumru et al. 2016a; Naro et al. 2022; Nogueira et al. 2024). Two RCTs found the same results; participants who had rTMS plus usual care improved significantly more than those who had sham rTMS and usual care on LEMS, but both groups improved on the 6MWT and 10MWT without statistical differences (Krogh et al. 2022; Kumru et al. 2016a). Benito et al. (2012) found similar results; all participants completed OGT and improved post-training in step length and TUG, but only the participants receiving rTMS improved post-training in LEMS and spasticity reduction.

Lastly, the RCT by Deng et al. (2024) compared real and sham intermittent theta burst stimulation (iTBS) (which is a mode of TMS) dual-target stimulation applied before conventional physical therapy in patients with incomplete and acute SCI. After 21 days of treatment, it was shown that there were statistically significant ($P < 0.05$) differences between groups, favoring the iTBS group, in the muscle strength of the knee flexors and knee extensors, LEMS, SCIM, step length and step frequency, and in the ground reaction force.

On the other hand, in patients with incomplete and chronic SCI, the RCT by Nogueira et al. (2024) compared a rTMS protocol followed by BWSTT (with visual feedback on the real-time stride length, provided through a mirror to maintain step symmetry and control postural compensation) for 12 sessions with the same intervention but with a sham rTMS application. After the 12th session, there was no difference between groups in walking independence (WISCI II) (Nogueira et al. 2024). Additionally, compared to baseline, LEMS and SCIM-III mobility scores were increased after 12 sessions in the BWSTT/rTMS real group but not in the sham group (Nogueira et al. 2024). The authors also showed that WISCI II scores after the 6th session were higher in the BWSTT/rTMS real than in the sham group; suggesting that combining BWSTT with rTMS could lead to earlier gait improvement in patients with chronic incomplete SCI.

It should be noted that rTMS seems to be safe; however, there were some side effects during the trials. Krogh et al. (2022) reported that one patient in the real stimulation group dropped out due to a seizure during stimulation, and two participants in the sham stimulation group reported mild and transitory headaches following their first treatment session. Kumru et al. (2016a) and Benito et al. (2012) stated that all participants tolerated the interventions, with the participants in real rTMS reported only mild undesired effects (slightly uncomfortable twitching of facial

muscles or difficulty to speak because of facial muscle contraction during real rTMS [n = 8 and n = 6, respectively], and mild headache one hour after the first rTMS session [n = 1 and n = 0, respectively]).

Conclusions

There is level 1 evidence (from 2 RCTs: Krogh et al. 2022; Kumru et al. 2016a) that the application of rTMS immediately before lower limb training sessions or BWSTT with Lokomat provides significant improvements in LEMS, but similar improvements in walking-related outcomes (6MWT and 10MWT) compared with the same intervention but with a sham rTMS application in participants with motor-incomplete and acute SCI.

There is level 1 evidence (from 1 RCT: Benito et al. 2012) that rTMS before overground LT provides significant improvements in lower limb strength (LEMS) and walking speed (10MWT) in patients with motor-incomplete SCI.

There is level 1 evidence (from 1 RCT: Deng et al. 2024) that iTBS (a mode of TMS) dual-target stimulation applied before conventional physical therapy for 21 days provides higher and significant improvements in the muscle strength of the knee flexors and knee extensors, LEMS, SCIM, step length and step frequency, and in the ground reaction force; compared with a sham iTBS intervention plus conventional physical therapy; in participants with incomplete and acute SCI.

There is level 1 evidence (from 1 RCT: Nogueira et al. 2024) that an rTMS protocol followed by BWSTT for 12 sessions provides significant improvements in LEMS and SCIM-III, but not in WISCI II, compared with a sham rTMS application followed by BWSTT in patients with incomplete and chronic SCI.

Key Points

Repetitive transcranial magnetic stimulation (rTMS) combined with locomotor or exercise training seem to provide more benefits in lower limb strength than exercise alone in patients with SCI, but results on improving functional walking were mixed.

6.4 Spinal Cord Stimulation Combined With Locomotor Training (LT)

The discovery of central pattern generators in the spinal cord has led to testing different methods of ES to restore or force patterned locomotion (Darrow et al. 2022). So, there is heightened interest in the effects of spinal cord stimulation (either via epidural or transcutaneous stimulation). Epidural spinal cord stimulation (ESCS) involves the application of an electrical current to the spinal cord through an electrode implanted in the epidural space and was first investigated in 1967 to treat pain (Rademeyer et al. 2021; Shealy et al. 1967).

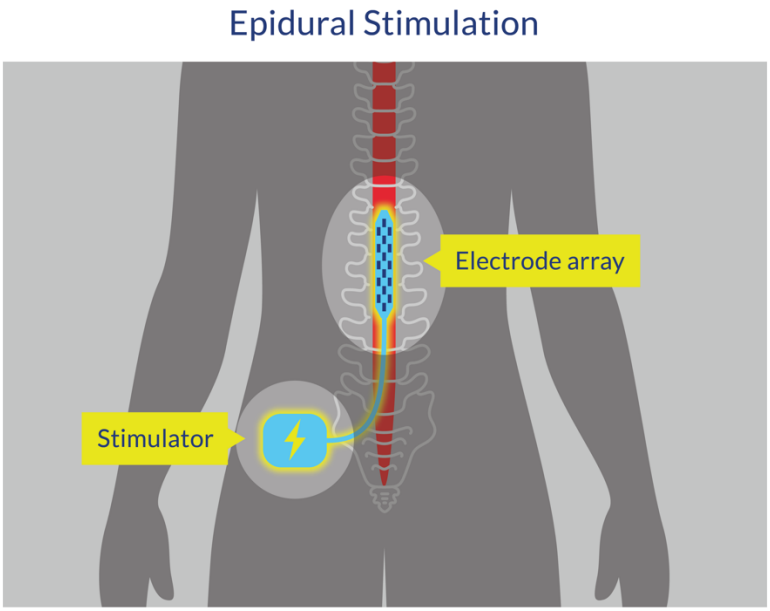


Figure 10. Epidural Spinal Cord Stimulation (ESCS)

Carhart et al. (2004) and Herman et al. (2002) were among the first to describe the effects of ESCS combined with gait training in one person with SCI (male with incomplete tetraplegia, 43 years old, injury level C5-C6, AIS C, 3.5 years post-injury). The participant first underwent 12 weeks of BWSTT, which resulted in some significant improvements in treadmill gait parameters, although his walking overground remained limited. Subsequently, the participant underwent surgical implantation of an epidural stimulation system placed over the T10-T12 vertebral level. After surgical healing had taken place, the participant resumed walking training with both BWSTT and OGT. The combination of ESCS with gait training resulted in a substantial improvement in treadmill gait parameters as well as in overground ambulation. The participant reported a decreased sense of effort, a doubling in walking speed, increased walking endurance, including walking outdoors in his community, when assisted by spinal cord stimulation.

More recently, Harkema et al. (2011) described the effect of ESCS in combination with LT in a single male participant with a motor complete spinal cord injury (23 years old, injury level C7-T1, AIS B, 3.4 years post-injury) (Harkema et al. 2011). Before implantation, the participant underwent 170 LT sessions and was unable to stand or walk independently or voluntarily move his legs. A 16-electrode array was surgically placed on the dura (L1-S1 cord segments). Optimal stimulation parameters for standing and stepping were tested. With stimulation, the participant was able to maintain standing unassisted with full weight-bearing. Locomotor-like muscle activity patterns emerged when epidural stimulation was combined with BWSTT (but not without stimulation). Interestingly, the participant was also able to regain some ability to voluntarily move the legs (but only in the presence of the epidural stimulation). Further studies have extended these initial findings to other people with motor-complete SCI (Angeli et al. 2018; Angeli et al. 2014; Calvert et al. 2019; Darrow et al. 2019; Gill et al. 2018; Gorgey et al. 2020b;

Rejc et al. 2015; Rejc et al. 2017), and even allowing for recovery of voluntary leg movement and standing without the ESCS (Reck & Landmann 2017).

Similar to ESCS, the laparoscopic implantation of neuroprosthesis (LION) procedure in the pelvic lumbosacral nerves (i.e., sciatic, pudendal, and femoral nerves) has been developed. LION consists of the laparoscopic implantation of fine wire electrodes (for simulation of the spinal cord or sacral nerve roots) in direct contact with the endopelvic portion of the nerves for neuromodulation (Possover 2014). In 2006, the first laparoscopic implantation of a neuroprosthesis to the pelvic nerves was performed on a patient with paraplegia for the control of bladder function (Possover et al. 2010). Over the last 10 years, several studies have revealed that stimulation of pelvic nerves might indeed be capable of inducing neurologic changes for the recovery of leg movements in people with chronic SCI (Possover 2014; Possover & Forman 2017; Possover 2021).

Transcutaneous spinal (direct) current stimulation (tSCS) is a mild, noninvasive form of ES targeting modulation of spinal reflexes, corticospinal excitability, and spinal processing of sensory inputs (Hawkins et al. 2022). tSCS uses non-invasive electrodes placed over the T12—L1 vertebrae and abdomen, and has been shown to recruit similar neural structures as ESCS (Al'joboori et al. 2020). This simple method removes the need for surgery, and can be readily transferable for clinical use; however, it can cause some discomfort and unwanted muscle contractions as the current passes through skin and trunk musculature, has less specificity than ESCS, and may be more affected by changes in body position (Al'joboori et al. 2020; Danner et al. 2016). tSCS, delivered at an intensity that is sub-threshold for generating lower limb activity (muscle contractions or whole-limb responses), but high enough to produce paresthesia in lower limb dermatomes, has also been shown to augment volitional stepping on a treadmill (Hofstoetter et al. 2013; Hofstoetter et al. 2015) in people with incomplete SCI (Al'joboori et al. 2020).

Table 17. Spinal Cord Stimulation Combined With Locomotor Training (LT)

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
tSCS Combined With Locomotor/Standing Training		
Hawkins et al. 2022 USA RCT PEDro = 6 Level 1	**Population:** 8 participants with chronic motor incomplete SCI and able to ambulate 3 m with or without the use of gait devices, braces, or the assistance of one person; mean age 52 years; level of injury C1 (n = 4), C6 (n = 1), T1 (n = 1), T3 (n = 1), and T7 (n = 1); AIS C	1. Both groups had similar average treadmill stepping times, overground stepping times, and levels of intensity. 2. The participants receiving tsDCS + LT during training tolerated the repeated exposure; with two

N = 8	(n = 1) and AIS D (n = 7); and mean time since injury 102.3 months. **Treatment:** Participants received 16 training sessions (4 times per week) and were randomly allocated to one of two groups: • tsDCS + LT (n = 4). • Sham tsDCS + LT (n = 4). During tsDCS + LT sessions, 30 min of tsDCS was delivered continuously over the spinous processes of T11 and T12. For LT, all participants were encouraged to achieve 30 min of BWSTT and 10 min of OLT with resting as needed. As walking performance improved, training intensity was adjusted for each participant by increasing walking speed and duration, or reducing rest duration, therapist assistance, and BWS. *Previously, a feasibility study was performed: All participants completed two sessions (on a separated days) in which they received either active tsDCS and LT or sham tsDCS and LT. **Outcome Measures:** Walking performance (10MWT and 6MWT) was assessed before and after the 16-session protocol. Feasibility (based on safety [adverse responses], tolerability [pain, spasticity, skin integrity], and protocol achievement [session duration, intensity)] was assessed during all sessions.	minor issues related to the skin under the electrodes. There was only one participant (in the sham + LT group) who reported a burning sensation during the stimulation (considered as a direct side effect from the stimulation). Other side effects (n = 4) (musculoskeletal pain and/or spasticity) were noted during training in both groups, more likely because of the LT program. 3. One participant in the sham + LT group had episodes consistent with onset of autonomic dysregulation during the first seven training sessions, but the issue subsided gradually and resolved for later training sessions. 4. 10MWT: An average walking speed change of 0.18 (0.29) m/s in the tsDCS + LT group compared to an average change of −0.05 (0.23) m/s in the sham + LT group was revealed. Three participants in the tsDCS + LT group exceeded the test's MCID (0.06 m/s) compared to only one participant in the sham + LT group. 5. 6MWT: An average improvement of 36.4 (69.0) m in the tsDCS + LT group and 4.9 (56.9) m in the sham + LT group was demonstrated. One participant in each group reached the MCID (0.10 m/s or 36 m).
Estes et al. 2021 USA RCT PEDro = 5 Level 2 N = 18	**Population:** 18 participants with subacute SCI, the ability to take at least one step with or without an assistive device, and the presence of at least mild spasticity; 14 males and 4 females; mean age 44.4 years; AIS B (n = 1), AIS C (n = 6), and AIS D (n = 11); injury level C1 (n = 1), C2 (n = 2), C3 (n = 2), C4 (n = 6), C5 (n = 3), C6 (n = 1), C7 (n = 2), and T11 (n = 1); and mean time since injury 100.3 days. **Treatment:** Participants received six bouts of LT for the first two weeks, and	1. No study-related AEs were experienced. 2. Between-group comparisons indicated that there were no differences in change following the wash-in phase ($p > 0.39$) or following the intervention phase ($p > 0.11$) for walking speed, walking distance, and step length asymmetry. 3. Within-group analyses of walking speed indicated that during the

	for the next two weeks, they were randomized to receive six bouts of either 30 min of tSCS coupled with LT (LT + tSCS; n = 8) or a sham-control stimulation coupled with LT (LT + $tSCS_{sham}$; n = 8). • LT approaches used in the study included treadmill-based training and OLT (with or without BWS and with or without manual or robotic assistance). The duration of the sessions was ≈ 1 hour. • tSCS was applied over vertebral levels T11/T12 for 30 min concomitantly with LT. **Outcome Measures:** 10MWT (speed and spatiotemporal gait characteristics [Step length asymmetry]) and 2MWT (distance) were assessed during overground walking at the beginning and at the end of each 2-week intervention block (first 2 weeks [wash-in phase] and second 2 weeks [intervention phase]). Pre- and post-training assessments of spasticity and assessments of tolerability were performed on each training day. * Walking data was collected only from 12 participants because 4 were unable to complete the walking tests.	wash-in phase, there were significant ($p \leq 0.05$) changes for each of the groups, with both groups exhibiting large effect sizes. However, during the intervention phase, only the LT + tSCS group showed a significant change ($p = 0.03$), with a large effect size ($g = 0.43$). 4. Within-group analyses of walking distance showed that during the wash-in phase, walking distance significantly improved only for the LT + $tSCS_{sham}$ group ($p = 0.04$), however, both groups exhibited large effect sizes. During the intervention phase, only the LT + tSCS group showed a significant change in walking distance ($p = 0.03$), with a large effect size ($g = 0.48$). 5. Within-group analyses of step symmetry revealed that this measure did not significantly change for either of the groups during the wash-in or intervention phases, however in the LT + $tSCS_{sham}$ group, large effect sizes were observed during both phases ($g = 0.49$ and 0.68, respectively).
Al'joboori et al. 2020 UK Prospective controlled trial Level 2 N = 7	**Population:** 9 participants with chronic SCI and unable to stand from a chair unaided; mean age 41.2 years; injury level C5 (n = 1), C6/7 (n = 1), T3 (n = 1), T5 (n = 2), T6 (n = 2), and T10 (n = 2); AIS A (n = 5), AIS B (n = 1), AIS C (n = 2), and AIS D (n = 1); and median time since injury 2 years 2 months. **Treatment:** Participants were assigned to: • tSCS combined with sit-to-stand training (STIM) (n =5). • Sit-to-stand training alone (NON-STIM) (n = 2). Training consisted of 3 sessions per week for 8 weeks. During each session,	1. Two participants were withdrawn due to a lower limb injury (n = 1) or early termination (n = 1). 2. Paraesthesia was experienced by all participants in the STIM group during training, and tSCS was tolerated in all participants, however, some reported discomfort due to the tSCS current. 3. For all participants in the STIM group (but none in the NON-STIM group), loading through the lower limbs increased progressively throughout the intervention.

	participants stood up 5 times (taking approximately one-hour) with BWS. Standing was maintained for 4–5 min, during which postural exercises such as deep and shallow squats, lateral and anterior/posterior weight shifts, squat holds, single leg bends, hip thrusts, kettle bell arm presses, trunk strengthening, hip rotations and squat rotations were performed. In the STIM group, continuous tSCS was applied during active standing. **Outcome Measures:** LEMS and motor responses by the Brain Motor Control Assessment were measured before and after the training program. BWS and upper- and lower-limb loading were recorded at 0, 4 and 8 weeks of training.	Unassisted standing was not achieved in any participant. 4. Participants in the STIM group also reported an evident enhanced voluntary control and proprioceptive feedback during tSCS standing activities by week 5. 5. For all participants, LEMS only increased in three of the five participants in the STIM group. 6. Recovery of volitional lower limb muscle activity and/or movement (with tSCS off) was noted in three STIM participants.
ESCS Combined With Locomotor Training		
Kathe et al. 2022 Switzerland, Canada, USA, Austria Pre – post N = 9	**Population:** 9 participants with chronic SCI (6 participants presented with severe or complete motor paralysis, but with some degree of sensation in the legs; and 3 participants presented complete sensorimotor paralysis). **Treatment:** Participants received surgically implanted neurostimulator interfaced to a multi-electrode paddle lead that enables closed-loop control of biomimetic ESCS protocols; followed by overground neurorehabilitation supported in a multidirectional body weight robotic support system (which consisted of standing, walking and performing various exercises with ESCS) 4-5 times per week (1-3 hours per session), for 5 months. **Outcome Measures:** LEMS; 6MWT with a standard four-wheel walker but without any external assistance; 10MWT with the preferred assistive device but without any external assistance; and EMG activity (recorded bilaterally from the iliopsoas, rectus femoris, vastus lateralis, semitendinosus, tibialis anterior,	1. LEMS were improved after the training in comparison with before the training (P = 0.0063). 2. Participants who exhibited residual function before training displayed a pronounced increase in LEMS that restored walking, even in the absence of ESCS in four participants. 3. Compared to before the training program, distance walked during the 6MWT increased after the training (P = 0.0076). 4. Weight-bearing capacities improved considerably over time, which enabled the participants to walk outdoors with ESCS ^{on} and an assistive device for stability.

	medial gastrocnemius and soleus) were assessed before and after the training with ESCS^{on} and ESCS^{off}.	
Rowald et al. 2022 Switzerland, Italy, Netherlands, France, UK, Germany, Austria, and USA Pre – post Level 4 N = 3	**Population:** Three participants with complete sensorimotor paralysis and unable to take any step; mean age 34 years; injury level T4 (n = 1), T5/T6 (n = 1), and T6/T7 (n = 1); AIS A (n = 2) and AIS B (n = 1); and mean time since injury 4.3 years. **Treatment:** A computational ESCS framework that informed the optimal arrangement of electrodes on a new paddle lead and guided its neurosurgical positioning and a software supporting the rapid configuration of activity-specific stimulation programs (i.e., walking, using the legs to swim in the water, pedaling actively on a motorized bike, or performing of rehabilitation exercises, among others) that reproduced the natural activation of motor neurons underlying each activity were established. Participants followed a personalized (according to participants' performance) rehabilitation program with this computational ESCS framework and software 4-5 times per week for 5 months. This period of rehabilitation comprised walking on a treadmill and overground with multiple assistive devices, sit-to-stand, standing, leg and trunk muscle exercises, swimming and cycling. **Outcome Measures:** • 6MWT and 10MWT were assessed at the beginning and at the end of the rehabilitation program. • Muscle mass at the abdominal and mid-thigh levels (by CT images) were acquired before surgery and after the period of rehabilitation.	1. Immediate recovery of walking: a. On the first day, all participants could step independently on a treadmill with BWS, as gait patterns exhibited poor extension components. b. After 1–3 days, gait patterns were sufficiently optimized to enable the participants to walk overground while supported in a multidirectional BWS system. Two out of the three participants could modulate the amplitude of leg movements when asked to increase their step length voluntarily. 2. Recovery of independence: All participants progressively regained full weight-bearing capacities, which translated into the ability to stand independently in community settings, walk independently with the help of a front-wheel walker for stability, ride a recumbent trike powered with the arms and legs, and practice leisure activities (e.g., boxing, enjoying a drink while standing at a bar or paddling a canoe on a lake). 3. These improvements coincided with a substantial increase in the mass of leg and trunk muscles. Moreover, two of the participants recovered the ability to activate proximal muscles voluntarily without ESCS.
Wagner et al. 2018	**Population:** 3 males with chronic cervical SCI who displayed severe lower	1. ESCS could be delivered in an open loop: Participants regulated

