

Review Article

A Systematic Review: Exercise Based Approaches to Activate Central Pattern Generator in Spinal Cord Injury Survivors

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Abstract

Background: Locomotion is a basic motor act which is essential for the survival of humans. The basic muscle synergies which are responsible for body propulsion are generated by the neurons in spinal cord collectively known as Central Pattern Generator for Locomotion. Spinal Cord is the major conduit for the transmission of information between brain and the rest of the body. Injury to the spinal cord is the insult to the neural elements of the spinal canal from foramen magnum to cauda equina. SCIs are heterogeneous in casualty, severity and location of injury but locomotion is the ultimate goal for the post-SCI survivors. In order for locomotion to occur, a complex CPG center of locomotion activation is required. Exercise based approach is the cornerstone in the treatment and management of individuals with SCI. **Objective:** To study the existing evidence on the effectiveness of Exercise-based approaches to activate Central Pattern Generator in Spinal Cord Injury Survivors with a focus on randomized controlled trials and cross over trials studies. **Methodology:** Literature published in English language. Original publications including RCTs and cross over trials published in peer-reviewed journals focused on traumatic or non-traumatic spinal cord injury published from 2014 to 2022. A key literature search adopted, for a more targeted search the following terms were used: effect of exercise, task-based approaches, body weight supported treadmill training, over ground training, balance and coordination training on the activation. **Search Strategy:** Database used were PubMed, Cochrane, Scopus, EMBASE, CINAHL and Medline. **Results:** Assessment of Risk of Bias was done using PeDro analysis. Eleven studies met the inclusion criteria out of 300 studies searched. **Discussion:** Exercise based approaches are highly essential and integrated part of the rehabilitation of spinal cord injury survivors. It has been concluded that activity-based therapies are highly effective but under-utilized by the rehabilitation specialists.

Keywords

Activity-Based Therapy (ABT), Central Pattern Generator (CPG), PubMed, PeDro

1. Introduction

The spinal cord plays a critical role in coordinating bodily functions via bidirectional communication between the auto-

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nomic, endocrine, and immune system. Thus, any damage to the spinal cord can result in widespread dysfunction in multiple organ system. Spinal Cord Injury (SCI) has been described as, “an acute, traumatic or non-traumatic lesion of neural elements of the spinal cord i.e. foramen magnum to cauda equina leading to temporary or permanent sensory, motor deficit or bladder/bowel/sexual dysfunction or autonomic dysfunction” [1]. The resultant paralysis and sensorimotor impairment can reduce mobility and functional independence which negatively impact quality of life.

SCI is a devastating form of neuro-trauma in which the level and type of injury can greatly influence the amount of dysfunction produced. As per the Global Burden of Diseases study, 0.9 million incident cases of SCI were reported in 2019 with the age standardized incidence rate of 12 [2]. Falls, road injuries and conflict & terrorism are the common leading causes of SCI. Spinal cord injury was found to be more prevalent in male population than female and also in elderly in comparison to young individuals [3]. The severity of spinal cord injury depends upon the extent of damage occurred in spinal cord (Wulf and Tom, 2023). The cause of damage to the spinal cord can be as a result of an intrinsic non-traumatic etiology (any space occupying lesion) or extrinsic etiology i.e. vehicle-related injuries, fall or violence [4].

SCI can be categorized into traumatic and non-traumatic spinal cord injuries. Traumatic SCI can be complete or incomplete spinal cord injuries. Complete SCI refers to the injury which results in the total lack of motor and sensory function below the level of lesion resulting in paraplegia and quadriplegia. Incomplete SCI refers to the spinal cord injury with some preserved motor or sensory function below the injury level including voluntary anal contraction (sacral sparing), palpable or visible muscle contraction below injury level or presence of peri-anal sensation [5]. It is a life-changing event that leads to impairments affecting sensory and motor function below an individual's level of injury [6].

SCI often results in systemic inflammation, immunosuppression and multiple organ dysfunction which left unresolved lead to exacerbated maladaptive responses of body systems and increased morbidity and mortality [7]. Current

treatment practices i.e. traditional therapies focus on the goals of returning the individual with SCI to independence as soon as possible while preventing secondary complications such as contractures and joint deformity. In clinical practice, the focus of neuro-rehabilitation is the use of compensatory strategies such as strengthening the unaffected side to assume more work, learning to dress one-handed and using devices like canes and braces for mechanical support. Thus, in traditional treatments most of the physical therapy actually discourages use of the affected body parts [8]. There is growing evidence that neurological improvements can be promoted through various exercise protocols which include stretching, strength training, Scheduling exercises, and activity-based therapy. However, there are perceived challenges regarding the principles of exercises and technologies, implementation, accessibility, and knowledge and there is a need for advocacy in terms of principles, type of exercises, training, and improvement to reflect the desire to maximize the potential for recovery in individuals with SCI [9, 10].

