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 N = 8	**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 (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	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 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

	safety [adverse responses], tolerability [pain, spasticity, skin integrity], and protocol achievement [session duration, intensity)] was assessed during all sessions.	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 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]).	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 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 ($g = 0.48$).

	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.	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, 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.	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. 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, medial gastrocnemius and soleus) were assessed before and after the training with ESCS^{on} and ESCS^{off}.	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.
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	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

	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.	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 Switzerland, USA and UK Pre – post Level 4 N = 3	**Population:** 3 males with chronic cervical SCI who displayed severe lower 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	1. ESCS could be delivered in an open loop: Participants regulated 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.

	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.	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. • 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	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 preoperative levels after a few weeks) (n = 3). d. Migration of the implantable pulse generator within 2 months after operation (repositioned within 2.5

	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.	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 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).	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 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.