Switzerland, USA and UK Pre – post Level 4 N = 3	limb deficits or complete paralysis that prevented them from walking overground; mean age 36.7 years; injury level C4 (n = 1) and C7 (n = 2); AIS C (n = 2) and AIS D (n = 1); and mean time since injury 5.3 years. **Treatment:** Targeted spinal cord stimulation (using an implanted pulse generator with real-time triggering capabilities, trains of spatially selective stimulation to the lumbosacral spinal cord with timing that coincided with the intended movement were used [spatiotemporal ESCS]) during a rehabilitation program 4-5 times per week for five months (focused on walking on a treadmill and overground and complemented with muscle strengthening and standing, each of which was enabled by task-specific epidural electrical stimulation). electrical stimulation). **Outcome Measures:** Walking capability was assessed.	the timing of their movements to pre-program ESCS sequences, which improved gait consistency. 2. Within five days, this procedure led to ESCS sequences that enabled robust EMG activity in otherwise quiescent muscles during stepping on a treadmill. 3. The stimulation enabled all participants to walk overground with BWS voluntarily while the stimulation was on. 4. All participants were able to adjust leg movements (enhance their step elevation and adjust the stride length to varying speeds) and could sustain more than 1200 steps (covering distances as long as 1.0 km) without showing muscle exhaustion or gait impairments. 5. After a few months, participants regained voluntary control over previously paralysed muscles without stimulation and could walk or cycle in ecological settings during spatiotemporal stimulation.
Laparoscopically Implanted Neurostimulator Combined With Locomotor Training		
Kasch et al. 2022 Denmark RCT PEDro = 4 Level 2 N = 16	**Population:** 16 participants with chronic complete (AIS A) SCI; 14 males and 2 females; mean age 37.15 years; injury level T4 (n = 3), T5 (n = 4), T6 (n = 2), T7 (n = 1), T8 (n = 1), T10 (n = 3), and T11 (n = 1); and mean time since injury 14.3 years. **Treatment:** Participants were assigned into one of two groups: • Intervention group (n = 8) receiving laparoscopic implantation of neuroprosthesis (the LION procedure) (to pelvic lumbosacral nerves) and subsequent neurostimulation and training.	1. At one year follow-up, the WISCI II score increased from 0 to 1 in 5 of 8 participants in the LION Group whereas, there was no change in the control group, p = 0.013. 2. AEs in the intervention group: a. Post-operative shoulder pain (resolved within the first 2 weeks) (n = 4). b. Gastrointestinal problems (resolved within 1-week post-operatively) (n = 3). c. Increased spasticity in lower extremities during the first two weeks after the continuous stimulation was initiated (resolved or restored to

	• Active control group (n = 8) receiving long-term home-based NMES. Approximately 6 weeks after the LION procedure, the training program was initiated, which consisted of stimulation for 20–30 min during home training sessions every other day. Participants were instructed to try to extend the knee during the ES. If the participants developed sufficient muscle strength to support standing at three months follow-up or subsequently, stand was allowed with concomitant stimulation on all four leads. In the control group, NMES (for the gluteal and the quadriceps muscle groups) was performed 2–3 times a week for 20–30 min. **Outcome Measures:** WISCI II was assessed at baseline and at 3 and 6 months, and at one-year follow-up.	preoperative levels after a few weeks) (n = 3). d. Migration of the implantable pulse generator within 2 months after operation (repositioned within 2.5 months post-operatively) (n = 1).
Lemos et al. 2023 Brazil and Canada Case series Level 4 N = 30	**Population:** 30 patients with chronic SCI; 23 males and 7 females; mean (± SD) age 35.5 (± 8.1); injury level cervical (n = 5), high thoracic (n = 11) and low thoracic (n = 14); AIS A (n = 21), AIS B (n = 8), and AIS C (n = 1); and mean (± SD) time since injury 7.3 (± 6.3) years. **Treatment:** Patients were submitted to the Possover-LION* surgical procedure for bilateral neuromodulation of femoral, sciatic, and pudendal nerves. After that, all patients underwent an intensive rehabilitation protocol to learn how to use the movements generated by the neuromodulator to enhance their rehabilitation and ADLs. This protocol comprised 15 to 20 weekly hours of multidisciplinary care. *LION: Laparoscopic implantation of neuromodulation. **Outcome Measures:** WISCI II and Mobility Assessment Tool for Evaluation of Rehabilitation (which assessed overall mobility based on the mobility landmarks identified by the	1. Median WISCI II score evolved from a median 0 to median 5 ($p < 0.0001$), and the median Mobility Assessment Tool for Evaluation of Rehabilitation score increased from four to seven ($p < 0.0001$). 2. All the patients improved mobility and all, but two patients managed to initiate gait training. 3. Qualitatively, 72% of patients with thoracic injury and 60% with cervical injury managed to establish independent walker-assisted gait (WISCI II score ≥ 7), using only supramaleolar AFO. 4. No intraoperative complications were registered. 5. Post-operative complications: a. Electrode displacement (n = 3) occurred within the first three months after the procedure and in situations where the movements that should be avoided were inadvertently performed. A reintervention for

	team as those with the most impact on patient's ADLs) were assessed before the surgical procedure (T0) and at three, six, and 12 months postoperatively (respectively, T3, T6, and T12).	electrode repositioning was performed. b. Infection of the neuromodulator (n = 1) resulted in the explantation it, with no further complications.
Possover 2021 Switzerland Pre – post Level 4 N = 29	**Population:** 29 patients with SCI; 27 males and 2 females; mean age 27 years; 27 with paraplegia and 2 with low tetraplegia; AIS A (n = 14); AIS B (n = 12), and AIS C (n = 2); and mean time since injury 57.4 months who were followed over the last 10 years. **Treatment:** This publication is a continuation of (Possover (2014), n = 4). Participants received the LION procedure of four pacing electrodes placed on the endopelvic portion of the sciatic, femoral, and pudendal nerves; and a pacemaker. In addition, the pacemaker programming consists of four programs with the aim of providing continuous selective stimulation of the abovementioned nerves, selective training of knee extension, and standing/walking. The patients trained at home (2-3 times 15-20 min/d) while a team of physiotherapists supervised the training for standing/walking. The same stimulation parameters and the same physical rehabilitation program was used than in Possover (2014). *LION: Laparoscopic implantation of neuromodulation. **Outcome Measures:** LEMS; WISCI II; and changes in thigh muscle mass were assessed.	1. The average postsurgery follow-up period is 45.92 ± 22.34 months (range, 12-84). 2. No intraoperative complications occurred, while few post-surgical complications were shown: a. Dislocation of a femoral electrode (n = 2) with a subsequent reimplantation. b. Massive spasticity (n = 1) (which had already been distinctly pronounced prior to surgery). c. Infection of the neuroprosthesis (n = 1) with explantation. 3. 71.4% of patients were able to demonstrate an electrically assisted voluntary extension of the knee and showed an increase in thigh circumference at 6 months of training of 2.1 cm on average (0-3.6 cm, P < 0.01). 4. It took, on average, two years of daily training until a patient could get up again and walk. 5. 26 (92.8%) patients could get to their feet when the pacemaker was switched on. 6. No patient in the study was able to walk before starting the study. At final examination, five patients could walk < 10 m (17.85 %) at the bar. Nineteen patients could walk > 10 m (67.8%), 8 of them only at the bar (28.5%) and 11 of them with the aid of crutches or a walker and without braces (40%). 7. The WISCI II scores increased from median 0 (IQR, 0-1) preoperatively to 2 (IQR, 0.25 - 4.75) at the follow-up when the stimulation was off (P < .001) and

		even to 5 (IQR, 1.25 - 13.00) when the stimulation was on (P < .001).
Possover 2014 Switzerland Case series Level 4 N = 4	**Population:** 4 patients with chronic SCI; 3 males and 1 female; mean age 34.7 years; level of injury T4/7 (n = 1), T7/8 (n = 1), T10/L1 (n = 1), and T12 (n = 1); and AIS A (n = 1), AIS B (n = 2), and AIS C (n = 1). **Treatment:** Participants received the LION procedure on the sciatic, pudendal, and femoral nerves. Continuous bilateral sciatic and femoral nerve stimulation was started on the first postoperative day; and in parallel, three further programs were installed to train the quadriceps muscles. Training was performed with concomitant sciatic and femoral stimulation (electrically induced knee extensions in seated position), 3 to 5 times per week at the patient's home. After a period of 12 weeks, assisted training for standing and finally walking was started, using first a bar table, then a walker. The configuration of the pacemaker was programmed such that modulation of the stimulation current could be controlled by the patients themselves to obtain optimum efferent patterns for standing and walking at home. The pacemaker was configured so that patients needed to use the remote control only at the beginning and end of the walking phase, thus providing the patients maximum autonomy. *LION: Laparoscopic implantation of neuromodulation. **Outcome Measures:** LEMS and WISCI II.	1. No pre- or postoperative complications occurred. 2. Compared to before the implantation, LEMS, WISCI II with FES and WISCI II without FES improved in all patients. 3. Within 12 weeks of FES-assisted training, the three patients with incomplete SCI had achieved substantial increases in lower limb skeletal muscle mass and developed adequate muscle strength for LT. 4. Each patient showed some degree of improvement in the ability to extend the knee, stand and walk.

6.4.1 Non-Invasive Stimulation

Discussion

Different approaches to stimulate the spinal cord have been used, including transcutaneous, which is a non-invasive method, and epidurally or laparoscopically, which are invasive methods requiring surgery.

As a non-invasive method, transcutaneous spinal cord stimulation (tSCS) is easier to study and comes with fewer risks. To date, tSCS studies have shown only minor AEs, such as discomfort, minor issues related to the skin under the electrodes, and one case of burning sensation during the stimulation (Al'joboori et al. 2020; Hawkins et al. 2022).

Two high-level studies assessed the effects of tSCS in combination with LT on walking outcomes (Hawkins et al. 2022; Estes et al. 2021). The RCT of Estes et al. (2021) included 18 participants with subacute (mean time since injury of 100.3 days) SCI and the ability to take at least one step with or without an assistive device and the presence of at least mild spasticity. Participants were randomized to receive 30 min of tSCS or sham stimulation, coupled with LT for another 2 weeks (Estes et al. 2021). After the intervention phase, the two groups were not significantly different from each other in walking speed or walking distance. However, the transcutaneous stimulation group improved significantly from baseline walking performance by 0.16m/s in walking speed and by 15.25m in walking distance, both clinically relevant changes (Lam et al. 2008; Estes et al. 2021). On the other hand, participants in the sham stimulation group showed more modest (non-significant) changes in walking speed (0.06 m/s) and in walking distance (6.85 m) (Estes et al. 2021).

Hawkins et al. (2022) included eight patients with chronic motor-incomplete SCI who were able to walk for three minutes with or without assistance. Participants engaged in 30 minutes of BWSTT and 10 minutes of OLT and were randomly assigned to receive either transcutaneous spinal direct current stimulation (tsDCS) or sham stimulation (Hawkins et al. 2022). After four weeks of training, both groups reached similar levels of training intensity but walking speed (10MWT) and walking distance (6MWT) were slightly better in the stimulation group than in the sham stimulation group (statistical analysis was not performed due to the small group sizes (n = 4) (Hawkins et al. 2022). Al'joboori et al. (2020) performed a prospective controlled trial in which seven patients with chronic SCI and unable to stand from a chair unaided were included. Participants were assigned to receive 24 sessions BWS sit-to-stand and standing training, either with tSCS or sham stimulation. After eight weeks, three of the five STIM group participants improved their LEMS and volitional lower limb muscle activity and/or movement (Al'joboori et al. 2020). However, more robust studies need to be conducted because the sample size was small, the allocation was not randomized, and no statistical analysis was performed (Al'joboori et al. 2020).

Conclusions

There is level 1 evidence (from 1 RCT: Estes et al. 2021) and level 2 evidence (from 1 RCT: Hawkins et al. 2022) that the simultaneous application of tSCS during LT (BWSTT or overground) training sessions is a safe procedure and may provide more improvements in walking speed (10MWT) and walking distance (2MWT and 6MWT) in comparison with the same intervention but with sham stimulation in patients with incomplete, and subacute and chronic SCI.

There is level 2 evidence (from 1 prospective controlled trial: Al'joboori et al. 2020) that an intervention based on tSCS combined with sit-to-stand and standing training may provide additional benefits in LEMS, in the recovery of volitional lower limb muscle activity and/or

movement, and in enhancing voluntary control of lower extremities and trunk, in comparison with the same training intervention but without tSCS in patients with chronic SCI.

6.4.2 Implantable Spinal Cord Stimulation and Walking

Discussion

Because implantable spinal cord stimulation, like epidural spinal cord stimulation (ESCS) and laparoscopic implantation of neuroprosthesis (LION), require surgery so there are no RCT studies in this area and the case series studies samples are small.

Wagner et al. (2018) included three males with chronic SCI who displayed severe lower limb deficits or complete paralysis that prevented them from walking overground; they implanted a pulse generator into all three participants to deliver spatially selective stimulation to the lumbosacral spinal cord with timing that coincided with the intended movement. After the implantation, the three participants received a rehabilitation program focused on walking on a treadmill and over ground, complemented with muscle strengthening and standing training (Wagner et al. 2018). In one week, spatiotemporal stimulation enabled all participants to walk overground (using the gravity assist) voluntarily while the stimulation was on, covering distances as long as 1.0 km without showing muscle exhaustion or gait impairments (Wagner et al. 2018). After a few months, rehabilitation promoted neurological recovery that translated into improvements in WISCI, in 6MWT, in 10MWT, or LEMS without stimulation; and they could even walk or cycle in ecological settings during spatiotemporal stimulation (Wagner et al. 2018).

In 2022, as part of the ongoing clinical trial 'Stimulation Movement Overground' (STIMO) (www.clinicaltrials.gov identifier NCT02936453), two pre-post studies were published (Kathe et al. 2022; Rowald et al. 2022). Kathe et al. (2022) included nine participants with chronic and severe or complete motor paralysis. Participants, after receiving spatiotemporal ESCS plus LT, showed that compared to before the training program, LEMS and walking distance (6MWT) were significantly improved (Kathe et al. 2022). Moreover, weight-bearing capacities improved considerably over time, which enabled the participants to walk outdoors with ESCS on and an assistive device for stability (Kathe et al. 2022). It should be noted that participants who exhibited residual function before training displayed a pronounced increase in lower limb motor scores that restored walking, even in the absence of ESCS in four participants (Kathe et al. 2022). This sustained recovery suggested that the stimulation triggered the remodeling of the spinal neurons to bring the locomotion network back online (Lewis 2022). Interestingly, when ESCS was active, nerve-cell activity at the site of stimulation decreased; and after further investigation, Kathe et al. (2022) discovered the neurons responsible for the rehabilitation enhancement and concluded that $SC^{Vsx2::Hoxa10}$ neurons located in the intermediate laminae of the lumbar spinal cord possess the anatomical and functional properties that are compatible with the key therapeutic features of ESCS rehabilitation.

Rowald et al. (2022) established a computational framework that informed the optimal arrangement of electrodes on a new paddle lead, guided its neurosurgical positioning, and developed software supporting the rapid configuration of activity-specific stimulation programs that reproduced the natural activation of motor neurons underlying each activity. Three

participants with chronic and complete sensorimotor paralysis and unable to take any step followed a rehabilitation program (which comprised walking on a treadmill and overground with multiple assistive devices, sit-to-stand, standing, leg and trunk muscle exercises, swimming and cycling) with this computational ESCS framework and software four to five times per week for five months (Rowald et al. 2022). Immediate recovery of walking was shown; on the first day, all three participants could step independently on a treadmill with BWS, and after 1–3 additional days, gait patterns were sufficiently optimized to enable the three participants to ambulate independently overground with BWS (Rowald et al. 2022). All three participants progressively regained full weight-bearing capacities, which translated into the ability to stand, walk, cycle, swim and control trunk movements in community settings (Rowald et al. 2022). Lastly, Rowald et al. (2022) showed that these improvements coincided with a substantial increase in the mass of leg and trunk muscles; moreover, two of the participants recovered the ability to activate proximal muscles voluntarily without ESCS, indicating neuroplastic recovery. These promising effects of different procedures of ESCS, should be confirmed with larger trials, which at time of writing, are currently underway ('Stimulation Movement Overground' (STIMO) (www.clinicaltrials.gov identifier NCT02936453).

The laparoscopic implantation of neuroprosthesis (LION) procedure has shown early and long-term effects in pre-post studies for regaining motor and sensory function in patients with paraplegia after SCI (Possover 2014; Possover 2021). In an RCT, Kasch et al. (2022) compared 16 participants with chronic complete (AIS A) SCI receiving the LION procedure were randomly allocated to subsequent neurostimulation and training or long-term home-based NMES for the gluteal and the quadriceps muscle groups (Kasch et al. 2022). At one-year follow-up, between-group comparisons in WISCI II scores were significant, as there was an increase from 0 to 1 in 5 of 8 participants in the LION Group, whereas there was no change in the control group participants (Kasch et al. 2022). More recently, a case series study by Lemos et al. (2023) included 30 patients with chronic and complete SCI who had received the LION surgical procedure and an intensive rehabilitation protocol to learn how to use the movements generated by the neuromodulator to enhance their rehabilitation and ADLs. At one year follow-up, median WISCI II score significantly improved from a median of 0 to median of 5. In addition, 18 of 25 (72%) patients with thoracic injury and three of five (60%) patients with cervical injury managed to establish independent walker-assisted gait (WISCI II score ≥ 7), using only ankle-foot orthosis (AFO) to stabilize their ankles (Lemos et al. 2023).

It should be noted that the majority of studies with patients who received ESCS did not report if there were any AEs (Wagner et al. 2018; Rowald et al. 2022; Kathe et al. 2022). Kasch et al. (2022) reported that in one participant, the implantable pulse generator in the LION procedure migrated within two months after the operation, although after the reposition during an outpatient clinic operative procedure, the implantable pulse generator was fully functioning and the training program was resumed. Lemos et al. (2023) and Possover (2021) registered no intraoperative complications, but the most frequent post-operative complication was electrode displacement (which occurred in situations where the movements that should be avoided were inadvertently performed), which happened in three (10%) cases and required a reintervention for electrode repositioning. Another complication observed by Lemos et al. (2023) and Possover (2021) was one case (3.3%) of infection of the neuromodulator, and after several antibiotic

courses attempted with no success, the neuromodulator was removed at five months postoperatively with no further complications. However, it should be noted that no discomfort or pain was reported by any patient, and no episodes of dysreflexia were observed as a result of nerve stimulation (Lemos et al. 2023).

Rademeyer et al. (2021) conducted a scoping review to synthesize the effects of ESCS on function in people living with SCI. From a total of 48 studies including 373 participants, 27.1% (n = 13) revealed promising (but preliminary) findings on lower extremity function (i.e., standing or locomotion) (Rademeyer et al. 2021). It was revealed that the epidural space posterior to the spinal cord was the optimal stimulation site to enable positive effects on lower extremity functional goals, with L2 as the preeminent level to stimulate locomotion and stimulation parameters being individually optimized often based on sensory and motor thresholds (Rademeyer et al. 2021). It was stated that ESCS may be combined with movement training (BWSTT, OGT or EAW) (Rademeyer et al. 2021).