Therapeutic activity is the mainstay of clinical neuro-rehabilitation however, it is typically unstructured and directed at compensation rather than restoration of central nervous system. Therefore, to potentiate recovery in physical independence in individuals with SCI and regaining the ambulation is of prime importance for individuals recovering from SCI.

2. Aim of the Study

To study the existing evidence on the effectiveness of Exercise-based approaches to activate Central Pattern Generator in Spinal Cord Injury Survivors with a focus on randomized controlled trials and cross over trials studies.

3. Methodology

3.1. Type of Studies Included

Randomized Controlled Trials and Cross Over Trials.

Table 1. Selection Criteria: Following is the selection criteria used for the study.

INCLUSION CRITERIA	EXCLUSION CRITERIA
1) Literature published in English language	1) Non-Experimental Studies such as review articles, editorials, letters to editors, commentaries, protocols or book chapters were excluded.
2) Original publications including RCTs and cross over trials published in peer-reviewed journals focused on traumatic or non-traumatic spinal cord injury published from 2014 to 2022.	2) Duplicated studies those with insufficient data for pooling and inaccessible full text articles.
3) A key literature search adopted, for a more targeted search the following terms were used: effect of exercise, task-based approaches, body weight supported treadmill training, over ground training, balance and coordination training on the activation of CPG of locomotion manifested as Inde-	3) Non-SCI participants i.e. able-bodied individuals, other neurological conditions/diseases.
	4) Peripheral Neuromodulation i.e. Functional Electrical

INCLUSION CRITERIA	EXCLUSION CRITERIA
<p>pendent or Co- Intervention in SCI survivors</p> <p>4) Studies focused on non-invasive interventions mainly exercise or activity based approaches.</p> <p>5) Adult Participants irrespective of gender, Age, Initial level of Impairment, Duration of SCI, Level of Injury and, the Mechanism involved.</p>	<p>Stimulation, Transcutaneous Electrical Nerve Stimulation. Brain Computer Interfaces, pharmacological additions.</p> <p>5) Involve invasive interventions (epidural spinal stimulation).</p>

Table 2. Search Strategy.

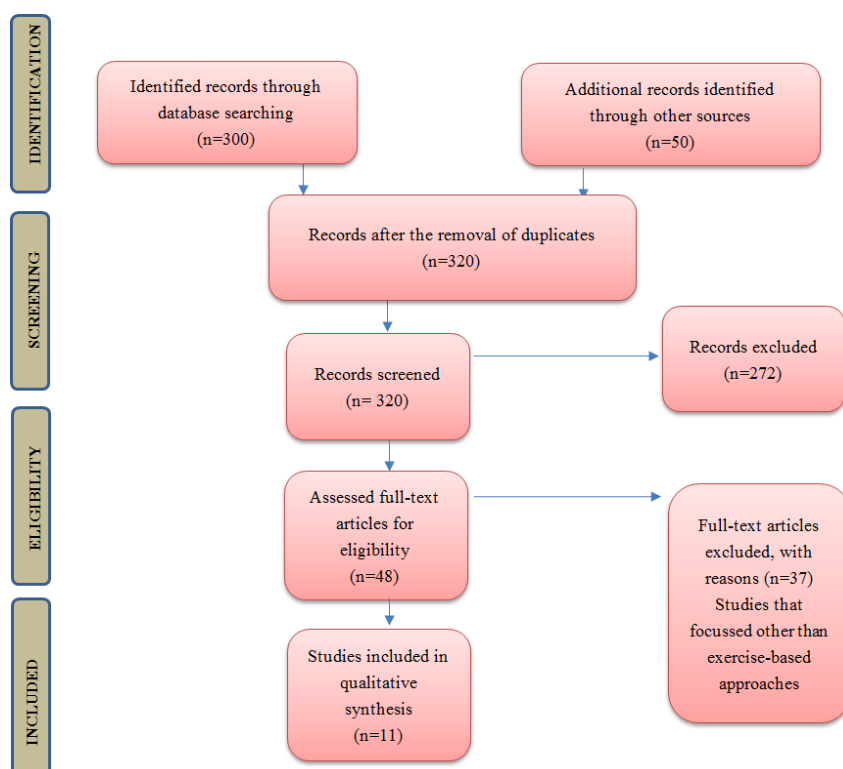
DATABASE	YEAR	SEARCH FOCUS
1) PubMed 2) Cochrane 3) Scopus 4) EMBASE 5) CINAHL 6) Medline	(2014-2022)	1) General Information 2) Participant Information 3) Trial Information 4) Intervention Information 5) Outcomes