Conclusions

There is level 2 evidence (from 1 RCT: Kasch et al. 2022) and level 4 evidence (from 1 case series and 1 pre-post study: Lemos et al. 2023; Possover 2021) that the LION procedure for bilateral neuromodulation of femoral, sciatic, and pudendal nerves followed by an intensive rehabilitation protocol; despite very few cases of complications (electrode displacement and infection of the neuromodulator); provides long-term beneficial effect on walking ability (WISCI II) in patients with chronic and complete SCI.

There is level 4 evidence (from 3 pre-post studies: Kathe et al. 2022; Rowald et al. 2022; Wagner et al. 2018) that ESCS (regardless of the process used) and a subsequent training program based on LT is relatively safe and provides improvements in walking capacity, LEMS, and independence in ADLs in patients with chronic SCI and complete or severe motor paralysis.

Key Points

Concurrent application of transcutaneous spinal cord stimulation (tSCS) seems to enhance the effects on walking and strength outcomes of locomotor training (LT) (bodyweight supported treadmill training (BWSTT) or overground) or sit-to-stand and standing training in patients with chronic SCI.

Epidural spinal cord stimulation (ESCS) is a relatively safe procedure, and combined with a subsequent LT, has promising but still preliminary effects on the recovery and improvements in walking capacity, LEMS, and independence in ADLs in patients with chronic and complete or severe motor paralysis.

The LION procedure in the pelvic lumbosacral nerves (i.e., sciatic, pudendal, and femoral nerves) is a relatively safe surgical approach, and, followed by an intensive rehabilitation protocol, provides long-term beneficial effects on walking ability in patients with chronic and complete SCI.

7 Biofeedback and Virtual Reality in Gait Rehabilitation

Biofeedback may be defined as a process that enables an individual to observe and subsequently learn how to change physiological activity for the purpose of improving health and performance (Schwartz 2010). Precise instruments measure physiological activity and rapidly and accurately "feed back" information to the user (Schwartz 2010). The presentation of this information supports desired physiological changes (Schwartz 2010), specifically gait movements in this chapter. Biofeedback techniques in publications include those based on Electromyography (EMG) recordings of muscle activation or position, or force sensors that provide feedback on joint motion or functional attributes such as weight-shifting.

In recent years, technological advances such as virtual reality (VR) are being used as a therapeutic tool in SCI rehabilitation (Abou et al. 2020). VR is a computer-based technology that allows users to interact in a computer-generated environment, allowing the practice of rehabilitation exercises in a safe, standardized, reproducible, and controlled environment (Abou et al. 2020). VR comprises two types of systems according to the immersion level: (i) semi-immersive or non-immersive systems, and (ii) immersive systems (De Miguel-Rubio et al. 2020). Semi-immersive and non-immersive systems use a screen to display the environment with a low level of immersion (e.g., commercial videogame consoles), and immersive systems offer full integration of the user into the virtual environment, providing sensory inputs to the patient (e.g., VR caves, large-screen projections, and head-mounted displays; De Miguel-Rubio et al. 2020; Henderson et al. 2007). VR therapy can help practitioners provide external feedback to their patients about their performance and increase adherence to intensive and repetitive exercise training in acute or chronic SCI treatment (Levin et al. 2015; Ionite et al. 2022; Leemhuis et al. 2021).

Table 18. Biofeedback Modalities

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Virtual Reality Biofeedback		
An & Park 2022 Republic of Korea RCT PEDro = 7 Level 1 N = 40	**Population:** 40 tetraplegic participants with incomplete SCI; 23 males and 17 females; mean age 42.6 years; level of injury C5-7 (n = 40); AIS C (n = 17) and AIS D (n = 23); and time since injury > 1 year. **Treatment:** Participants were randomly divided into two groups and received 12 sessions of a 30 min	1. There were significant differences between groups at the end of the intervention, favoring the experimental group for chair stand test time (p = 0.03), and for 10MWT (p = 0.03). 2. Within-group improvements were significant in both groups (p < 0.02) for all the outcome measures, but

	therapy three days/week for four weeks in their homes: • Participants in the experimental group (n = 20) participated in 'virtual soccer games.' While seated in their wheelchair, they performed kicking motions with their legs. • Participants in the control group (n = 20) underwent a similar rehabilitation intervention but without the VR content. **Outcome Measures:** Stability during a pattern of five sit-to-stand movements (by the chair stand test); and walking speed (by 10MWT) were assessed before and after the intervention protocol.	greater decreases were seen in the experimental group for all of them (p< 0.04): a. Chair stand test times had a large effect size (Cohen's d = 0.71). b. 10MWT had a medium effect size (Cohen's d = 0.61).
Zwijgers et al. 2024 The Netherlands RCT PEDro = 5 Level 2 N = 35	**Population:** 35 participants with incomplete SCI with the ability to walk at least 10m with or without a walking aid (but without physical assistance) and the ability to walk at comfortable speed between 0.3 and 1.0m/s. • Walking adaptability training group (n = 17): Median (IQR) age: 62 (56-71) years. 10M, 7F Level of injury: Cervical (n = 8), thoracic (n = 3), and lumbar (n = 6). AIS C (n = 2) and AIS D (n = 15). Cause of injury: Traumatic (n = 6) and non-traumatic (n = 11). Median (IQR) time post injury: 47 (20-120) months. • Conventional locomotor and strength training group (n = 18): Median (IQR) age: 67 (60-72) years. 9M, 9F Level of injury: Cervical (n = 10), thoracic (n = 5), and lumbar (n = 3). AIS C (n = 1) and AIS D (n = 17). Cause of injury: Traumatic (n = 9) and non-traumatic (n = 9).	1. Participant's adherence and experience: a. The number of steps per training session was significantly higher for the walking adaptability training group (median [IQR] = 2670 [2261-3352]) compared to the conventional locomotor and strength training group (median [IQR] = 2400 [1490-2555]; P = 0.03). b. The perceived intensity (defined as the difference between the ratings of physical tiredness before and after) was significantly higher for the walking adaptability training group (mean ± SD = 5.3 ± 1.9) compared to the conventional locomotor and strength training group (mean ± SD = 3.8 ± 2.0; P = .03). 2. Walking capacity: a. Independent of intervention, maximal walking speed increased by 0.07m/s (95% CI=0.03-0.11) at post-intervention (P < 0.01) and by 0.10 m/s (95% CI = 0.06-0.14) at follow-up (P < 0.01) relative to baseline.

	Median (IQR) time post injury: 66 (20-135) months. **Treatment:** Participants were randomly assigned to receive either walking adaptability (n = 17) or conventional locomotor and strength training (n = 18). Both interventions consisted of 11 training sessions of 60 minutes over a period of 6 weeks (on average 2 training sessions per week). The training interventions were designed to contain approximately 20 minutes of active walking to ensure a similar number of steps per session for both interventions. • Walking Adaptability Training: It was conducted using the Gait Real-time Analysis Interactive Lab (GRAIL). The GRAIL incorporates an instrumented split-belt treadmill with adjustable pitch and sway, an 10-camera motion capture system, and a 180° semi-cylindrical screen for the projection of synchronized VR environments. For safety reasons, participants wore a safety harness attached to a rail on the ceiling without BWS. During a training session, multiple walking adaptability tasks were performed, including precision stepping, obstacle avoidance, and/or reacting to perturbations for 20 minutes. In the remaining time available (0-10 minutes), standing balance tasks were included. • Conventional Locomotor and Strength Training: It consisted of treadmill training (20 minutes) and lower-body strength exercises (10-20 minutes). **Outcome Measures:** Maximal walking speed (2MWT) was measured at baseline, immediately post-intervention, and at follow-up (at 6weeks post-intervention). The SCI-FAP, the ABC scale, and the USER-P	b. No significant difference (P = 0.23) in maximal walking speed between both training groups was found 6 weeks after training at follow-up (−0.05 m/s; 95% CI = −0.12-0.03). 3. Functional ambulation: a. Independent of intervention, significant improvements across time between baseline and follow-up (median difference = −3.3 points, IQR = −6.0 to −0.3, P < .01) were found. b. No significant difference (P = 0.79) in SCI-FAP between groups was found 6 weeks after training at follow-up.

	were measured at baseline and during the follow-up assessment.	
Duffell et al. 2019 UK Pre – post Level 4 N = 11	**Population:** 11 participants with incomplete SCI who were using a wheelchair for at least 2 hours per day; 10 males and one female; mean age 56.5 years; injury level C1 (n = 2), C3 (n = 1), C4 (n = 1), T2 (n = 3), T3 (n = 1), T5 (n = 1), T7 (n = 1), and T12 (n = 1); AIS C (n = 7) and AIS D (n = 3); and median time since injury 1 year and 1 month. **Treatment:** Participants trained three 1-h sessions per week over 4 weeks on the iCycle (which is a FES ergometer) with biofeedback through a VR game (in which the speed of the avatar depends on the actual crankshaft torque while motion is maintained by a motor) to encourage voluntary drive during pedalling. **Outcome Measures:** Voluntary motor function (assessed using ISNCSCI motor scores); Oxford scale motor power grading (carried out for knee extension/flexion and ankle plantarflexion/dorsiflexion); WISCI II; and 10MWT were assessed pre- and post- training, and 4 weeks after completing training.	1. Participants did not report serious AEs. Only two participants noticed skin redness at the end of a session. 2. There was an improvement in ISNCSCI motor scores by 10% in participants with chronic injuries (n = 6) and by 16% in participants with subacute SCI (n = 5). 3. Changes in ISNCSCI motor score did not correlate with age, time since injury, baseline ISNCSCI motor score, baseline power output during cycling, time spent training, or stimulation amplitude. 4. Median (range) improvement in Oxford scale motor power grading from baseline to follow-up for knee flexion was 0.5 (- 1.0 to + 2.0), for knee extension was 1.0 (- 1.0 to + 2.0), for ankle dorsiflexion was 0.5 (- 1.0 to + 2.0), and for ankle plantarflexion was 0.5 (- 1.0 to + 3.0). 5. Only two of the participants included were ambulatory; and only one of them demonstrated an improvement in WISCI II score of 5 points at end of training compared with baseline, and 10MWT time improved from 82 s at baseline to 41 s at end of training.
van Dijsseldonk et al. 2018 The Netherlands Pre-post Level N = 15	**Population:** 15 participants with incomplete and chronic SCI who could walk independently for 2 min without assistance; 11 males and 4 females; mean (± SD) age 59 (± 12) years; AIS level C (n = 2) and D (n = 13); and mean (± SD) time since injury 42 (± 48) months. **Treatment:** Individualized VR gait training on the GRAIL for 12 1-h training sessions spread over a 6-week period. The GRAIL consisted of an instrumented dual belt treadmill with two embedded force plates and an eight-camera motion capture system.	1. Spatiotemporal parameters: a. The mean walking speed was significantly higher at post measurement (1.04 ± 0.38 m/s) compared to baseline 1 (0.85 ± 0.41 m/s, $p < 0.001$) and baseline 2 (0.93 ± 0.37 m/s, $p = 0.003$). b. Stride length was significantly larger at the post measurement (112 ± 31cm) compared to baseline 1 (94 ± 39 cm, $p < 0.001$) and baseline 2 (101 ± 33 cm, $p = 0.002$). c. Stride frequency and step width were not significantly affected.

	The platform was able to move in several directions to generate mechanical perturbations. In front of the treadmill, VR environments were projected on a 180° semi-cylindrical screen. Reflective markers were adhered to the patients to interact with the virtual environment and to capture kinematic data. The GRAIL system was controlled, and the visual information was matched to the treadmill speed. During the GRAIL training multiple applications (categorized in three themes; "gait adaptability" and "walking" were performed in an individualized pattern. **Outcome Measures:** 2MWT on the GRAIL; spatiotemporal parameters (walking speed, stride length, step width, and stride frequency); and gait stability measures; were assessed at the last training session (post measurement) and at 6 months after the last training session (follow-up measurement).	2. The follow-up data was performed in 10 of the 15 patients: a. There was no significant difference in patient's walking speed, stride length, step width, or stride frequency between post and follow-up measurement.
An & Park 2018 Republic of Korea Pre-post Level 4 N = 10	**Population:** 10 participants with chronic SCI; 6 males and 4 females; mean (± SD) age 44.20 (± 8.66) years; level of injury C2 (n = 1), C4 (n = 3), C6 (n = 2), C7 (n = 2), and T1 (n = 1); AIS level C (n = 4) and D (n = 6); and mean (± SD) time since injury 19.20 (± 3.93) months. **Treatment:** Participants underwent semi-immersive VR therapy (using an Interactive Rehabilitation Exercise 30 min per day, 3 times a week for 6 weeks. Six programs were included: "soccer", "conveyor", "volleyball", "formula racer", "airborne", and "snowboard". Each program was performed for 4 min with a 1-min break between programs. **Outcome Measures:** Upright mobility function (ABC scale and WISCI II) was assessed before and after the intervention.	1. There were no AEs during the semi-immersive VR therapy. 2. The WISCI II score after intervention showed significant improvement from 16.30 to 17.90 ($P < 0.05$).

Villiger et al. 2017 Switzerland Pre-post Level 4 N = 11	**Population:** 11 participants with motor-incomplete SCI and able to sit in a chair without assistive and supporting systems; mean (± SD) age 60 (± 10.2) years; level of injury C4 (n = 1), C5 (n = 3), C7 (n = 2), T4 (n = 1), T9 (n = 1), T12 (n = 2), and L3 (n = 1); AIS C (n = 1) and AIS D (n = 10); and mean time since injury 7.6 years. **Treatment:** All participants were trained at home on the VR tasks over a period of 4 weeks, with 16–20 sessions of 30–45 min each, and with the mobile prototype of the YouKicker system. Around 500 repetitions of ankle movements and 100 knee movements with each leg were performed through different blocks by a typical patient during a training session. **Outcome Measures:** LEMS, 10MWT, 6MWT, SCIM-III, and WISCI II were tested 4 weeks before treatment (pre-baseline), directly before treatment (baseline), after finishing the training program (post-assessment), and 2-3 months after the treatment program (follow-up).	1. None of the participants had any pain while playing the games or after the sessions. 2. One participant was unable to perform the walking assessments. 3. At post-assessment, significant increases in comparison with the averaged pre-baseline and baseline were found in LEMS (P = 0.008) 4. There were no significant effects on 10MWT (P = 0.169), 6MWT (P = 0.037); SCIM-III mobility (P = 0.18), and WISCI II (P = 0.180). 5. At follow-up assessment, no significant changes were found in muscle strength (LEMS, P = 0.065), or walking speed/distance and mobility (10MWT [P = 0.169], 6MWT [P = 0.32], SCIM-III mobility [P = 0.026], and WISCI II [P = 0.317]).
Villiger et al. 2015 Switzerland Pre-post Level 4 N = 23	**Population**: 9 participants with SCI - 5 males and 4 females; incomplete SCI; all AIS D; Lesion level between C4 to T12; mean age= 55.1 ± 15.8y; years post injury= 1-5y; 14 healthy persons were in the control group - 8 males and 7 females; mean age= 47.1 ± 14.4y. **Treatment**: Patients underwent 4 weeks of intensive VR-augmented lower limb training. The patients with incomplete SCI were trained with the VR movement tasks 16–20 times during the 4 weeks (4–5 × 45 min. per week). The training used a VR-augmented therapy system for lower limbs combining action observation, imagination and execution. Before and after the training period a structural volumetric 3D MRI data set was acquired in patients. Retention of the performance improvements was	1. The intense VR-augmented training of limb control improved significantly walking speed, ambulation, and muscle strength in patients. 2. Retention of clinical improvements was confirmed by the 3–4 months follow-up.

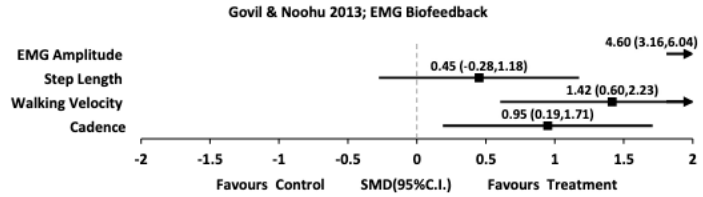
	assessed in a 3–4 month follow-up session **Outcome Measures:** 10MWT, BBS, LEMS, and SCIM mobility.	
Villiger et al. 2013 Switzerland Pre-post Level 4 N = 14	**Population:** 14 participants - 9 males and 5 females; chronic SCI; 2 AIS C and 12 AIS D; level of injury: C4-T12. mean age= 53y; median years post-injury= 4y. **Treatment:** Participants received 4-5 45-min sessions of intensive VR augmented training sessions per week for a total of 16-20 sessions. **Outcome Measures:** BBS, 10MWT and WISCI II.	1. Significant improvements in 10MWT, BBS and WISCI II were shown after intervention.
Other Biofeedback Approaches		
Mollà-Casanova et al. 2024 Spain RCT PEDro = 7 Level 1 N = 12	**Population:** 12 volunteers with chronic incomplete SCI and the ability to walk with or without aids. Mean age: 52 years Level of injury: C2-S1 AIS C (n = 3) and AIS D (n = 9) Mean time since injury: 5.25 years **Treatment:** Participants were divided into two intervention arms (experimental intervention and control intervention). Both interventions lasted 6 weeks (3 days a week), and the session were carried out in groups of three people. • Experimental intervention (n = 6) consisted in a visual illusion therapy intervention based on virtual walking for 10 minutes. The patient was facing a mirror (from the waist up), and a standing frame set-up provided support for the lower body. For the lower body, a screen (from the waist down) where a video of legs walking on a treadmill was projected. • Control intervention (n = 6) included placebo virtual walking. The set-up and	1. All participants completed at least 80% of the intervention sessions and none of the participants dropped out before the end of the intervention. 2. With regard to unwanted effects, all participants reported fatigue at the end of each session. Moreover, one participant in the control intervention group suffered dizziness while viewing placebo virtual walking video on the second session of the intervention. 3. Significant ($p < 0.05$) improvements in the experimental intervention were found for tibialis anterior mean and maximum strength (Cohen's d = -0.51 [medium effect size] and -0.18, respectively), 10MWT (Cohen's d = 0.52 [medium effect size]) and WISCI (Cohen's d = 0.13), while no significant ($p > 0.05$) differences were found between assessments in the control group.

	duration were the same as in the experimental virtual walking, but videos of landscapes without featuring any type of human or animal movement were projected. Both groups performed a therapeutic exercise program which was divided into two parts: i) gait technique training (i.e., coordination exercises), and ii) multicomponent training (i.e., strength, balance and stretching exercises); with a total duration of 35 min. **Outcome Measures:** 10MWT, WISCI, and isometric strength (using a load cell) of the least affected leg tibialis anterior and quadriceps were measured at baseline and at the end of the 6-week treatment.	
Amatachaya et al. 2023 Thailand RCT PEDro = 6 Level 1 N = 44	**Population:** 44 ambulatory individuals with chronic SCI and with the ability of independent walking with or without a walking device over a distance of at least 15m: • Control group (n=22): Mean (SD) age: 53.3 (12.1) years; 15M, 7F; ASIA: ASIA C (n=8) and ASIA D (n=14); level of injury: Tetraplegia (n=5) and paraplegia (n=17); and mean (SD) time since injury: 57.6 (34.7) months • Experimental group (n=22): Mean (SD) age: 51.2 (14.9) years; 18M, 4F; ASIA: ASIA C (n=10) and ASIA D (n=12); Level of injury: Tetraplegia (n=8) and paraplegia (n=14); and mean (SD) time since injury: 51.7 (31.4) months **Treatment:** Participants were assigned to the control intervention group (i.e., bodyweight shifting and lower limb loading training [LLLT] without augmented loading feedback) or the experimental intervention group (i.e., bodyweight shifting and lower limb loading	1. Mobility outcomes: a. After the training programs, participants demonstrated significant improvement in all mobility outcomes at week two and week four (within-group analysis) ($p<0.05$). The mobility outcomes of participants in the experimental intervention group also showed significant improvement at six-month follow-up. b. When adjusted for the baseline data, the mobility improvement of participants in the experimental intervention group at week two and week four was significantly greater than that of the participants in the control intervention group ($p<0.05$). However, this difference was not found at six months after the training programs. 2. Fall data: During the six months after the training, there were nine participants who fell in the control intervention group and four participants who fell in the

	training with augmented loading feedback) for 30min/day, 5days/week, over 4weeks. • Control intervention program (n=22): The participants in this group engaged in stepping training while in a step-standing position, for each leg continuously, as long as they could without fatigue, for 10min/leg. They were then trained to walk on a smooth, flat, and firm surface for 10min. • Experimental intervention group (n=22): The participants were trained using the same protocols as those used in the control intervention group; however, in this group, external augmented loading feedback was also obtained using a visual weight-taking machine. **Outcome Measures:** Incidence of falls was measured 6 months before the start of the intervention and 6 months after finishing the intervention. Mobility outcomes (TUG test, 10MWT, FTSTS test, and 6MWT) were assessed at baseline, at week two and week four, and after 6 months follow-up.	experimental intervention group. The number of faller participants was significantly different between the groups (p=0.044).
Nithiatthawanon et al. 2020 Thailand RCT cross-over PEDro = 6 Level 1 N = 30	**Population:** 30 community-dwelling participants with SCI who had the ability to walk independently, with or without a walking device, over at least 17 m (FIM-L Score of 5–7); 22 males and 8 females; mean age (± SD) 53.2 (± 11.8) years; level of injury paraplegia (n = 20) and tetraplegia (n = 10); AIS C (n = 12) and AIS D (n = 18); and mean (± SD) time since injury 71.9 (± 74.5) months. **Treatment:** All participants involved in a single control and a single experimental session with a 2-week washout period between them: • Control intervention session, consisting of:	1. Both training programs significantly improved all the outcome measures, excepting lower limb loading of the less-affected leg following the control intervention training program. 2. The improvement after the experimental intervention program was significantly greater than that following the control intervention program for all the outcome measures ($p < 0.05$).