3.2. Medical Subject Headings and Keywords

Exercise-based approaches, post-SCI locomotive Impairment, CPG pattern in SCI, Motor and sensory Impairment, Activity-based therapy, Body weight supported treadmill training.

3.3. Quality Assessment and Data Extraction (Assessment of Risk of Bias)

Physiotherapy Evidence Database (PEDRO).

**Figure 1.** PRISMA-Flow Diagram.

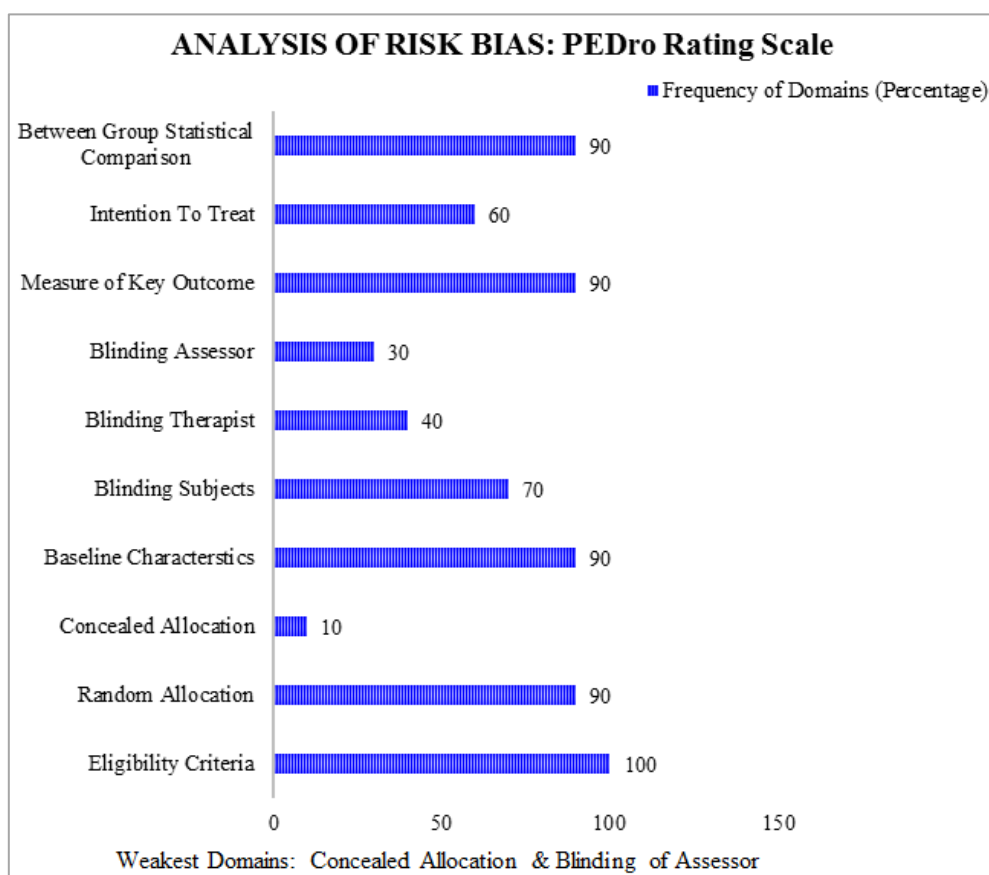


Figure 2. Analysis of risk of bias- PEDro rating Scale.

4. Discussion

Modern clinical neuro-rehabilitation is grounded in the premise that exercises-based approaches is beneficial for individuals suffering from spinal cord injury [11]. The notion of exercises having therapeutic properties is so deeply ingrained within the field that it is vital for augmenting the recovery in the individuals with spinal cord injury [12]. Data of Included Trials revealed that exercise-based approaches or Interventions comprising intense repetitive rehabilitative treatment sessions can only induce Potential activity dependent plasticity of the neural axis in the spinal cord promoting the therapeutic utility of exercise directed interventions by targeting Central Pattern Generator for Locomotion in individuals with SCI [13-17].