	○ Bodyweight shifting and lower limb loading training during stepping (forward and backward) without external feedback for 10 min for each leg. ○ OWT with an emphasis on lower limb loading, with or without a walking device, according to their ability for 10 min. • Experimental intervention session: The participants were trained using the same protocols as those of the control intervention program but with visual feedback relating to the amount of lower limb loading of the stance leg from a visual weight-taking machine to alert the participants and the therapist of the adequate amount of lower limb loading on the stance limb (at least 80% of the participant's bodyweight). **Outcome Measures:** 10MWT, FTSTS test and maximal lower limb loading ability were assessed prior and immediately following each training session (four times).	
Cheung et al. 2019 China RCT PEDro = 8 Level 1 N = 16	**Population:** 16 participants with incomplete SCI and able to perform BWSTT; 11 males and 5 females; mean age 54.3 ± 9.6 years; level of injury C1-L2; AIS C (n = 11) and AIS D (n = 5); and mean time since injury 13.7 ± 7.4 months. **Treatment:** All participants received, twice a week, one hour of standard physiotherapy program, including limbs mobilization and strengthening, trunk stabilization, wheelchair maneuver training and OWT. Additionally, 3 times per week, for 8 weeks, participants were randomly allocated to: • 30 min of BWSTT with Lokomat system, at comfortable walking speed, with assist-as-needed	1. No AE or discomfort was reported by participants. 2. Significant ($p < 0.025$) improvements in BWSTT group in the mobility sub-score of SCIM-III and bilateral symmetry were shown, but none of these outcome measures were improved in the control group. 3. No significant time X group interaction was found in other outcomes with no significant between group difference.

	guidance force, and 40% of BWS. Additionally, EMG-biofeedback system was applied to the bilateral vastus lateralis and audio feedback was generated if the muscle activation was less than 30% of maximal recruitment to encourage active participation during the stance phase of the gait cycle. • Control group: Participants received passive lower limb mobilization training by using lower limb active-passive exerciser. **Outcome Measures:** WISCI II, SCIM-III, LEMS, Lower limb-force (L-force) function in Lokomat system, and quality of gait pattern (by gait analysis system) (walking speed, heel-heel base support, bilateral stance duration and bilateral symmetry [ratio of stride length of two legs]) were collected within 1 week before the start of intervention and within 1 week after the completion of the 8 weeks program.	
Govil & Noohu 2013 India PEDro = 5 RCT Level 2 N = 30	**Population:** 30 participants with incomplete SCI; randomized to 2 groups. For Group 1: mean (SD) age = 38.73 (10.75); DOI= 17.87 (8.37). For Group 2: mean (SD) age=38.03 (7.45); DOI = 16.93 (7.10). **Treatment:** Group 1 received EMG biofeedback to the gluteus maximus muscle, as well as traditional rehabilitation and gait training for 5 days/wk for 4 wks. Group 2 received traditional rehabilitation and gait training for 5 days/wk for 4 wks. **Outcome Measures:** Walking speed, step length, cadence, EMG.	1. Significant differences were found between the two groups in: - Walking velocity (m/s): Group 1 pre=0.12(0.11), post=0.27 (0.25); Group 2 pre=0.11(0.08), post=0.12(0.10); (p=0.043) - Cadence: Group 1 pre=22.15(16.18), post=40.40(28.27); Group 2 pre=21.67 (20.71), post=22.04(21.71); (p=0.05). 2. Group 1 showed significant changes for EMG amplitude, step length, walking velocity and cadence pre and post. 3. Group 2 showed significant changes for EMG amplitude, walking velocity and step length, but not cadence pre and post.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data.	

		
[Petrofsky 2001] USA Prospective Controlled Trial Level 2 N = 10	**Population:** 10 males; age 22-30 yrs; incomplete, T3-T12 lesion level. **Treatment:** The control group (n=5) had 2-hour daily conventional physical therapy, including 30 min biofeedback of more affected gluteus medius for 2 months. Experimental treatment (n=5) had same program and used a portable home biofeedback device. **Outcome Measures:** Muscle strength (isometric strain gauge transducer) and gait analysis.	1. Gains in strength (in quadriceps, gluteus medius and hamstring) were seen for both groups but were greater for the experimental group than controls. 2. After two months of therapy the reduction in Trendelenburg gait was greater for the experimental group than for the control group and the experimental group showed almost normal gait.
[Tamburella et al. 2013] Italy Case Control Level 3 N = 12	**Population:** 12 participants with SCI; 6 in the visual biofeedback task-specific balance training (vBFB) group and 6 in control group. vBFB group: mean (SD) age: 52 (11.74); 3M 3F. Control group: mean (SD) age: 53.5 (13.21); 3M 3F. **Treatment:** 2 groups: vBFB and Rehab group (control). vFBF and control groups underwent 8 wks of rehab 5 times/wk (control: 60 min devoted to Rehab; vBFB: 40 min of rehab plus 20 of vBFB). **Outcome Measures:** BBS; WISCI; 6MWT; 10MWT; and kinematic spatiotemporal gait parameters.	1. Only the vBFB group experienced a significant improvement in gait: a. BBS: 26 (10.69) at baseline to 41 (7.8) at end of intervention. b. WISCI: 14.17 (1.83) at baseline to 17.15 (1.64) at end of intervention. c. 6MWT: 193.18 (68.08) at baseline to 259.64 (82.84) at end of intervention. 2. The improvement in gait for the vBFB group was maintained at follow-up examinations. 3. vBFB participants experienced greater improvements than control participants for all measures 4. vBFB treatment demonstrated a significantly higher level of effectiveness than conventional rehabilitation.
[Sayenko et al. 2010] Canada, Japan Pre-post Level 4 N = 6	**Population:** 6 participants- 5 males and 1 female; chronic SCI; 4 AIS C and 2 AIS D; level of injury: C4-T12; mean age= 41y; median years post-injury= 7y **Treatment:** Patients participated in 3 60-min visual feedback training	1. All participants showed substantial improvements in the scores, which varied between 236±94 and 130±14% of the initial values for different exercises. 2. Improvements were all statistically significant for both eyes open and

	sessions, totaling 12 sessions. During training, participants stood on a force platform and were asked to shift their center of pressure (COP) in the indicated directions as represented by a cursor on the monitor. **Outcome Measures:** Static standing eyes open and closed as measured by COP displacement; Dynamic standing as measured by voluntary COP displacement.	closed except mean velocity in the medial/lateral direction.

Discussion

Several studies have been conducted including patients with chronic SCI, who performed different training programs using virtual reality (VR) (An & Park 2018, 2022; Donati et al. 2016; Duffell et al. 2019; van Dijsseldonk et al. 2018; Villiger et al. 2017; Zwijgers et al. 2024), or standing and walking programs coupled with biofeedback (Amatachaya et al. 2023; Cheung et al. 2019; Govil & Noohu 2013; Mollà-Casanova et al. 2024; Nithiatthawanon et al. 2020; Sayenko et al. 2010; Tamburella et al. 2013). Though VR training has been incorporated more often in studies training sitting balance or standing balance in people with SCI, some studies show that VR and biofeedback training can improve walking as well.

An and Park (2022) compared a rehabilitation protocol that included kicking motions to participants in a virtual soccer game in 40 people with incomplete tetraplegia. At the end of the intervention, both groups showed improvements in walking speed (10MWT), but the VR group improved significantly more than the control group (reduction in time to complete test from before to after intervention: 13.75 seconds vs. 9.45, $P < .01$; An & Park 2022).

Another type of walking training with VR biofeedback, Gait Real-time Analysis Interactive Lab (GRAIL), has been tested in people with SCI (Zwijgers et al. 2024; van Dijsseldonk et al. 2018). GRAIL consists of an instrumented dual belt treadmill with two embedded force plates capable of moving in multiple directions and of generating mechanical perturbations with an eight-camera VICON motion capture system (van Dijsseldonk et al. 2018). In a multicenter RCT, Zwijgers et al. (2024) randomly assigned 35 participants with incomplete, chronic SCI to either 11 hours of walking training using the GRAIL system or to conventional walking and strength training. After six weeks, both groups' maximal walking speed increased by 0.07 m/s at post-intervention and by 0.10 m/s at follow-up relative to baseline. A small pre-post study found slightly higher gains in walking speed (0.14-0.19 m/s) after GRAIL training (van Dijsseldonk et al. 2018).

In a longer-term approach to assessing walking training with VR, Donati et al. (2016) enrolled eight people with SCI into a year-long gait neurorehabilitation program that included immersive VR, enriched visual-tactile feedback, and custom-designed exoskeletons. Among other outcome measures assessed, all patients experienced a three-to-six-point gain in WISCI scores (on a scale of 1-20, greater than 1 SD of 3.4 points; Donati et al. 2016).

The RCT of Cheung et al. (2019) included 16 participants with incomplete SCI who received standard physiotherapy; in addition, participants either received BWSTT plus biofeedback three times per week for eight weeks (active group, n=8) or passive lower limb mobilization (control group, n=8). BWSTT was performed with the Lokomat system and an EMG biofeedback system was applied to the bilateral vastus lateralis with generated audio signals if the muscle activation was less than 30% of maximal recruitment, encouraging active participation during the stance phase of the gait cycle (Cheung et al. 2019). The experimental group improved more in WISCI II and SCIM-III mobility scores, however, it should be noted that they received 40% more walking training hours than the control group; it is therefore difficult to determine the effects of the EMG biofeedback system for these participants.

Other studies, it would appear, provide evidence that biofeedback may be helpful in muscle activation when attempting walking in people with SCI. In the study by Govil and Noohu (2013), biofeedback was provided in the form of EMG from the gluteus maximus muscle. Participants (N=30) were randomized into two groups, either receiving biofeedback and gait rehabilitation or just gait rehabilitation. Both groups significantly improved from baseline in EMG amplitude, walking velocity and step length, but the group receiving biofeedback improved cadence too. In an RCT, Amatachaya et al. (2023) tested a lower limb loading training (LLLT) program with or without biofeedback over four weeks (30 min per day, 5 days per week) in participants with incomplete and chronic SCI. At the end of the intervention, the mobility improvement (10MWT, 6MWT, and FTSTS test) of participants in the experimental group was significantly greater than that of the participants in the control group ($p<0.05$); however, this difference was not found at six months after the training programs (Amatachaya et al. 2023).

VR and biofeedback-based physical therapy have been employed in home-based rehabilitation in order to improve access, increase adherence and uniformity in interventions, and the ability to remotely monitor and solve problems (Reilly et al. 2021). Exercise through home-based video games, such as Nintendo Wii (Nintendo, Kyoto, Japan) and Xbox Kinect (Microsoft®, Redmond, WA, USA) have been used by clinicians to offer moderate intensity exercises (Mat Rosly et al. 2017), task-oriented training and high repetition to maximize motor learning and neuroplasticity (Levin et al. 2015), along with increased motivation and enjoyment, and the ability to be used independently by the patient (Perrochon et al. 2019). Villiger et al. (2017) tested the feasibility of a home-based (i.e., unsupervised) VR-augmented training intervention (in sitting and standing positions) for 4 weeks in participants with motor-incomplete SCI. The intervention was well-accepted by participants, and the results revealed significant improvements in muscle strength (LEMS) at short-term assessment (Villiger et al. 2017).

There remains a strong need for further well-designed RCTs investigating the effect of VR therapy on different mobility outcomes among people with SCI and providing information about VR long-term effects in order to develop robust and detailed recommendations (Abou et al. 2020; Yeo et al. 2019).

Conclusions

There is level 1 evidence (from 1 RCT: An & Park 2022) that participants who performed kicking motions in a virtual soccer game improved their walking speed (10MWT) more than the participants who performed the same number of kicking motions without the VR component.

There is level 1 evidence (from 1 RCT: Cheung et al. 2019) that BWSTT (performed with the Lokomat system and an EMG biofeedback system) provided greater improvements in WISCI II walking scores and SCIM-III mobility subscores than passive lower limb mobilization in participants with incomplete SCI.

There is level 2 evidence (from 1 RCT: Zwijgers et al. 2024) and level 4 evidence (from 1 pre-post study: van Dijsseldonk et al. 2018) that individualized VR gait training on an instrumented dual belt treadmill with the capacity to move in several directions to generate mechanical perturbations and the utilization of the GRAIL system for 6 weeks, provides significant improvements in walking speed (2MWT) and functional ambulation (SCI-FAP); however, these improvements are not superior to the ones obtained after a conventional locomotor and strength training program; in participants with incomplete and chronic SCI.

There is level 2 evidence (from 1 longitudinal study: Villiger et al. 2015) and level 4 evidence (from 1 pre-post study: Villiger et al. 2013) that lower limb training augmented by biofeedback of ankle and knee movements can improve gait and muscle strength.

There is level 1 evidence (from 2 cross-over RCTs: Amatachaya et al. 2023; Nithiatthawanon et al. 2020) that adding visual feedback relating to the amount of lower limb loading during bodyweight shifting, stepping, and OWT provides improvements on 10MWT, 6MWT, and FTSTS test in participants with chronic SCI.

There is level 1 evidence (from 1 RCT: Mollà-Casanova et al. 2024) that six weeks of visual illusion therapy based on virtual walking (quiet standing watching a video projection of legs walking on a treadmill) plus a therapeutic exercise program (including gait and multicomponent training exercises) provides significant improvements in tibialis anterior strength and in walking speed (10MWT) and walking ability (WISCI II) than a placebo visual illusion intervention plus the same therapeutic exercise program, in participants with incomplete and chronic SCI.

There is level 2 evidence (from 1 RCT: Govil & Noohu 2013) that EMG biofeedback may improve gait outcomes in patients with SCI.

There is level 4 evidence (from 1 pre-post study: An & Park 2018) that a semi-immersive VR intervention for 6 weeks provides significant improvements in walking ability (WISCI II) in patients with incomplete and chronic SCI.

Key Points

Virtual reality (VR) training is an effective strategy to improve walking performance in patients with chronic and incomplete SCI, and may afford further benefits compared with the same training interventions without the VR biofeedback.

EMG Biofeedback, visual feedback, visual illusion, or visuotemporal cue feedback adding to standing, stepping, or body weight supported treadmill training protocols may improve gait and lower limb muscle strength in people with incomplete and chronic SCI.

8 Whole-Body Vibration (WBV)

The use of whole-body vibration (WBV) has become more common in the last decade as a method for improving postural control, muscle strength, and power in numerous healthy and pathological people (Alashram et al. 2019). It can be defined as standing or training on a vibrating platform, which transmits sinusoidal oscillations to the whole body via feet (Cardinale & Bosco 2003).

Table 19. Whole-Body Vibration (WBV)

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
In et al. 2018 Republic of Korea RCT PEDro = 7 Level 1 N = 28	**Population:** 28 participants with cervical (level C6 or C7) SCI; 19 males and 9 females; mean age 48 years; AIS D; and mean time since injury 14 months. **Treatment:** All patients were randomly assigned to two groups: • Whole-body vibration (WBV) group (n = 14): Participants received 16 min of WBV training, twice a day, 5 days a week for 8 weeks. The frequency was set at 30 Hz, and a vertical displacement was 2–4 mm. Patients were required to stand on the platform and were instructed to hold a semi-squatting position. WBV	1. Both groups showed significant improvements in walking ability. 2. The WBV group improved on the 10MWT significantly more than the control group (3.5±2.3 vs 1.3±1.4; p = 0.005).

	training consisted of four sets of 45 s of stimulation, and a minute break between each session. • Control group (n = 14): Participants received the same WBV procedure but without vibration (placebo). Both groups were treated with a conventional physical therapy protocol consisting of ROM and mat exercises, and gait training for 30 min per day. **Outcome Measures:** Postural imbalance (analyzed based on postural sway length using a force plate device) and walking ability (by 10MWT) were assessed at baseline and at post training.	
Estes et al. 2018 USA RCT crossover PEDro = 4 Level 1 N = 34	**Population:** 34 participants with SCI and at least mild spasticity affecting leg muscles; 28 males and 6 females; mean age 46.3 years; injury level C1 (n = 1), C3 (n = 4), C4 (n = 4), C5 (n = 6), C7 (n = 5), C8 (n =1), T1 (n = 1), T3 (n = 1), T4 (n = 1), T6 (n = 1), and T8 (n = 1); AIS C (n = 9) and AIS D (n = 25); and mean time since injury 6.1 years. **Treatment:** Participants received four different WBV frequency/duration dose conditions and one sham-control stimulation (single sessions): • Low frequency, short duration: 30 Hz; four 45-s bouts (180 s total). • High frequency, short duration: 50 Hz; four 45-s bouts (180 s total). • Low frequency, long duration: 30 Hz; eight 45-s bouts (360 s total). • High frequency, long duration: 50 Hz; eight 45-s bouts (360 s total). • Sham-control: ES with electrodes placed in the posterior thoracic region while standing; eight 45-s bouts. During each WBV session, participants stood on the vibration platform with knees slightly flexed. **Outcome Measures:** 10MWT was measured at three time points during each session: (1) prior to the start of the intervention (baseline), (2) immediately	1. 29 participants completed all sessions. 2. Mean baseline walking speed was not different among any of the five intervention sessions (p = 0.992). 3. The change in walking speed from baseline to either of the two postintervention assessment time points (immediate and 45-min delayed) was not different when comparing each WBV frequency/duration dose condition to the sham-control at each of the time points. 4. When participants were stratified according to baseline spasticity, there were no significant differences in the change in walking speed from baseline to either of the two post-intervention assessments when comparing each WBV frequency/duration dose condition to the sham-control in either the high spasticity or low spasticity subgroups.

	after intervention (immediate), and (3) 45 min after the conclusion of the intervention (45-min delayed).	
Bosveld & Field-Fote 2015 USA RCT PEDro = 8 Level 1 N = 25	**Population**: 25 participants; chronic SCI; age =49.7 ± 12.5 years; years post injury= >1y. **Treatment**: Participants were randomized into two groups. Group 1 (n = 13) received WBV treatment (frequency: 50 Hz, amplitude: 2 mm) comprising of four 45-s bouts with 1-min rest periods after each bout. Group 2 (n = 12) received sham ES. Maximal voluntary isometric quadriceps force was measured with a fixed dynamometer. A modified FTSTS test was used to assess functional lower extremity strength. Measures were made at pre-test, immediate post-test, and delayed post-test 20 min later. **Outcome Measures:** Maximal voluntary isometric quadriceps force, modified FTSTS test.	1. When comparing the pre-test and immediate post-test data, the difference in mean quadriceps strength between the two groups approached significance (P = 0.10). However, between the pre-test and delayed post-test, there were no significant difference between groups (P = 0.82). 2. The within-group change for the WBV group was significant with a moderate effect size (P = 0.05; ES = 0.60). 3. Between the pre-test and immediate post-test, the time from sit to stand between the two groups approached significance (P = 0.10). Between the pre-test and delayed post-test, there was no significant difference between groups (P = 0.32).
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data. 	
Ness & Field-Fote 2009 USA Pre-Post N = 17	**Population:** 3 women, 14 men; aged 28-65 years; all participants had a motor-incomplete SCI; C3-T8 lesion level; ≥1 year duration. **Treatment:** WBV 3 days/week for 4 weeks with four 45 s bouts of 50 Hz frequency and 2-4mm intensity each session, while standing on a vibration platform with one minute of seated rest in between. **Outcome Measures:** 3-D motion capture system used to measure walking function (walking speed; step length;	1. Walking speed significantly increased by mean (SD) 0.062 (0.011) m/s from 0.259 ± 0.248 m/s in the initial test to 0.321 ± 0.260 m/s in the final test ($p<0.001$). 2. All participants tolerated the 12-session of WBV, were able to maintain the standing posture for the 45-s bouts of WBV, and reported no adverse effects.

	cadence (steps/min); hip-knee intralimb coordination).	

Discussion

Even though whole-body vibration (WBV) is more common than it once was, the research supporting its usage in people with SCI is somewhat limited. In 2009, Ness and Field-Fote first demonstrated the feasibility and potential benefits of WBV on walking function in people with SCI (Ness & Field-Fote 2009). This small pre-post study found a mean improvement in walking speed of 0.062 m/s, which although statistically significant, was considered a small effect size. Herrero et al. (2010) suggested that that peak blood flow in the femoral artery increased with higher vibration frequencies (20 or 30 Hz), thus promoting circulation in the legs and increasing muscle activation.

In an RCT, In et al. (2018) measured walking speed comparing WBV plus conventional physical therapy (30 minutes of ROM mat exercises, and gait training) versus sham WBV and the same physical therapy program. Both groups improved walking ability, but people in the WBV group improved significantly more on the 10MWT. However, two other RCTs (Estes et al. 2018; Bosveld & Field-Fote 2015) found no differences in walking speed (10MWT), though potential benefits of WBV through improvements in muscle force output and sit-to-stand function were found in Bosveld & Field-Fote (2015).

Conclusions

There is level 1 evidence (from 1 RCT: In et al. 2018) and level 4 evidence (from 1 pre-post study: Ness & Field-Fote 2009) that a minimum of 4 weeks of WBV training could have beneficial effects on walking speed in patients with chronic and motor-incomplete SCI.

There is level 1 evidence (from 1 RCT: Bosveld & Field-Fote 2015) that WBV improved muscle force output and Sit to Stand test scores, though neither of these differences was significant.

Key Points

There is limited evidence that whole body vibration plus physical therapy improves walking velocity in people with incomplete SCI but stronger evidence, possibly by improving muscle force output.

9 Telerehabilitation

Telemedicine involves using information and communication technologies to provide care and education at a distance (Solomon et al. 2022). Telerehabilitation is a subset of telemedicine defined as the provision of rehabilitation services at a distance using telecommunication technology, incorporating prevention and treatment (Russell 2007). The first-known

telerehabilitation study involving people with SCI was an RCT by Soopramanien et al. (2005) testing the effectiveness of post-discharge support. The COVID-19 pandemic resulted in a significant shift in the adoption trajectory of telerehabilitation and remote monitoring technologies for many health professionals, including physical therapists (Ferguson 2022).

Recently, some systematic reviews (Lee et al. 2021; Touchett et al. 2022; Solomon et al. 2022) have been published evaluating the effectiveness and potential barriers of "telespinalcordinjury" or "teleSCI" (term coined at the International Spinal Cord Society Annual Scientific Meeting in Vienna, Austria on 2016); however, only one study (Villiger et al. 2017) assessed walking interventions/outcome measures. Most recently, two studies have been conducted to test telerehabilitation using walking outcome measures, among other outcomes, in people with SCI whose rehabilitation plan was affected because of COVID-19 (García-Rudolph et al. 2024a) or due to war conflicts (Fathe et al. 2024).

Table 20. Telerehabilitation

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Fathe et al. 2024 Iraq Prospective controlled trial Level 2 N = 18	**Population:** 18 individuals with SCI who had experienced an interruption in rehabilitation services 4 and 5 years earlier (because of war and/or COVID-19 pandemic): • Experimental group (n = 8): 5M, 3F Mean (SD) age: 32.25 (5.91) years. Injury level: C6-L2; tetraplegia (n = 1) and paraplegia (n = 7). ASIA A (n = 7), ASIA B (n = 1). Mean (SD) time since injury: 55 (4.78) months. • Control group 1 (n = 5): 3M, 2F Mean (SD) age: 26.80 (6.19) years. Injury level: T5-L2; tetraplegia (n = 5) and paraplegia (n = 0). ASIA A (n = 5), ASIA B (n = 0). Mean (SD) time since injury: 53.4 (5.81) months. • Control group 2 (n = 5): 3M, 2F Mean (SD) age: 21.20 (8.18) years. Healthy sample.	1. The analysis indicates a lack of statistically significant impact on anthropometric measures and most muscle strength evaluations. Specifically, the p-values exceeded 0.05 (ranging between $p < 0.166$ and 1.000), except for the test assessing pelvis elevation from lying-down position and closing lower limbs. 2. The secondary assessments indicate no significant effect of the HTRP on anthropometric measures of abdomen/waist, both thighs, both legs circumferences, weight and BMI. The only significant effect on anthropometric measures was on pelvic circumference ($p < 0.001$).

	Treatment: A personalized rehabilitation plan for each participant was provided for 6 months. The home telerehabilitation program focused on different exercises (bed exercises, rubber ball exercises for strength and balance, trunk flexibility exercises, crawling, rolling, ball-related movements, and exercises on parallel-bar), weight exercises (focused on the upper limbs, shoulders, chest, and back), and aerobic training targeting cardiorespiratory fitness. Program was five weekly sessions gradually increasing the intensity and volume (from 45 to 120 min). Control group 1 (SCI only) underwent the assessment test and the control group 2 (non-SCI) was included to establish baseline levels of study variables for people without SCI. **Outcome Measures:** Anthropometric measurements for body parts circumferences and muscle strength tests (performed on participants' lower and upper extremities, head, and trunk to measure various movements using a handheld muscle tester) were assessed at baseline, at three months and at 6 months.	
García-Rudolph et al. 2024a Spain Case control Level 3 N = 84	**Population:** 84 participants with acute (within 2 months after injury) SCI. • Telerehabilitation (tele) SCI group (n = 42): 26M, 16F Median (Q1-Q3) age: 51 (35-60) years. Cause of injury: Traumatic (n = 18) and non-traumatic (n = 24). Injury level: Paraplegia (n = 30) and tetraplegia (n = 12). AIS A (n = 11), B (n = 0), C (n = 9), and D (n = 22). Median (Q1-Q3) time since injury: 39 (34-49) days. • Traditional rehabilitation inpatients (controls) matched for age, time since injury to rehabilitation admission, level of	1. The teleSCI group showed no significant differences compared with traditional rehabilitation group in gains, efficiency and effectiveness in FIM, SCIM, or WISCI.

	injury, complete or incomplete injury, and etiology (n = 42): 22M, 20F Median (Q1-Q3) age: 55 (36-62) years. Cause of injury: Traumatic (n = 16) and non-traumatic (n = 26). Injury level: Paraplegia (n = 31) and tetraplegia (n = 11). AIS A (n = 11), B (n = 5), C (n = 4), and D (n = 22). Median (Q1-Q3) time since injury: 42 (30-51) days. **Treatment:** Historical controls who had completed in-person rehabilitation were compared with a specific group of patients who followed teleSCI during the COVID-19 lockdown. • In-person rehabilitation: The rehabilitation program includes intensive treatment from the multidisciplinary team oriented toward training in activities of daily living and physical rehabilitation, respiratory management, training for bladder and bowel management, and psychological support. Physical rehabilitation, training of activities of daily living, and respiratory management constitute 3–4 hours of rehabilitation input daily, 5 days per week. • Intervention group: The focus of the teleSCI input was on physical rehabilitation and training of activities of daily living, which had three components: o TeleNeuroFitness (TNF) involved fitness exercises classes of 60 minutes with five patients connected online together with a medical fitness instructor. o TeleNeuroRehab (TNR) involved 30-minute one-to-one sessions with a physiotherapist or occupational therapist to	

	explain exercises, provide advice, and resolve doubts. ○ TeleNeuroMov (TNM) utilized 15-minute 41 exercise (SCI-specific, and with different level of difficulty) videos that the patient could access during their day at home. The videos covered a wide range of exercise training including sessions for balance, upper limb and lower limb strengthening, respiratory exercises, trunk exercises, dynamic gait, fine hand training, hand strengthening, and bed mobility practice. All included patients received 3.5 hours of teleSCI a day, 5 days a week, for the duration of their rehabilitation that included 1 hour of TNF, three 30-minute sessions of TNR, and four 15-minute TNM sessions. *While at home, patients received a daily phone call from a member of the rehab nursing team and a weekly call from their physician to monitor any problems, and patients also attended the center once a month to be seen by their physician. The potential to be readmitted to the center because of medical complications that could not be managed at home was considered on a case-by-case basis. **Outcome Measures:** Gain, efficiency, and effectiveness for the FIM, SCIM-III, and WISCI II were calculated: • Gain = score at discharge – score at admission • Efficacy: difference between score at admission and score at discharge. • Efficiency: gain divided by length of stay and OM effectiveness as: (final score-initial score)/maximum score-initial score) x 100.	

Villiger et al. 2017 Switzerland Pre-post Level 4 N = 11	**Population:** 11 participants with motor-incomplete SCI and able to sit in a chair without assistive and supporting systems; mean (± SD) age 60 (± 10.2) years; level of injury C4 (n = 1), C5 (n = 3), C7 (n = 2), T4 (n = 1), T9 (n = 1), T12 (n = 2), and L3 (n = 1); AIS C (n = 1) and AIS D (n = 10); and mean time since injury 7.6 years. **Treatment:** All participants were trained at home on the VR tasks over a period of 4 weeks, with 16–20 sessions of 30–45 min each, and with the mobile prototype of the YouKicker system. Around 500 repetitions of ankle movements and 100 knee movements with each leg were performed through different blocks by a typical patient during a training session. **Outcome Measures:** LEMS, 10MWT, 6MWT, SCIM-III, and WISCI II were tested 4 weeks before treatment (pre-baseline), directly before treatment (baseline), after finishing the training program (post-assessment), and 2-3 months after the treatment program (follow-up).	1. At post-assessment, significant increases in comparison with the averaged pre-baseline and baseline were found in LEMS (P = 0.008) 2. There were no significant effects on 10MWT (P = 0.169), 6MWT (P = 0.037); SCIM-III mobility (P = 0.018), and WISCI II (P = 0.180). 3. At follow-up assessment, no significant changes were found in muscle strength (LEMS, P = 0.065), or walking speed/distance and mobility (10MWT [P = 0.169], 6MWT [P = 0.32], SCIM-III mobility [P = 0.026], and WISCI II [P = 0.317]).

Discussion

There are too few studies currently to determine the effectiveness of a telerehabilitation approach on walking (or precursors to walking) in people with SCI.

One case control study by García-Rudolph et al. (2024a) found no significant differences on FIM, SCIM, or WISCI scores whether people were in the 'teleSCI' group or in the traditional rehabilitation control group. A small prospective controlled trial tested a 6-month at home rehabilitation program with war veterans; Fathe et al. (2024) largely found no significant differences between telerehab and in-person groups on muscle strength or other anthropomorphic measures. In a small pre-post study, Villiger et al (2017) tested the feasibility and effectiveness of an at-home VR lower limb rehabilitation program called 'YouKicker'; after 4 weeks, they found significant improvements in LEMS, but not in 6MWT, WISCI II, or SCIM scores.

Conclusions

There is level 2 evidence (from 1 prospective controlled trial: Fathe et al. 2024) that a 6-month home telerehabilitation program focused on different whole-body exercises, resistance exercises, and aerobic training provides few differences in muscle strength or other anthropomorphic measures compared to controls in people with complete chronic SCI.

There is level 3 evidence (from 1 case control study: García-Rudolph et al. 2024a) that a teleSCI intervention (comprising fitness exercises classes, one-to-one physiotherapy/occupational therapy sessions, SCI-specific exercises prepared videos, and scheduled phone-calls with nurses and physicians) provides similar improvements in mobility (WISCI) and functional outcomes (FIM and SCIM) as traditional rehabilitation in patients with acute SCI.

There is level 4 evidence (from 1 pre-post study: Villiger et al. 2017) that a home VR intervention focused on lower limb exercises for four weeks provides significant improvements in LEMS but not in 10MWT, 6MWT, WISCI, and SCIM in participants with incomplete and chronic SCI.

Key Points

Limited research to date shows that telerehabilitation provides similar improvements as traditional rehabilitation in people with SCI.

Further research with higher-quality studies is necessary to test these results.

10 Acute Intermittent Hypoxia (AIH)

Acute intermittent hypoxia (AIH) refers to brief (acute), repetitive (intermittent) episodes of breathing oxygen-deprived air (hypoxia) alternating with breathing ambient room air (Tan et al. 2020). AIH is a novel, noninvasive means to induce spinal plasticity, strengthening spared pathways to motoneurons after incomplete SCI (Hayes et al. 2014). Recent studies have provided foundational support that AIH also induces improvements in breathing capacity, lower limb, and upper limb function in people with SCI, suggesting its translational potential as a therapeutic strategy in people with SCI (Tan et al. 2020).

Table 21. Acute Intermittent Hypoxia (AIH)

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Tan et al. 2021 USA RCT cross-over PEDro = 8 Level 1 N = 11	**Population:** 11 participants with incomplete SCI and the ability to walk at least one step without human assistance; 9 males and 2 females; mean age 46.8 years; injury level C4 (n = 4), C5 (n = 2), C6 (n = 1), C8 (n = 1), T3 (n = 1), T5 (n	1. No serious AEs occurred during the interventions. 2. Participants significantly improved overground walking speed and endurance following the daily AIH + WALK intervention relative to their

	= 1), and T9 (n = 1); and mean time since injury 8.5 years. **Treatment:** Participants received AIH + WALK or AIH_{sham} + WALK (SHAM + WALK) with a washout period of 2 weeks. Interventions consisted in five consecutive days receiving: • The single AIH protocol session consisted of 15, 90s episodes of breathing at a fraction of inspired oxygen (FiO_2) = 0.10 ± 0.02 with 60s room air intervals at a FiO_2 of 0.21 ± 0.02; and the SHAM breathing protocol session consisted in the same breathing episodes but always set at a FiO_2 of 0.21 ± 0.02 (room air). • Walking practice during 30 min at their perceived maximum voluntary walking speed, approximately 15 min following completion of the breathing protocol. **Outcome Measures:** Walking performance (10MWT and 6MWT) and intralimb motor coordination using kinematic variability measures of foot trajectory (i.e., endpoint variability), and of inter-joint coupling between the hip and knee, as well as between the knee and ankle joints (i.e., angular coefficient of correspondence) were assessed at baseline (BL), 1-week (F1), and 2-weeks (F2) following each combinatorial intervention*. *Walking performance was also assessed at the end of the fifth day of the treatment intervention (T5).	baselines (with these improvements persisting at F1 and at F2), but not following daily SHAM+WALK. 3. Improvements in the 10MWT and 6MWT following daily AIH + WALK did not result in more consistent foot trajectories of the more impaired leg. 4. Comparison of changes between participants who used bilateral walking aids (n = 5) and those who did not (n = 6) showed that participants achieved comparable gains in walking endurance following daily AIH + WALK; however, those participants who used bilateral arm-driven walking aids achieved greater change in their 10MWT time following daily AIH + WALK as compared to those participants who did not.
McKenzie et al. 2024 USA RCT crossover PEDro = 5 Level 2 N = 10	**Population:** 10 participants with incomplete (ASIA D) and chronic SCI and with the ability to ambulate at least 14 m without physical assistance. 8M, 2F Mean (SD) age: 46.90 (16.53) years. Injury level: C4-T12 Mean (SD) time since injury: 8.75 (9.44) years	1. No AEs occurred throughout the trial. 2. Walking speed at self-selected velocity: At 3 days postintervention, the improvement for self-selected velocity in the AIH + tSCS arm was significantly greater than the improvements in the SHAM

	Treatment: Participants completed 3 arms of the study in random order, with a minimum of a 4-week washout between arms: • Real AIH with tSCS during gait training (AIH + tSCS). • SHAM AIH with tSCS during gait training (SHAM AIH + tSCS). • Gait training alone (SHAM + SHAM). Participants completed 5 intervention sessions for each arm. Each intervention session consisted of: • AIH delivery: 15 cycles of AIH (9% O_2, fraction of inspired air [FiO_2]: 0.09; alternating with 15 cycles of normoxia (Nx) [21% O_2, FiO_2: 0.21] or SHAM AIH (15 alternating exposures of normoxic air [21% O_2]). Each hypoxia cycle was administered until the participant's oxygen saturation reached this nadir or for up to 90 seconds. Nx was delivered for up to 90 seconds. • 30 minutes of rest. • 30 minutes of OGT (Borg Rating of Perceived Exertion 14-17 out of 20) with tSCS or SHAM tSCS. tSCS was delivered medially between the C6-6, T11-12, and L1-L2 levels. Continuous stimulation was applied during gait training consisting of biphasic, rectangular 1-ms pulses at a frequency of 30 Hz with a carrier frequency of 10kHz. Stimulation intensity was determined by assessing spinal motor evoked responses at baseline. For SHAM stimulation, tSCS was turned on for the first 5-10 seconds of walking and then deactivated by the clinician without notifying the participant. **Outcome Measures:** • Walking speed at self-selected velocity and fast velocity using the 10MWT; 6MWT; and TUG test	AIH + tSCS arm (between-group MD: 0.08 m/s, 95% CI: 0.02-0.14 m/s, P=0.04, g=0.31). Additionally, within the AIH + tSCS arm, the MCID of 0.06 m/s was met at 3 days postintervention with an average improvement from baseline of 0.06 m/s (95% CI: 0.00-0.12 m/s, P=0.18, g=0.14), and approached the MCID at 1WK (within MD 1WK-baseline: 0.05 m/s, 95% CI: 0.01 to 0.12 m/s, P=0.34, g=0.17). 3. Walking speed at fast velocity: The fast velocity improvements of the AIH + tSCS arm at each time point compared with the other two arms were insignificant and had small effect sizes. The same trend was seen for within arm comparisons for improvements over time compared with baseline. However, the improvements from baseline to 1WK of the AIH + tSCS arm, although small, had greater effect sizes (1WK-baseline g=0.12) compared with the other 2 arms (1WK-baseline g=0.09, g=0.03). Regardless of the order of arms, the final arm baseline fast velocity was significantly greater than the first (0.10 m/s, P=0.02) and second (0.06 m/s, P=0.01) baseline. 4. 6MWT: For the 6MWT, there were no significant between-group improvements. For the within improvements of the AIH + tSCS arm there was a meaningful change for people with neurologic injuries with an improvement from baseline to 1WK of 21.5 m (95% CI: 3.4-39.6 m, P=0.06, g=0.22). The baseline mean 6MWT distance at the final arm was significantly greater than the first baseline (39.18 m, P=0.02).