Physical activity i.e. exercises based training is vital for augmenting recovery after spinal cord injury [18, 19]. Activity dependent plasticity of the neural axis including spinal cord and has provided new perspective on the role of physical rehabilitation for the recovery of motor function after spinal cord injury. Exercise based rehabilitation act as a compensation for irremediable deficits and also as a strategy for new skill development [20-23]. Exercise based therapeutic strategies are key part of maintaining and enhancing the quality of life of individual with SCI. These exercise-based rehabilita-

tion provided significant neurological recovery, physical health benefits, independence, mental health benefits, hope and motivation.

Exercise also acts as neuroprotective therapy. Findings of the studies have been justified with the fact that exercise-based approach cannot induce neural firing however it is believed to modulate the increased rate of spontaneous neuronal firing specific to activate the CPG for Locomotion thus justifying the synergistic effects with the better functional outcome at the end [24-27]. However, extensive variability was observed in terms of intervention dosage, frequency and variety of exercises such as intensity of activity, duration of activity, repetition of activity, number and frequency of sessions [28, 29]. In fact, substantial heterogeneity was found among the studies in which exercises was intended to treat similar locomotor domains [30-33]. Possible reason could be that most of the studies have been limited by the small sample size a thus difficulty in generalizability of results.

5. Conclusion

Exercise-based therapy plays a multifaceted role in promoting the formation, refinement, and function of central pattern generators in individuals with spinal cord injury, ultimately leading to improvements in motor con-

trol, mobility, and quality of life. Exercise promotes neural plasticity, which refers to the brain and spinal cord's ability to reorganize and form new connections in response to stimuli or experiences. Through repetitive movement patterns, exercise can stimulate the reorganization of neural circuits involved in motor control, including the CPGs. Regular participation in exercise-based therapy can lead to long-term adaptations in the nervous system, including structural and functional changes within the spinal cord. Over time, these adaptations can contribute to the establishment of more robust and efficient CPGs, enhancing motor function and mobility in individuals with SCI. Thus, targeted Exercise based strategies forms the foundation of neurorehabilitation of SCI by harnessing the principles of neural plasticity, task-specific training, sensory-motor integration, and neurotrophic effects to optimize recovery, enhance function, and improve quality of life for individuals living with spinal cord injury.

Abbreviations

SCI: Spinal Cord Injury

CPG: Central Pattern Generator

Appendix

Description of the Studies

Table 3. The following is the description of the studies.

Author and Year	Aim of the Study	Intervention	Outcome Measure	Conclusion
Edwards <i>et al.</i> (2022)	To investigate the effectiveness of Exoskeleton-based robotic gait training regime in individuals with incomplete spinal cord injury	N= 25 Experimental Group Exoskeleton-based robotic gait training regime 12 weeks' regime (26 sessions) of intervention Control Group Conventional Physiotherapy 12 weeks' regime (26 sessions)	10 Minute Walk Test (MWT) Time Up Go Walking Index for Spinal Cord Injury-II (WISCI-II)	1) Improved clinical ambulatory status 2) Improved Quality of Life in the experimental group
Young <i>et al.</i> (2021)	To study the effect of Spinal Cord Injury Program in Exercise (SCIFE) on the functional independence in individuals with spinal cord injury	N= 109 Experimental Group 8 weeks of SCIFE 1-2 hrs/week Control Group Standard exercise training for 8 weeks 1-2 hrs/week	Changes in Physical Activity Level-PAR-Q	1) Address several barriers to exercise 2) Improved functional ambulation and quality of life in the experimental group
Pirra <i>et al.</i>	To determine the effectiveness	(N=24)	WISCI-II	Improvement in pos-

ABT: Activity- Based Therapy

RCT: Randomized Clinical Trials

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Author Contributions

All authors equally contributed in the preparation of the article.

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Conflicts of Interest

The authors declare no conflicts of interest.