	were measured at baseline before intervention, intervention session 5 (INT5), 3 days postintervention (POST), and 1-week following POST assessment (1WK). • Maximum isometric ankle plantarflexion torque was assessed within each arm at baseline and 3 days postintervention using a strength testing dynamometer.	5. Isometric ankle torque: The results for isometric plantarflexion showed that maximal torque increased an average of 23.8% (95% CI: 2.6 to 50.3%, P=0.66) for the weak side and 11.3% (95% CI: 5.3 to 28.0%, P=0.25) on the strong side after AIH + tSCS arm. However, there was no significant difference in strength percent change between the arms.
Navarrete-Opazo et al. 2017a Chile RCT PEDro = 4 Level 2 N = 35	**Population:** 35 participants with chronic and incomplete SCI; 31 males and 4 females; mean (± SD) age 41 (± 17) years; injury level C4 (n = 1), C5 (n = 3), C6 (n = 6), C7 (n = 2), T1 (n = 1), T3 (n = 2), T4 (n = 1), T6 (n = 3), T9 (n = 3), T10 (n = 1), T12 (n = 4), L1 (n = 3), L3 (n = 3), L4 (n = 1); AIS C (n = 13) and AIS D (n = 22); and mean (± SD) time since injury 53 (± 40) months. **Treatment:** Participants were randomly allocated into two groups: • Experimental group (n = 18): The intermittent hypoxia (IH) protocol consisted of 90sec of 9% O_2 interspersed with 90 sec of 21% O_2, 15 times a day, for 5 consecutive days, followed by IH three times per week for 3 additional weeks. • Control group (n = 17): The placebo protocol consisted of continuous Nx (21% O_2) for 45 min for 5 consecutive days followed by three times per week for 3 weeks. Following the IH/Nx protocol, all participants performed BWSTT for 45 min (for 5 consecutive days the first week and 3 times per week for 3 additional weeks). **Outcome Measures:** 10MWT and 6MWT were assessed at baseline, day 5, weekly from weeks 2–4, and at a 2-week follow-up.	1. The interventions were well tolerated by all participants; with no side effects being reported. 2. Within-group comparisons showed that overall, the IH group had a significant decrease in 10MWT time from day 5 to week 2 (-10.2 – 3.0 vs. -15.5 – 4.8 sec, p = 0.03), which was maintained up to the 2-week follow-up (-15.5–4.8 vs. -20.3–6.9s, p = 0.09). 3. Between-group comparisons showed that the IH group had a greater walking speed than the control group, between baseline vs. at 5 days after the interventions (IH: -10.2 – 3.0 vs. Nx: -1.8 – 1.7 sec, p = 0.006). This trend was maintained at week 2 and week 3 but not at week 4 (p = 0.54). A 2-week follow-up showed that both groups maintained a walking speed significantly faster than baseline (p < 0.05), and differences between groups approached statistical significance (p = 0.06). 4. Within-group comparisons showed that the IH group had a progressive increase in walking distance from day 5 to week 4 (43.1 – 10.7 vs. 70.5 – 13.2 m, p = 0.007), and this increase persisted for 2 weeks after the completion of the study (70.5 – 13.2 vs. 65.7 – 11.5, p = 0.49).

		5. Between-group comparisons showed that there was a greater walking endurance in the IH group compared with the control group at day 5 (IH: 43.1–10.7 vs. Nx: 6.1–3.4m, p = 0.012) and at later time points.
Hayes et al. 2014 USA RCT PEDro = 8 Level 1 N = 22	**Population:** 22 participants with chronic incomplete SCI; 16 males and 3 females; mean (± SD) age 43 (± 4) years; injury level C2 (n = 1), C4 (n = 5), C5 (n = 5), C6 (n = 3), C7 (n = 1), T3 (n = 1), T4 (n = 1), T7 (n = 2), and T8 (n = 1); AIS C (n = 1) and AIS D (n = 17); and mean (± SD) time since injury 9 (± 2) years. **Treatment:** The study consisted of 2 experimental blocks: • In block 1, participants were randomly assigned to first receive either daily AIH (dAIH) (n = 6) or daily SHAM (dSHAM) (n = 5), and then the other intervention a minimum of 2 weeks later. • In block 2, participants were randomly assigned to first receive either daily AIH + walking (n = 5) or daily SHAM + walking (n = 6), and then the other intervention a minimum of 2 weeks later. Daily AIH (5 consecutive days) consisted of 15, 90-s hypoxic episodes (FIO_2 = 0.09) with 60-s normoxic intervals (FIO_2 = 0.21). Daily SHAM, consisted of 15, 90-s simulated normoxic episodes (FIO_2 = 0.21) with 60-s normoxic intervals (FIO_2 = 0.21). In block 2, participants received the daily AIH or daily SHAM, followed within 60 min by OWT. **Outcome Measures:** 10MWT and 6MWT were assessed at baseline, at day 1 (D1), day 5 (D5), and at follow-up at 1 week (F1) and 2 weeks (F2).	1. The intervention was well tolerated with no AEs being reported. 2. dAIH vs. dSHAM: a. Decreases in time in 10MWT were greater for dAIH compared with dSHAM after only one AIH exposure (p = 0.006) and this difference persisted at F2 (p = 0.010). b. Walking endurance significantly increased in both groups, with no differences between-groups at F1 and F2. 3. dAIH + walking vs. dSHAM + walking: a. Participants receiving dAIH + walking increased walking endurance more than dSHAM + walking at D5 (p = 0.017) and F1 (p = 0.014). b. 10MWT times remained unchanged from baseline after AIH + walking, but with a greater decrease than dSHAM + walking after one exposure (p = 0.013). 4. dAIH vs. dAIH + walking: a. Combined dAIH + walking increased walking distance more than dAIH alone at D1 (p = 0.046), D5 (p = 0.002), and F1 (p = 0.001). b. Combined dAIH + walking did not improve speed more than dAIH alone.

Discussion

Four RCTs have tested walking with an AIH intervention in participants with chronic and incomplete SCI; most studies find that AIH plus walking training improves walking speed (as measured by the 10MWT), however, the results are mixed for walking endurance (6MWT) and the studies are small (N's range from 10-35 participants; Hayes et al. 2014; McKenzie et al. 2024; Navarrete-Opazo et al. 2017a; Tan et al. 2021).

In an RCT, Tan et al. (2021) compared a single AIH session plus walking practice versus sham AIH plus walking practice in 11 people with SCI. After the intervention and at 1 and 2 weeks of follow-up, people in the AIH group showed significant improvements in walking speed (10MWT) and endurance (6MWT) while those who received the sham protocol did not show any changes (Tan et al. 2021). Similar results were found by Hayes et al (2014); 11 participants with SCI received AIH or normal oxygen (21% - acting as sham hypoxia) but without walking practice. Those who received AIH had significantly better improvements in walking speed (10MWT) but similar gains in walking endurance (6MWT) than those in the normal oxygen group.

In an RCT, Navarrete-Opazo et al. (2017a) tested a protocol alternating IH and normal oxygen levels (versus sham IH) 15 times/day for one week followed by 3 times/week for 3 weeks. Navarrete-Opazo et al. (2017a) found that those in the repetitive IH group had a greater walking speed compared with the sham intervention; the IH group decreased their 10MWT time by an average of 17 seconds at week 3 (versus 7 seconds decrease in the sham group), however the groups were much closer and no longer had statistically significant differences in walking speed by week 4. The IH group also had significantly higher distances walked than the sham group up to and including week 4 (IH: 70.5 ± 13.2 m vs. Nx: 22.4 ± 10.6 m, $p = 0.005$). There were no differences between groups however in timed up and go test scores.

It is possible that the addition of AIH to walking training provides benefits, especially if the regimen is more intense as in Navarrete-Opazo et al. (2017a). More research in a larger cohort of people with SCI is recommended to better determine the generalizability of AIH, the specific protocols tested already, and any of the treatment's enduring effects (Tan et al. 2020).

Conclusions

There is level 1 evidence (from 2 RCTs: Hayes et al. 2014; Tan et al. 2021) that a period of five consecutive days of daily AIH followed by walking overground provides significantly better improvements in walking speed and endurance, compared with sham AIH plus walking in patients with incomplete and chronic SCI.

There is level 2 evidence (from 1 RCT: Navarrete-Opazo et al. 2017a) that a repetitive IH protocol followed by BWSTT (first, for five consecutive days, and then three times per week for three additional weeks) provides a greater walking speed and endurance than sham IH plus BWSTT.

There is level 2 evidence (from 1 pilot study: McKenzie et al. 2024) that a combination of AHI, tSCS and overground training for five consecutive days provides higher significant improvements in self-selected walking speed (during 10MWT), but not in fast velocity (during

10MWT), walking endurance (6MWT), or maximum isometric ankle plantarflexion, in comparison with sham AHI plus tSCS + gait training or gait training alone (sham AHI and sham tSCS) in people with incomplete and chronic SCI.

Key Points

Acute Intermittent Hypoxia (AIH) has the potential to improve walking in people with SCI, particularly if it is paired with intensive walking training.

More research is recommended with larger cohorts of people with SCI to assess generalizability, to flesh out ideal AIH protocols, and determine the treatment's enduring effects.

11 Emerging Experimental Approaches

Researchers and scientists are always looking for ways to innovate and to better treat SCI. New approaches can come from studies on high-performance athletes, animals, or biological material (e.g., stem cell therapy). Specifically, greater understanding of the mechanisms underlying locomotor pattern generation, neuroplasticity, and motor recovery has led to the development of new experimental approaches for improving locomotor function following spinal cord injury. However, until there are enough studies testing an intervention with an adequately large sample size, it is difficult to determine if an approach should be recommended or not. In this section, we highlight some newer research on walking in people with SCI as "emerging experimental approaches."

11.1 Eccentric Resistance Exercise Using the Eccentron

Active lower body eccentric resistance training (RT) may improve ambulatory capacity after incomplete SCI; however, the attenuated muscular force capacity following more severe incomplete SCI may be insufficient to stimulate muscular adaptations necessary for RT or ambulation (Stone et al. 2019). As seen in previous sections, those with incomplete SCI often perform RT alone (Labruyère & van Hedel 2014), through NMES (Stone et al. 2019), or paired with gait training (Gorgey & Sheherd 2010) to improve ambulatory capacity. Eccentric RT may be an optimal training regimen for those with incomplete SCI seeking increased muscular strength without external NMES or therapist-assisted training (Stone et al. 2019). Few studies assessed the effects on walking capacity and lower limb strength after a training intervention based on eccentric exercise using the Eccentron in participants with SCI (Stone et al. 2018; Stone et al. 2019).

The Eccentron (BTETech, Hanover, MD, USA; see figure 11) is a motor driven eccentric recumbent stepper (Stone et al. 2019). Originally designed to train older adults, athletes, or those who have had cardiopulmonary complications, the Eccentron delivers a controlled and measurable negative muscular overload (Stone et al. 2019). Training on the Eccentron allows a

person with incomplete SCI to bilaterally work the limbs and visually track the accuracy of force production during repetitions (Stone et al. 2019). The Eccentron may assist in concurrently improving lower extremity muscle strength and reciprocal limb activation, both of which may improve ambulatory function (Stone et al. 2019).

Figure 11. The Eccentron. From www.btetechnologies.com

Table 22. Eccentric Resistance Exercise Using the Eccentron

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Stone et al. 2019 USA Pre - post Level 4 N = 11	**Population:** 11 participants; 7 males and 4 females; mean (± SD) age 39.0 (± 15.9) years; AIS B (n = 4), AIS C (n = 4), and AIS D (n = 3); level of injury cervical (n = 6), thoracic (n = 4) and lumbar (n = 1); and mean (± SD) time since injury 9.5 (± 4.7) years. **Treatment:** Participants trained twice a week for 12 weeks on an eccentrically biased recumbent stepper (Eccentron), which targets the gluteal, hamstring, and quadriceps muscles. Participants started training at 50% 1RM (intensity was individually adjusted) for 2 to 3 sets of 8 repetitions at 12 rpm.	1. There were no AEs or elevated pain associated with the eccentric resistance training (ERT). 2. There was a significant (P = .027) ERT effect on 10MWT speed with these changes occurring from pre-test (0.34 ± 0.42 m/s) to post-test (0.43 ± 0.50 m/s). 3. Participants also improved in WISCI II scores from pre-test (8 ± 7) to post-test (13 ± 7) (P = .004).

	Outcome Measures: 10MWT, and WISCI II during 10MWT were assessed at baseline, after 6 weeks, and after 12 weeks. Daily step physical activity on four consecutive days was also assessed.	4. The improvement in 10MWT performance across the ERT was positively correlated with the change identified in daily step physical activity (r = .649, P = .04).
Stone et al. 2018 USA Pre-post Level 4 N = 11	**Population:** 11 participants with incomplete and chronic SCI; mean (± SD) age 39.1 (± 15.9) years; injury level cervical (n = 6), thoracic (n = 4), and lumbar (n = 1); and mean (± SD) time since injury 9.5 (± 4.7) years. **Treatment:** Participants trained two times a week for 12 weeks on the eccentric stepping ergometer (Eccentron) with a progression in resistance training (RT) parameters. **Outcome Measures:** Isometric strength of the flexors and extensors of the knees and hip and plantar- and dorsiflexors (using a hand-held, digital dynamometer); eccentric strength (using the Eccentron); and daily step physical activity (using a step activity monitor) during three consecutive weekdays and one weekend day were assessed at baseline, at the end of weeks 6 and 12.	1. Average step physical activity did not differ following RT (p = 0.092). 2. Eccentric strength significantly improved from pretest to midtest (p = 0.034) and from pretest to posttest (p = 0.038); with no changes between midtest and posttest (p = 0.15). 3. Isometric strength significantly improved from pretest to posttest data (p = 0.031).

Discussion

The pre-post studies of Stone et al. (2019) and Stone et al. (2018) used an eccentric recumbent stepper (i.e., Eccentron, which targets the gluteal, hamstring, and quadriceps muscles) for resistance training twice a week, with an intensity of 50% 1RM and a dosage of 2-3 sets of 8 repetitions at 12 rpm (Stone et al. 2019; Stone et al. 2018). Compared to baseline, at 6 weeks and at 12 weeks of training, participants significantly improved their walking speed (10MWT) and walking ability (WISCI II) (Stone et al. 2019). It should be noted that the improvement in 10MWT performance across the intervention was positively correlated with the change identified in daily step physical activity (Stone et al. 2019). Lastly, lower limb eccentric and isometric strength also improved; however, daily step physical activity remained unchanged (Stone et al. 2018).

Conclusions

There is level 4 evidence (from 2 pre-post studies: Stone et al. 2018; Stone et al. 2019) that an eccentric RT program for the lower limbs, using the device Eccentron, performed twice a week for 12 weeks with an intensity of 50% 1RM improves walking speed, walking ability, and

isometric and eccentric strength, but not daily step physical activity on participants with chronic SCI.

Key Points

An eccentric resistance training program for the lower limbs, using the device Eccentron, provides improvements in walking function and lower limb strength in participants with chronic SCI, but further high-quality studies need to be performed to confirm these promising effects.

11.2 Underwater Treadmill Training (UTT) and Aquatic Therapy (AT)

An intervention that has remained largely unexamined as a means of improving walking performance in people with SCI is underwater treadmill training (UTT) (Morgan & Stevens 2022). Primarily used in animal rehabilitation and sports medicine facilities, the use of a treadmill submerged in a self-contained, water-filled tank allows for the precise control of water depth, walking speed, and water temperature, a trio of variables that can markedly influence training responses (Stevens et al. 2015). In a typical overground treadmill harnessing system, a given percentage of body weight is supported, but the weight of the legs remains unchanged (Morgan & Stevens 2022). Hence, if leg strength is inadequate, external assistance is required to move the lower extremities during walking (Morgan & Stevens 2022). Conversely, use of water as an unloading medium during treadmill exercise reduces the weight of the legs and core weight, thus decreasing the strength needed for walking and body support while providing challenging, yet manageable, levels of resistance (Morgan & Stevens 2022). There are few studies assessing the effects on walking capacity and strength after an UTT intervention in persons with complete (Morgan & Stevens 2022) and incomplete (Stevens et al. 2015) SCI.

On the other hand, aquatic exercise has been reported to improve physical function and quality of life for patients with neurological disorders (Oh & Lee 2021). However, in people with SCI, the available evidence for aquatic therapy (AT) is scarce (García-Rudolph et al. 2024b). This has been shown in a systematic review from 2023, as only three studies with a total of 71 participants, using the FIM as an outcome measure, were included (Palladino et al. 2023). There is one recent study assessing the effects on walking ability and independence of AT in participants with acute SCI.