Author and Year	Aim of the Study	Intervention	Outcome Measure	Conclusion
(2019)	of Robot-assisted locomotor training on the CPG of locomotion in individuals with incomplete spinal cord injury with ASIA C and D, >2 years post-SCI	Experimental Group Robot-assisted locomotor training With conventional physiotherapy interventions (n=12) locomotor training, 30Min/Session, 5times/week x 60 days Control Group Conventional Physiotherapy (n=12) locomotor training, 30Min/Session, 5times/week x 60 days	Lower Extremity Motor Score (LEMS) Balance	tural control of the control group Improved lower limb muscle strength Improved walking speed in the experimental group
Hubscher <i>et al.</i> (2019)	To study the efficacy of Task-specific locomotor training using body weight support treadmill training on bladder function in individuals with incomplete spinal cord injury	N=8 Task-oriented locomotor training using Body Weight Support Treadmill Training (BWSTT) 80 daily one-hour session of BWSTT for 3 months' duration+ Conventional Physiotherapy (N= 91)	Urodynamics Lower Extremity Motor Score	Improvement in Bladder, bowel, and sexual outcomes in the experimental group
Oliveria <i>et al.</i> (2019)	To study the effectiveness of Activity Based Therapy (ABT) on CPG of locomotion in individuals with incomplete spinal cord injury in community settings	ABT in Community Setting Independent mobility Sitting balance 3-12 months 1-4 times per week Assessment every 3 monthly N=16 -Experimental Group	Spinal Cord Independence Measure Seated Reach Distance Outcome	Significant Improvement in sitting balance, and mobility of patients with SCI
Wu <i>et al.</i> (2018)	To investigate the effectiveness of Dynamic weight shifting and treadmill training using 3DCaLT on the postural control in individuals with incomplete spinal cord injury	Dynamic weight shifting and treadmill training using 3DCaLT -Control Group Body-weight supported treadmill training with manual assistance 6 weeks of training 3 times per week of 45 minutes per session (N=40) -Experimental group	6 MWT SCIM-III WISCI-II	Improved postural control, trunk control, balance, and confidence in the experimental group
Bedi <i>et al.</i> (2018)	To study the effectiveness of Activity Based Therapy in comparison to Surface Spinal Stimulation (SSS) in individuals with incomplete spinal cord injury	ABT + SSS for 24 weeks Thrice weekly basis -Control group ABT for 24 weeks thrice weekly basis	ASIA WISCI-II SCIM-III	Improvement in the walking speed Significant improvement in the quality of life of the individuals with SCI in the experimental group
Lin <i>et al.</i> (2016)	To study the effectiveness of Overground Treadmill Training using BWSTT with whole-body vibration, WBV in individuals with incomplete spinal cord injury 12-week duration thrice weekly program of BWSTT	(N=40) BWSTT + WBV for 12 weeks Thrice weekly basis +BWSTT for 12 weeks thrice weekly basis	ASIA WISCI-II SCIM-III	Improvement in the walking speed of the patient Improvement in the tone of the lower limb musculature in the experimental group

Author and Year	Aim of the Study	Intervention	Outcome Measure	Conclusion
Senthilvelkumar <i>et al.</i> (2015)	To determine the effectiveness of Spinal Cord Injury Locomotor Trial (SCILT) in individuals with spinal cord injury with ASIA C & D	(N= 107) Experimental Group Spinal Cord Injury Locomotor Trial (SCILT) 12 weeks of Training with BWSTT Control Group Conventional Overground mobility intervention (CONT)	ASIA Functional Independence Measure (FIM) – lower extremity 15-minute walking speed LEMS	Improved postural control, sitting balance. Improved functional independence Improvement in the tone and strength of lower limb musculature in the experimental group
Dobkin <i>et al.</i> (2014)	To determine the efficacy of Spinal Cord Injury Locomotor Trial (SCILT) in individuals with spinal cord injury with ASIA C & D	N= 107 Experimental Group Spinal Cord Injury Locomotor Trial (SCILT) 12 weeks of Training with BWSTT Control Group Conventional Overground mobility intervention (CONT)	ASIA FIM-L 15-minute walking speed LEMS Outcome	Improved walking speed, endurance, and muscular strength of lower extremity in the experimental group
Jones <i>et al.</i> (2014)	To study the effectiveness of Activity based therapy on the Walking speed in Post SCI survivors.	Experiment Group ABT within 2 weeks & continued for 24 weeks N=48 Developmental sequencing + strengthening exercises + locomotor training	LEMS 10-meter walk test 6-minute walk test Timed Up and Go Test SCIM-III	Improvement in the walking speed of the patient Improvement in the tone of the lower limb musculature in the experimental group

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