Table 23. Underwater Treadmill Training (UTT) and Aquatic Therapy (AT)

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Aquatic Therapy (AT)		
García-Rudolph et al. 2024b Spain Case control Level 3 N = 58	**Population:** 580 participants with acute (within 2 months after injury) SCI. • Aquatic therapy (AT) group (n = 29): 15M, 14F Mean (SD) age: 52.7 years. Cause of injury: Traumatic (n = 7) and non-traumatic (n = 22). Injury level: Paraplegia (n = 24) and tetraplegia (n = 5). AIS A (n = 4), B (n = 3), C (n =4), and D (n = 18). Mean time since injury: 37.6 days. • Matched historical controls (n = 29): 18M, 11F Mean age: 48.2 years. Cause of injury: Traumatic (n = 9) and non-traumatic (n = 20). Injury level: Paraplegia (n = 24) and tetraplegia (n = 5). AIS A (n = 5), B (n = 5), C (n = 8), and D (n = 13). Mean time since injury: 31.6 days. **Treatment:** A group of patients who received inpatient rehabilitation that included AT were compared to matched controls who had received inpatient rehabilitation that did not include AT (non-AT). • Inpatient rehabilitation: This program totalizes 4 h daily of intensive treatment from the multidisciplinary team oriented toward training in ADLs (1 h), physical rehabilitation (2 h) and gait rehabilitation (1 h) for a total of 10 weeks. o ADL training involved activities targeted at the patients' needs such as transfer practice, washing,	1. Gains, efficiency, effectiveness and MCID: 1:1 matching (n = 58): No significant differences were observed for FIM or SCIM-III gains, efficiency and effectiveness. Significant differences were observed in WISCI II gain (p = 0.018) and WISCI II efficiency (p = 0.046), in favor of the AT group, and quasi-significant differences were observed in WISCI II effectiveness (p = 0.088) also in favor of the AT group. Furthermore, the proportion of individuals achieving MCID (i.e., a change of two WISCI II points) was significantly higher (p = 0.030) for the AT group (75.9% vs. 48.3%).

	dressing, grooming and wheelchair skills. ○ Physical rehabilitation included strengthening, stretching, and joint mobilization exercises. ○ Gait rehabilitation incorporates the use of BWSTT (Lokomat®), BWSOGT using the Andago®, as well as the use of standard treadmills, and orthosis-walking with the aid of walking frames as appropriate to the patient's evolution • Intervention group (AT): Individuals in the intervention group received rehabilitation as explained before, but in their case AT sessions replaced 1 h of physical rehabilitation within the daily 4 h of total therapy. All interventions consisted of 60-min sessions, three times per week, for a total of 10 weeks. The intervention was based on the Halliwick concept. **Outcome Measures:** Gain, efficiency, and effectiveness for the FIM, SCIM-III and WISCI II were calculated as follows: • Gain = score at discharge − score at admission. • Efficiency = Gain/length of stay (LOS). • Effectiveness = Gain/(maximum scale score − score at admission) x 100.	
Underwater Treadmill Training (UTT)		
Morgan & Stevens 2022 USA Pre-post Level 4 N = 5	**Population:** 5 participants with AIS A SCI; 4 males and one female; mean age 41.6 years; level of injury T4 (n = 1), T9 (n = 1), T10 (n = 1), and T11 (n = 2); and mean time since injury 3.18 years. **Treatment:** Participants embarked on a year-long training program of 2 to 3 sessions of underwater treadmill training (UTT) per week performed on alternate days, and supplemental OWT, which were distributed in the following manner: • UTT: Walking speed or duration, trainer's facilitation of gait, and reliance on upper-extremity support	1. An average of 29 training sessions (range = 9–62 sessions) was required for participants to register unassisted stepping activity during UTT. 2. There were significant improvements in WISCI II levels from T3 (8.40 ± 1.34), compared to T1 (0.20 ± 0.45) (P = .039), but not between T1 and T2 or T2 and T3. 3. Individual data revealed that all study participants

	while walking were progressed individually until independent walking in the water for 45 min without experiencing fatigue and without need for assistance of the trainers was achieved. • After independent stepping was recorded during UTT, a systematic and individualized program of supplemental OWT for 30 min was performed before the UTT (with 5 stages of different functional exercises and tasks). **Outcome Measures:** WISCI II was assessed prior to UTT (T1), six months after starting UTT (T2), and immediately following completion of UTT (T3).	registered a marked improvement in WISCI II level over the 12-month training program (mean change = 8.2; range = 6–9) that corresponded with a large effect size (r = .65). 4. All participants progressed to the fourth level of OWT and one of them, progressed to the fifth level of OWT.
Stevens et al. 2015 USA Pre-Post Level 4 N = 11	**Population**: 7 males and 5 females; average age 47.7y; >1y post injury; AIS C and D. **Treatment**: Participants completed 8 weeks (3 × /week) of UTT. Each training session consisted of three walks performed at a personalized speed, with adequate rest between walks. BWS remained constant for each participant and ranged from 29 to 47% of land body weight. Increases in walking speed and duration were staggered and imposed in a gradual and systematic fashion. **Outcome Measures:** Lower-extremity strength, preferred and rapid walking speeds, 6MWT, and daily step activity.	1. Participants improved in leg strength (57%), preferred walking speed (34%), rapid walking speed (61%), 6MWT (82%), and daily step activity (121%) following UTT.

Discussion

Treadmill training performed in a water environment has been shown to serve as an effective alternative or support to land-based physical activity and walking programs in adults who experienced lower-limb muscle weakness (Stevens et al. 2015); however, there is limited research on this intervention for persons with SCI. Stevens et al. (2015) included 11 participants with incomplete SCI who completed eight weeks of UTT featuring personalized levels of BWS and incremental gains in walking speed and duration. There were reported gains ($p < 0.05$) of moderate to large magnitude in leg strength (57%) and preferred and rapid walking speed (34% and 61% respectively), 6-min walk distance (82%), and daily step activity (121%). Another pre-post by Morgan and Stevens (2022) included five participants with complete (AIS A) SCI; participants received a one-year training program that consisted of 2-3 UTT weekly sessions and, once independent stepping was accomplished for each participant during UTT, supplemental OWT with five stages of different functional exercises and tasks (Morgan & Stevens 2022). All

participants registered a marked improvement in WISCI II scores over the 12-month training program with a large effect size (mean change = 8.2; range = 6–9; r = 0.65).

Although more research is needed, mainly because the sample size and quality of studies were low; the use of smaller, portable underwater treadmills may also extend the accessibility of UTT into public fitness settings to enhance ambulatory status and physical function in persons with SCI and other severe neuromuscular disorders (Morgan & Stevens 2022).

We only found one study assessing aquatic therapy (AT) and its effects on walking in people with SCI. García-Rudolph et al. (2024b) used a 10-step, 3-stage process using different positioning and progressive exercises to help individuals become independent with their movement in the water (based on the Halliwick concept). They found that after 10 weeks, the group of patients who received AT (n = 29) showed significantly higher gains in WISCI II (and in the proportion of individuals achieving the MCID [two points]) than the matched-controls (n = 29); however, no significant between-groups differences were observed in SCIM-III and FIM. Larger and randomized studies (e.g., RCTs) should be carried out to replicate these promising effects. Marinho-Buzelli et al. (2019) interviewed rehabilitation professionals on the use of AT in people with SCI and reported the lack of knowledge about the benefits of this approach as a barrier to its successful integration into clinical practice.

Conclusions

There is level 4 evidence (from 1 pre-post study: Morgan & Stevens 2022) that a one-year period of UTT (with supplementary OWT once independent stepping was recorded during UTT) provides a significant improvement in walking ability (WISCI II) in persons with complete (AIS A) and chronic SCI.

There is level 4 evidence (from 1 pre-post study: Stevens et al. 2015) that eight weeks of UTT provides significant gains of moderate to large magnitude in leg strength, preferred and rapid walking speed, 6MWT, and daily step activity in participants with incomplete and chronic SCI.

There is level 3 evidence (from 1 case control study: García-Rudolph et al. 2024b) that one hour of daily AT (in the form of the Halliwick concept), replacing one hour of physical rehabilitation from the four daily hours of the usual inpatient rehabilitation program, provides higher significant improvements in walking ability (WISCI II), but not in functional independence (FIM and SCIM-III), than only receiving the four-hour of the daily usual inpatient rehabilitation program in patients within two months of having a SCI.

Key Points

Underwater Treadmill Training (UTT) and Aquatic Therapy (AT) could be interesting alternative approaches to dry land Bodyweight Supported Treadmill Training (BWSTT) for improving walking performance and lower limb strength in persons with complete and incomplete, and acute or chronic SCI.

Further high-quality studies need to be performed to confirm these promising effects.

11.3 Conditioning Reflex Protocols

Traditional tenets about the hard-wired nervous system have long been dispelled with mounting evidence for activity-dependent plasticity throughout the central nervous system. Fascinating results from animal, and more recently, human studies have shown that even the "simplest" spinal cord reflex, the stretch reflex pathway or its electrical analog, the H-reflex, can be altered to increase or decrease in size through operant conditioning (Wolpaw 2010). Humans can also learn to increase or decrease the size of the soleus H-reflex (Thompson et al. 2009). Some gait impairments following SCI could be associated with hyperreflexia and abnormal reflex responses in the ankle plantarflexors (Dietz & Sinkjaer 2007). The possibility that H-reflex amplitude could be down-conditioned raises the compelling question of whether such protocols may benefit persons with SCI who present with spastic gait disorder.

This idea was tested in a group of 13 people with chronic (>8 months) motor-incomplete SCI who were all ambulatory and presented with spasticity (e.g., ≥1 on Modified Ashworth Score) and weak ankle dorsiflexion (Thompson et al. 2013). Participants were randomly assigned at a 2:1 ratio to the down-conditioning (DC) group (n = 9) or the unconditioned group (n = 4). Each participant completed 6 baseline sessions followed by 30 sessions (3 sessions/week) of control (unconditioned group) or conditioning (DC group). Visual feedback was provided to the DC group to inform them of whether they were successful in reducing their H-reflex amplitude to within the target range. In the unconditioned group, each session involved H-reflex recordings without any visual feedback or instructions about H-reflex amplitude. Note that in this study, no LT was provided; training sessions consisted of only the H-reflex down-conditioning (or control protocol). More recently, a similar RCT performed by Thompson and Wolpaw (2021) assessed a new protocol, in which the H-reflex during the late-swing phase of walking on a treadmill with BWS was elicited (Thompson & Wolpaw 2021). However, the number of conditioning and control sessions, the number of reflex trials per session, and the session schedule were identical in both protocols (Thompson & Wolpaw 2021; Thompson et al. 2013).

Table 24. Conditioning Reflex Protocols

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Thompson & Wolpaw 2021 USA RCT PEDro = 5 Level 2 N = 13	**Population:** 13 participants with chronic and incomplete (AIS D) SCI, signs of spasticity and the ability to walk on the treadmill for > 160 steps without stopping; 9 males and 4 females; mean (± SD) age 49.8 ± 13.5 years; injury level C1 (n = 1), C4 (n = 2), C (n = 2), C6 (n = 2), C7 (n = 3), C8 (n = 1), T1 (n = 1), and T5 (n = 1); and mean time since injury 1.4 years. **Treatment:** The participants were randomly assigned to the Down-Conditioning (DC) group (n = 7) or the No-Stimulation (NS) control group (n = 6). Each person completed 6 baseline sessions and 30 control (NS group) or conditioning (DC group) sessions at a rate of 3 sessions per week. • In the DC group, the soleus H-reflex was down-conditioned during the swing-phase of walking on a treadmill with BWS. • In the NS group, the sessions consisted of walking on the treadmill with BWS for three blocks of 160 steps each without H-reflex elicitation and without any special instructions. **Outcome Measures:** 10MWT (during overground) and locomotor H-reflexes across the entire step cycle (during treadmill) were measured before and after the training program. For the DC group, a follow-up session (identical to the conditioning sessions) occurred 1 month (n = 6), 3 months (n = 4)	1. Swing-phase H-reflex down-conditioning was successful in 6 of 7 DC participants, which is similar those for previous, steady-state operant conditioning studies in people with SCI (Thompson et al. 2013). 2. With swing-phase down-conditioning, the H-reflex (both the conditioned and the control) decreased much faster and much more than did the H-reflex in previous human studies with the steady-state protocol (Thompson et al. 2013), and the decrease persisted for at least 6 months after conditioning ended. 3. The locomotor H-reflex across the step cycle: a. The modulation index (MI) of the locomotor H-reflex over the step cycle was high before the 30 conditioning sessions (DC participants: 90 ± 8 %) or the 30 control sessions (NS participants: 93 ± 13%) and did not change significantly after the 30 sessions. b. In the successful DC participants, the average locomotor H-reflex over the entire step cycle decreased by 29% (P = 0.007); the average stance-phase H-reflex decreased by 34% (P = 0.04); and the average swing-phase H-reflex decreased by 43% (P = 0.02). By contrast, the locomotor H-reflexes of the NS participants did not change significantly. 4. In the six successful DC participants, 10MWT increased significantly over the 30 conditioning sessions (with an average increase from 1.04 to 1.16 m/s, [P = 0.02]). Walking speed increase

	and 6 months (n = 4) after the final conditioning session.	was not correlated with the final H-reflex size (r = 0.33). By contrast, in the NS participants, walking speed did not change.
Thompson et al. 2013 USA RCT PEDro = 7 Level 1 N = 13	**Population:** 13 ambulatory participants with SCI (9M 4F); mean (SD) age: 48.4 (13.9) yrs; DOI ranging from 8 months to 50 yrs. **Treatment:** Participants randomly assigned at a 2:1 ratio to the DC group (6M 3F) or the unconditioned group (3M 1F). Each participant completed 6 baseline sessions and 30 control (unconditioned participants) or conditioning (DC participants) sessions at a rate of 3 sessions/week. ES of the soleus H-reflex was elicited by a 1ms square pulse stimulus. **Outcome Measures:** Locomotion (participant asked to walk 10 m at comfortable speed 3 times; average walking time determined); locomotor symmetry; EMG activity; H-reflex modulation.	1. Success (average conditioned H-reflexes significantly less for session 25-30 than baseline) rate for participants with SCI = 67%, which is slightly, but not significantly, less than that for neurologically normal participants (89%). 2. Conditioned H-reflex for unconditioned group as a whole showed a slight by significant increase (to (mean [SE]) 116 [7]%). Down-conditioning was achieved in 6 of 9 participants. 3. Over the 30 conditioning or control sessions, the participants' 10m walking speeds increased by 0-123%. The increase was significant in the 6 DC participants in whom the H-reflex decreased. For the 7 participants in whom H-reflex did not decrease, walking speed increased less and not significantly. 4. For DC participants with decreased H-reflex (n=6), locomotion became faster and more symmetrical and the modulation of EMG activity across the step cycle increased bilaterally.

Discussion

In the RCT of Thompson and Wolpaw (2021), six of the seven participants in the DC group were able to successfully down-condition (decrease) their H-reflex amplitude; however, there was no reduction in H-reflex amplitude in the unconditioned group. These success rates were similar to those of previous steady-rate operant conditioning studies in people with SCI (Thompson et al. 2013). However, with the swing-phase down-conditioning, the H-reflex decreased much faster and much more than did the H-reflex in previous human studies with the steady-state protocol (Thompson et al. 2013), and the decrease persisted for at least six months after conditioning ended (Thompson & Wolpaw 2021). Across both of these studies, the participants who could successful down-condition their soleus H-reflex amplitude experienced significant increases in their 10MWT speeds (average of 59% (range: 0-123%) in Thompson et al. (2013); 112% ± 9% in Thompson & Wolpaw (2021). For the seven participants in whom H-

reflex did not decrease, walking speed also increased, though less and not significantly (Thompson et al. 2013).

Conditioning reflex protocols have been published many years ago for the upper extremity in SCI (Segal & Wolf 1994) to reduce spasticity and are an important neuroscience observation. However, they have not been accepted into practice likely due to the variable results and laborious number of sessions to get a small effect. This one small RCT for the lower extremity shows similar findings as the upper extremity – that soleus spinal reflexes can be down-conditioned in about 2/3 of the participants, although a few of these participants did demonstrate large improvements in gait speed. The success rate of down-conditioning in participants with SCI was comparable to previous studies in participants without SCI. Unfortunately, absolute values were not reported here, making the clinical significance of these results difficult to ascertain. Furthermore, the complexity of this approach may make it inaccessible for most clinicians. Nevertheless, these results are intriguing and point towards another potential approach of directly manipulating spinal cord plasticity to enhance functional recovery.

Conclusions

There is level 1 evidence (from 1 RCT: Thompson et al. 2013) and level 2 evidence (from 1 RCT: Thompson & Wolpaw 2021) that down-conditioning reflex protocols of the soleus could increase walking speed and improve gait symmetry.

Key Points

Down-conditioning (DC) reflex protocols of the soleus could facilitate walking speed and gain symmetry in people with SCI.

The process to achieve gains via down-conditioning reflex protocols may take time and multiple session (though standards have yet to be established).

11.4 Robot-aided Ankle Rehabilitation

Ankle rehabilitation can be important for people with SCI as it may address drop foot consequences and/or weakened lower limb muscles (Calabrò et al. 2022). Improving ankle functionality generally means targeting the ranges and directionality of motion (i.e., plantar/dorsiflexion, inversion/eversion, and abduction/adduction) as well as ankle plantar and dorsiflexion muscle strength, and proprioceptive capacity of the ankle (Calabrò et al. 2022).

The rationale of adopting robot-aided ankle rehab for patients with incomplete SCI is to provide the patient's ankle with regular and assisted-as-needed movements (mainly inversion–eversion and dorsiflexion–plantarflexion) and to train muscle strength with mechanical support and some control over force distribution (Calabrò et al. 2022). Goals may include minimizing the risk of falls and improving walking speed and efficiency (Calabrò et al. 2022).

One platform-based robot system, the Hunova®, is made of two electromechanical and sensorized platforms with two planes of movement (forward/backward and left/right) that monitor and train postural and joint movements, including the ankle. Two training modes are available - a 'static' mode, where the platform does not move, but offers resistance to the user's movements, or a 'dynamic' mode where the platform itself moves and the user has to adapt (Calabrò et al. 2022). Exercises may be performed seated, on the attached armchair with optional strap support, or standing on the platform with optional handrail support (Calabrò et al. 2022). The Hunova® also provides the user with visual and audio feedback, from devices like an accelerometer, gyroscope, and magnetometer located on/attached to the person's torso (Calabrò et al. 2022).

Table 25. Robot-aided Ankle Rehabilitation

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Calabrò et al. 2022 Italy Case control (pre-post for the experimental group and retrospective for the control [matched group]) Level 3 N = 20	**Population:** • Experimental group (n = 10): Participants with SCI and at least a palpable or visible contraction of ankle plantar and dorsal flexor muscle groups, and without severe ankle instability; 6 males and 4 females; mean (± SD) age 39 (± 13) years; level of injury C5 (n = 2), C6 (n = 1), C7 (n = 1), T6 (n = 1), T7 (n = 3), and T10 (n = 1); AIS C (n = 5) and AIS D (n = 5); and mean (± SD) time since injury 8 (± 4) months. • Control group (n = 10): Participants who previously underwent conventional ankle rehabilitation were retrospectively matched: 5 males and 5 females; mean (± SD) age 39 (± 7) years; level of injury C5 (n = 1), C6 (n = 2), T1 (n = 1), T2 (n = 2), T5 (n = 2), T6 (n = 1), and T9 (n = 1); AIS C (n = 4) and AIS D (n = 6); and mean (± SD) time since injury 9 (± 3) months. **Treatment:** All persons underwent an intensive treatment (6 days weekly) consisting of FES of lower limb muscles (a daily 30-min session), conventional physiotherapy (two 1-h sessions daily), and	1. None of the participants reported any side effects during the rehabilitative sessions. 2. None of the persons achieved a complete recovery of walking function. However, there were more significant improvements in experimental group (vs. the control group) for: a. 10MWT: experimental group from 0.43 ± 0.11 to 0.51 ± 0.09 m/s, p = 0.006; control group from 0.4 ± 0.13 to 0.45 ± 0.12, p = 0.01; group-comparison p = 0.006. b. 6MWT: experimental group from 231 ± 13 to 274 ± 15 m, p < 0.001; control group from 236 ± 13 to 262 ± 15 m, p = 0.003; group-comparison p = 0.01.

	occupational therapy (a 1-h session, three times weekly) for 4 weeks. Additionally: • The experimental group received robot-aided ankle rehabilitation using Hunova® device for a one-hour daily session. • The control group underwent an equal amount of conventional ankle rehabilitation. **Outcome Measures:** 10MWT; 6MWT; were assessed at baseline and after the trial completion.	

Discussion

There was only one study that evaluated the effects of robot-aided ankle rehabilitation in people with incomplete SCI using corticomuscular coherence data. The case control study (with a prospective design for the experimental group and a retrospective design for the matched-control group) compared the effects on gait performance after engaging in robot-aided ankle rehabilitation or conventional ankle rehabilitation in patients with acute SCI (Calabrò et al. 2022). All participants underwent an intensive treatment program (six days/week) consisting of FES of lower limb muscles, conventional physiotherapy and occupational therapy sessions; participants in the experimental group used the Hunova® device for ankle rehabilitation (Calabrò et al. 2022). After 4 weeks of training, there were more significant improvements in the experimental group than in the control group for walking speed (10MWT) and walking distance (6MWT), independence in daily living activities (SCIM-III), and muscle activation of dorsal and plantar flexors (Calabrò et al. 2022).

Conclusions

There is level 3 evidence (from 1 case control study: Calabrò et al. 2022) that the addition of a robot-aided ankle rehabilitation to an intensive program consisting of FES, conventional physiotherapy and occupational therapy provides more significant improvements on walking (10MWT and 6MWT) than conventional physiotherapy in patients with acute SCI.

Key Points

The addition of a robot-aided ankle rehabilitation to an intensive therapy program seems to represent an effective approach for improving walking performance in patients with acute SC. However, further high-quality studies need to be performed to confirm these promising effects.

11.5 Cellular Transplantation Therapies

Experimental animal research utilizing stem cells and other cells or tissue to treat severe SCI is now being translated to human clinical studies. Recent systematic reviews have been published assessing the evidence of different stem cell transplantation therapies (from various sources such as bone mesenchymal stem cells, bone marrow mononuclear cells and umbilical cord-derived mesenchymal stem cells) (Chen et al. 2021; Liu et al. 2022; Xu et al. 2022) or, specifically, of mesenchymal stem cell therapy (Muthu et al. 2021; Xu & Yang 2019), to help increase motor function and reduce impairments in the recovery of people with chronic SCI.

Safety and efficacy of stem cell treatment in SCI have not yet been established, particularly with regard to the improvement of walking. In a meta-analysis, Xu and Yang (2019) found 11 studies using mesenchymal stem cells treating 499 patients with SCI. Although no gait outcomes were assessed, results were mixed; significant improvements of total AIS grade, ASIA sensory score and reduction of residual urine volume were observed in experimental groups versus control groups, but there were no changes in motor scores nor in ADL scores (Xu & Yang 2019). Though no serious or permanent adverse events occurred, the experimental groups were 20 times more likely to experience toxicity than those in the control groups; common AEs like fever, headache, backache, and abdominal distension usually resolved spontaneously or post-treatment (Xu & Yang 2019; RR: 20.34; 95% CI 8.09–51.18, $P < 0.001$).

Table 26. Cellular Transplantation Therapies

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Albu et al. 2021 Spain RCT PEDro = 8 Level 1 N = 10	**Population:** 10 patients with chronic and complete (AIS D) thoracic SCI; 7 males and 3 females; mean age 32.7 years; injury level T3 (n = 1), T4 (n = 3), T5 (n = 2), T6 (n = 1), and T11 (n = 3); and mean time since injury 31.9 months. **Treatment:** Participants were randomly assigned to first receive an intrathecal infusion of Wharton jelly mesenchymal stromal cells isolated from human umbilical cord or placebo. After 6 months of the first infusion, participants received the opposite treatment. *Stem cell transplantation. **Outcome Measures:** AIS motor and motor evoked potentials of the tibialis anterior and abductor hallucis	1. Intrathecal administration of mesenchymal stromal cells was well tolerated, and only non-severe side effects, such as an episode of headache and vomiting and local pain after lumbar puncture, were reported the day after intrathecal infusion. 2. Specifically, change in pinprick sensation on the right side was significant at 3 months (P = 0.03) and reached maximum improvement at 6 months (P = 0.013), compared with baseline, following WJ-MSC infusion though no sensory changes were significant on the left side in either group. Improvement in pinprick score was not predicted by the

	muscles bilaterally were assessed at baseline, 1 month, 3 months and 6 months after each intervention.	level of spinal injury or time after injury. MEPs and SEPs from the lower limbs were absent at baseline and 6 months after either MSC or placebo infusion. 3. There were no significant changes in motor or independence measures in either group.
Kishk et al. 2010 Egypt Case Control Level 3 N = 64	**Population:** Treated Group – 36 males, 7 females; mean (SD) age 31.7(10.4); 12 complete, 31 incomplete SCI Control Group – 15 males, 5 females; mean (SD) age 33.8(11.8); 3 complete, 17 incomplete SCI. **Treatment:** Monthly intrathecal injection of autologous bone marrow mesenchymal stromal cells for 6 months, all participants received 3 rehabilitation therapies per week. **Outcome Measures:** Trunk muscle assessment, Modified Ashworth Spasticity Scale, FAC, AIS sensorimotor, motor and sensory scores, lower-limb somatosensory evoked potentials. Participants were evaluated at entry and at 12 months after completing the 6-month intervention.	1. A significantly greater proportion of the treatment group showed improved motor scores, but this is not clinically relevant as it was only by 1-2 points in 18/44 participants (48.7(9.1) to 49.3(9.2)). 2. There were no significant differences between-groups for trunk support, Functional Ambulatory Categories, sensory exam (pin prick), scores, tone, bladder control questionnaire, bowel control, and AIS changes. 3. Adverse effects of injections included spasticity (significantly more often in treatment group; p<.01) and 24 out of the 43 patients developed neuropathic pain. One participant with a history of post-infectious myelitis developed encephalomyelitis after her third injection and was forced to withdraw from the study.
Lima et al. 2010 Portugal Pre-post Level 4 N = 20	**Population:** 17 males, 3 females; mean (SD) age 30.2(5.7); 15 patients AIS grade A, 5 patients AIS grad B; all > 1 YPI. **Treatment:** Olfactory mucosal autografts into the area of the SCI a mean of 49 months after injury, with pre-operative rehabilitation (mean (SD) 31.8(6.8) hours/week for 34.7(30) weeks) and post-operative rehabilitation (mean (SD) 32.7(5.2) hours/week for 92(37.6) weeks) with BIONT or robotic BWSTT. **Outcome Measures:** AIS score and AIS grade, FIM, WISCI. The mean duration of follow-up was 27.7 months (range = 12-45 months).	1. Estimated mean change in all ASIA neurological measures (pink prick, light touch, motor arms, motor legs) was statistically significant. ASIA motor LEMS score improved from 0 to 4.95(7.1) post intervention. 2. 11 patients improved their AIS grades (6 by 2 grades), and 1 patient's score deteriorated and suffered ARs (aseptic meningitis, spinal cord edema). 3. 9 of the patients with an AIS score of 0 at baseline improved from 4 to 22 at last evaluation. 4. Of the 13 patients assessed for functional studies, all had improvements on FIM scores

		(mean (SD) 71(23) to 85(28)) and WISCI scores (0.2(0.4) to 7.4(2.6)). 5. Patients at facilities focusing on BIONT showed better motor recovery compared with those at facilities focusing on BWSTT. 6. Voluntary motor potentials of the lower limb muscles were found in 11/20 patients.

Discussion

We found three studies assessing the effects of cellular transplantation in people with SCI where walking outcomes were measured. In an RCT, Albu et al. (2021) tested the effects of cellular transplantation on muscle strength and independence in 10 people with AIS A thoracic level SCI. Participants either received a single dose of intrathecal ex vivo-expanded Wharton jelly mesenchymal stromal cells (MSC) from human umbilical cord or a placebo injection (Albu et al. 2021). Participants in the experimental group showed a significant improvement in pinprick sensation in the dermatomes below the level of injury compared with those in the placebo group, but there were no significant changes in motor function or independence measures in either group (Albu et al. 2021). Specifically, change in pinprick sensation on the right side was significant at 3 months (P = 0.03) and at 6 months (P = 0.013), compared with baseline following WJ-MSC infusion, though no sensory changes were significant on the left side in either group. Improvement in pinprick score was not predicted by the level of spinal injury or time after injury. MEPs and SEPs from the lower limbs were absent at baseline and 6 months after either MSC or placebo infusion.

One case control study investigated the effects of monthly intrathecal injections of mesenchymal cells in combination with 6 months of rehabilitation therapies on muscle strength and function (Kishk et al. 2010). There were no differences between groups for functional ambulation; motor scores were only slightly (but significantly) greater in the treatment group.

In a pre-post study, olfactory mucosal autografts were transplanted into the site of injury in persons with chronic complete or motor-complete SCI (Lima et al. 2010). Patients then underwent LT (either robotic-assisted treadmill training or assisted OWT). FIM and WISCI II scores improved in 13 participants tested, and this improvement correlated with increases in leg strength. However, as this was an uncontrolled pilot study, it is impossible to attribute improvements to mucosal grafts or to the extensive walking training (average of 24-39 hours/week for a median of 4 months).

Multiple participants in both Kishk et al. (2010) and Lima et al. (2010) experienced adverse events (AEs). In Kishk et al. (2010), the adverse effects of injections included spasticity (which occurred significantly more often in the treatment group) and 24 and the 43 participants developed neuropathic pain. One participant with a history of myelitis developed encephalomyelitis after their third injection and was forced to withdraw from the study. In Lima

et al. (2010), 5 of 20 participants experienced AEs including one person with aseptic meningitis, and another with irritable bowel syndrome.

Further pre-clinical studies are needed to establish safety and efficacy of cellular transplantation, and subsequently in randomized controlled trials in humans, before they can realistically be recommended for rehabilitation. For a more in-depth and plain language description of stem cell treatment in SCI, visit Stem Cells in SCI on SCIRE Community.

Conclusions

There is level 1 evidence (from 1 RCT: Albu et al. 2021) that the administration of a single dose of intrathecal ex vivo-expanded Wharton jelly mesenchymal stromal cells from human umbilical cord did not provide any improvements (compared with placebo) on motor function or independence of patients with chronic complete SCI.

There is level 3 evidence (from 1 case control study: Kishk et al. 2010) that monthly intrathecal injections of mesenchymal cells in combination with 6 months of rehabilitation therapies provided significantly greater improvements in motor scores, but not in functional ambulation in participants with chronic SCI, though multiple participants experienced adverse events like spasticity and pain.

There is level 4 evidence (from 1 pre-post study: Lima et al. 2010) that the implantation of olfactory mucosa autografts in combination with LT could produce some AEs, and could improve FIM and WISCI, in correlation with leg strength in patients with chronic, sensorimotor complete or motor complete SCI.

Key Points

There is a lack of evidence regarding different stem cell transplantation therapies and their derivate effects on walking function in patients with SCI.

Further pre-clinical studies are needed to establish safety and efficacy of cellular transplantation, and subsequently in randomized controlled trials in humans, before they can realistically be recommended for rehabilitation.

For a more in-depth and plain language description of stem cell treatment in SCI, visit Stem Cells in SCI on SCIRE Community.

11.6 Brain-Spine Interface (BSI)

Brain-spine interfaces (BSI) use brain activity, combined with implantable electrical spinal cord stimulation (ESCS), to mimic the command transfers from the brain itself to the spinal cord (Lakshmipriya & Gopinath 2024). In BSI technology, a command originating in the brain is linked to neurons with motor intent, decoded into commands with movement patterns, and then transmitted to an implanted electrode along the spinal cord. This electrode activates the spinal

circuits by generating electrical pulses, helping to initiate movement based on the person's intent. This system is designed to enable voluntary control over leg movements to walk, stand, and climb stairs.

Table 27. Brain-Spine Interface (BSI)

Author Year Country Research Design Score Total Sample Size	**Methods**	**Outcome**
Lorach et al. 2023 Switzerland Case Report Level 5 N = 1	**Population:** One male with incomplete and chronic SCI and able to step with the help of a front-wheel walker; 38 years old of age; injury level C5/C6; and time since injury 10 years. **Treatment:** The communication between the brain and the region of the spinal cord that produces walking has been restored with a digital bridge between the brain and the spinal cord. This brain–spine interface (BSI) consists of fully implanted recording and stimulation systems that establish a direct link between cortical signals and the analogue modulation of ESCS targeting the spinal cord regions involved in the production of walking. The participant completed 40 sessions of neurorehabilitation, which involved walking, single-joint movements, and standard physiotherapy (with a focus on the control of hip flexor muscles). **Outcome Measures:** Immediate recovery of natural walking (walking capacity); navigation over complex terrain (climbing up and down a steep ramp with ease capacity, climbing over a succession of stairs, negotiate obstacles and traverse changing terrains capacity); long-term stability of the BSI; neurological recovery (volitional control of hip flexor muscles and associated hip flexion movements without stimulation, motor scores, WISCI II, clinical assessment [6MWT, weight-bearing capacities, BBS, and walking quality assessed using the observational gait analysis scale], and quality of life); and integration of the BSI in daily life.	1. The BSI was calibrated within a few minutes with high reliability. This reliability has remained stable over one year, including during independent use at home. 2. The BSI enabled natural control over the movements of the participant's legs to stand, walk, climb stairs and traverse complex terrains. 3. The participant regained the ability to walk overground independently with crutches, even when the BSI was switched off. 4. Neurorehabilitation supported by the BSI improved neurological recovery: a. An improvement in the volitional control of hip flexor muscles and associated hip flexion movements without stimulation was shown. b. Gains in motor scores, and in walking ability (WISCI II). Concretely, the participant exhibited improvements in 6MWT, weight-bearing capacities, BBS and walking quality without stimulation.

Discussion

We found one published case report by Lorach et al. (2023) that is a part of an ongoing clinical feasibility study STIMO-BSI ('Brain-controlled Spinal Cord Stimulation in Patients with Spinal Cord Injury'), which investigates the safety and preliminary efficacy of brain-controlled spinal cord stimulation after SCI (clinicaltrials.gov, NCT04632290). This one participant was implanted with a spinal cord stimulation system (ESCS), then completed a five-month intensive neurorehabilitation program, followed by a two-year period of independent use at home (Lorach et al. 2023). The results showed that the reliability of the brain–spine interface (BSI) remained stable over one year (including during independent use at home), that the BSI enabled natural control over the movements of the legs of the participant to stand, walk, climb stairs and even traverse complex terrains (Lorach et al. 2023).

Although these results are promising, they need to be replicated in larger studies and the digital bridge will require several developments, which will require time and resources.

Conclusions

There is level 5 evidence (from 1 case report study: Lorach et al. 2023) that a BSI coupled with ESCS and months of rehabilitation/walking training enabled natural control over standing and walking in one participant with chronic, incomplete tetraplegia.

Key Points

One case report reported that Brain-Spine Interface (BSI) technology, coupled with implanted epidural spinal cord stimulation and rehabilitation/walking training, enabled voluntary control over standing and walking in one person with incomplete SCI.

Further studies establishing safety, feasibility, and effectiveness of BSI technology are required to confirm initial promising effects.

11.7 Hypothalamic Deep Brain Stimulation (DBS^{LH})

SCI alters the communication between the brain and the neurons in the lumbar spinal cord that must be activated to produce walking (Arber & Costa 2018; Courtine & Sofroniew 2019). When the SCI is incomplete, the reorganization of residual projections from spinal cord-projecting neuronal populations located in the brain may restore enough communication for partial recovery of walking (Cho et al. 2024).

Table 28. Hypothalamic Deep Brain Stimulation (DBS^{LH})

Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Cho et al. 2024 Switzerland Pre-post Level 4 N = 2	**Population:** 2 participants with chronic incomplete SCI who could walk with assistive aids but exhibited persistent gait deficits despite their prior participation in standard rehabilitation programs. **Treatment:** Deep brain stimulation therapy of the lateral hypothalamus (DBS^{LH}) and then a 3-month structured rehabilitation program involving 3 days of gait training per week, for a total of 3 h per session. **Outcome Measures:** LEMS, 6MWT, and 10MWT.	1. In both participants, DBS^{LH} immediately augmented the activity of lower-limb muscles. This increase in muscle activation translated into improved kinematics and endurance. The participants also reported a perceived reduction in effort to walk. 2. Results after the rehabilitation program: a. Pronounced improvement in walking was shown as demonstrated by 10MWT, 6MWT, and increases in LEMS, including while DBS^{LH} was turned off. b. Both participants achieved their respective pre-rehabilitation goals of walking without orthoses and being able to climb stairs independently. c. All procedures throughout the trial were tolerated by both participants and no serious AEs were observed.

Discussion

Cho et al. (2024) aimed to identify brain regions that steer the recovery of walking after incomplete SCI. Before conducting the pilot clinical trial, the authors acquired functional magnetic resonance imaging (fMRI) data from 21 healthy people showing bilateral activations of the lateral hypothalamus (LH) during walking (Cho et al. 2024). Following this, the authors translated this discovery into a pilot clinical trial with deep brain stimulation therapy of the LH (DBS^{LH}) in two individuals with incomplete SCI (Cho et al. 2024). It was shown that DBS^{LH} immediately improved walking and, in conjunction with rehabilitation, mediated functional recovery that persisted when DBS^{LH} was turned off, without serious AEs (Cho et al. 2024). Further trials should be performed in larger studies to more firmly establish the safety and efficacy of DBS^{LH}, including potential changes in body weight, psychological status, hormonal profiles and autonomic functions (Cho et al. 2024).

Conclusions

There is level 4 evidence (from 1 pre-post study: Cho et al. 2024) that a DBS^{LH} was safe and, with the addition of rehabilitation, that improved walking and functional recovery (10MWT, 6MWT, and LEMS) in two participants with chronic and incomplete SCI.

Key Points

There is promising, but preliminary, evidence that Hypothalamic Deep Brain Stimulation (DBS^{LH}) paired with rehabilitation could provide functional improvements in walking (10MWT and 6MWT) and strength (LEMS) in people with chronic and incomplete SCI; however further trials must establish the safety and efficacy of this approach.

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Abbreviations

2MWT	2-minute walk test
6MWT	6-minute walk test
10MWT	10 meter walk test
ABC scale	activity-specific balance confidence scale
ABT	activity-based therapy
AE	adverse event
AIH	acute intermittent hypoxia
AIS	American Spinal Injury Association Impairment Scale
AFO	ankle-foot orthosis
ASIA	American Spinal Injury Association
AT	aquatic therapy
BBS	Berg Balance Scale
BSI	brain-spine interface
BWS	body weight support
BWSOGT	body-weight supported overground training
BWSTT	body-weight supported treadmill training
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval
COP	center of pressure
CSA	cross-sectional area
DC	down-conditioning

EAW	exoskeleton-assisted walking
EMG	electromyography
ES	electrical stimulation
ES-LCE	electrical stimulation-induced leg cycle ergometer
ESCS	epidural spinal cord stimulation
FAC	functional ambulation category
FDA	Food and Drug Administration
FES	functional electrical stimulation
FES-I	Falls Efficacy Scale-International
FES-LCE	functional electrical stimulation-induced leg cycling exercise
FIM	Functional Independence Measure
FIM-L	Functional Independence Measure-Locomotor
FiO_2	Fraction of inspired oxygen
FTSTS test	Five Times Sit to Stand test
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAL	hybrid assistive limb
HKAFO	hip-knee-ankle-foot orthosis
HR	heart rate
HRR	heart rate reserve
IH	intermittent hypoxia
ISNCSCI	International Standards for Neurological Classification of SCI
iTBS	intermittent theta burst stimulation
MCID	minimal clinically important difference
KAFO	knee-ankle-foot orthosis
LEMS	lower extremity motor score
LH	lateral hypothalamus
LION	laparoscopic implantation of neuroprosthesis
LT	locomotor training
LT-RGO	locomotor training with a robot-assisted gait orthosis
MD	mean difference

MMT	manual muscle testing
MRI	magnetic resonance imaging
MST	motor skill training
MVC	maximum voluntary contraction
NMES	neuromuscular electrical stimulation
NRN	NeuroRecovery Network
Nx	normoxia
OGT	overground gait training
OWT	overground walking training
PAS	navigated TMS and Peripheral Nerve Stimulation
PCMS	paired corticospinal-motoneuronal stimulation
PEDro	Physiotherapy Evidence Database
RAGT	robotic-assisted gait training
RCT	randomized controlled trial
RM	repetition maximum
ROM	range of motion
RPE	rate of perceived exertion
rpm	revolutions per minute
RT	resistance training
rTMS	repetitive transcranial magnetic stimulation
SCI-FAP	SCI-Functional Ambulation Profile
SCIM	Spinal Cord Independence Measure
SD	standard deviation
SMD	standardized mean difference
tDCS	transcranial direct current stimulation
TENS	transcutaneous electrical nerve stimulation
TMS	transcranial magnetic stimulation
tSCS	transcutaneous spinal current stimulation
tsDCS	transcutaneous spinal direct current stimulation
TUG test	Timed Up and Go Test

tvDCS	transvertebral direct current stimulation
UEMS	upper extremity motor score
UTT	underwater treadmill training
vBFB	visual biofeedback task-specific balance training
VO_2	oxygen uptake
VR	virtual reality
WBV	whole-body vibration
WISCI	Walking Index for Spinal Cord Injury
WPE	wearable powered exoskeleton