REVIEW ARTICLE

Brain-derived Neurotrophic Factor (BDNF) Responses to Exercise in Individuals with Spinal Cord Injury: A Systematic Review.

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Abstract

Introduction: Spinal Cord Injury (SCI) leads to debilitating effects. This study aimed to conduct a systematic review examining the correlation between exercise, physical activity, and levels of Brain-Derived Neurotrophic Factor (BDNF) in individuals with SCI. **Method:** A search was conducted between 2013 and 2023 using the PubMed, CENTRAL, Medline, and Wiley Online Library databases, along with bibliographic searching. The evaluation process was conducted at each stage to identify eligible studies. Methodological quality assessments were performed on each eligible study, and the data were presented in tabular form. **Results:** Out of 2,928 papers, only five met the eligibility criteria for inclusion in the review. The methodological quality of the included studies ranged from low to moderate. The demographic variables of the participants, including age, years since injury, gender, level and severity of injury, sample size, study design, intervention, outcome measures, and findings, were organized into a table. All the included studies exhibited heterogeneity. **Conclusion:** The findings suggest a potential association between exercise and physical activity and BDNF concentration levels in individuals with SCI. However, further research with larger sample sizes and rigorous methodology is necessary to establish the long-term effects of exercise and physical activity on BDNF concentration levels. Clinically, this review underscores the importance of tailored exercise interventions in enhancing neuroplasticity and recovery in SCI patients.
Keywords: *Brain-Derived Neurotrophic Factor (BDNF), cord Injury, exercise, physical activity, spinal.*

Introduction

Spinal Cord Injury (SCI) presents significant challenges, leading to permanent disabilities like paralysis and loss of sensation [1]. These injuries not only cause physical impairments but also lead to complex physiological changes, such as autonomic dysregulation, which further complicates the overall health and well-being of individuals with SCI [2]. The annual incidence of SCI is estimated to be between 250,000 and 500,000 cases, with a prevalence of 40 to 80 cases per million individuals [3]. Despite advances in medical research and rehabilitation, individuals with SCI continue to face substantial functional limitations that hinder their ability to perform activities of daily living (ADLs) such as self-care, feeding, and mobility [4]. These impairments also restrict participation in employment [5], sports [6], and social activities [7, 8], often resulting in a diminished quality of life [9].

Exercise and physical activity are known to mitigate some of these impairments, improving muscle strength [10], balance [11], and overall physical fitness [5], which in turn can enhance participation and quality of life [18]. However, the impact of exercise on neuroplasticity and neuronal regeneration in SCI remains underexplored. One key factor in this area is Brain-Derived Neurotrophic Factor (BDNF), which plays a crucial role in the survival, excitability, and regeneration of neurons [6]. BDNF is particularly important in the context of SCI, where neurological impairment and autonomic dysregulation may alter the body's typical physiological responses, including the production of BDNF.

Given BDNF's role in supporting neuroplasticity, its potential to enhance locomotor function through exercise and physical activity makes it a promising target for rehabilitation in SCI patients. BDNF is known to influence brain structures, including the hippocampus and prefrontal cortex, which are involved in synaptic neurotransmission and neuronal proliferation [19]. Although the benefits of BDNF are well-documented in healthy individuals [24], the elderly [25], and other clinical populations such as stroke [27] and multiple sclerosis patients [28], the responses of BDNF to exercise in individuals with SCI are less consistent and robust. This inconsistency may be due to several factors specific to the SCI population, including the extent of neurological impairment, the level and completeness of the injury, and the adapted nature of exercise modalities used.

Research on the effects of exercise and physical activity on BDNF levels in SCI individuals is scarce, leaving a significant gap in our understanding of how these interventions might influence neuroplasticity and neuronal recovery in this population [3]. In light of these gaps in knowledge, this review aims to provide a thorough analysis of current scientific literature to clarify the potential benefits and mechanisms associated with exercise and physical activity in enhancing BDNF-mediated neuroplasticity and neuronal reconstruction in individuals with SCI. Our hypothesis is that the intensity and duration of exercise may differentially regulate BDNF levels, with more intense or longer-duration activities potentially leading to more pronounced neuroplastic effects.

Materials and Method

Literature search strategy

To comprehensively identify relevant studies, a systematic literature search was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search covered studies published between January 1993 and January 2023. This search was executed across key health-related databases, including PubMed, CENTRAL, Medline, and the Wiley Online Library. Search terms were selected from three categories: Population (Spinal Cord Injury OR Paraplegia OR Tetraplegia), Intervention (Exercise OR Physical Activity), and Outcome (Brain-Derived Neurotrophic Factor OR Neurotrophic). These terms were combined using Boolean operators (AND, OR) to refine the search results effectively. The search was

restricted to studies published in English, which could introduce a language bias, and this should be considered a potential limitation. A secondary search was also conducted through the reference lists of relevant studies to identify additional potential sources. Table 1 below outlines the study search strategy.

Inclusion and Exclusion Criteria

The inclusion criteria were meticulously defined to ensure the relevance and quality of the studies included in this systematic review. Eligible studies met the following criteria: participants were aged 18 years or older, had chronic or subacute SCI, the study was conducted on human subjects, and full articles were available in English. Additionally, studies were required to be published in academic journals between 1993 and 2023. Studies that were systematic reviews, scoping reviews, and narrative reviews were excluded from the analysis. Furthermore, studies were excluded if their outcomes did not include an assessment of BDNF concentration.

The Review and Data Extraction Process

The review process involved three phases to ensure the reliability and validity of the findings. Initially, the main author screened the titles of retrieved papers to identify potentially relevant articles, eliminating irrelevant or duplicate studies. Abstracts of remaining articles were then screened against the inclusion and exclusion criteria. Discrepancies were resolved through discussion and consensus among the reviewers, with a third reviewer consulted if needed. Full texts of eligible studies were retrieved and assessed by the main author. Each article was critically evaluated by two reviewers to ensure alignment with the research question, extract relevant data, and determine the quality of the studies. The data extraction process involved creating a structured table that included information on participants (age, gender, years since injury), study characteristics (design, sample size, intervention, outcome measures), and outcomes (BDNF concentration changes, exercise effects).

Methodological Quality Assessment

The methodological quality of each study was assessed using the Joanna Briggs Institute (JBI) checklist, which is designed to evaluate a wide range of study types, including experimental, observational, and cross-sectional studies. The JBI checklist is comprehensive, covering key aspects such as sample selection, study design, data collection methods, statistical analysis, and the appropriateness of conclusions. Its use ensured a consistent and rigorous assessment of methodological quality across studies, systematically identifying potential biases and limitations. The checklist's flexibility and comprehensiveness enhanced the transparency and robustness of the review, making it a suitable tool for evaluating the quality of included studies. The JBI instrument exhibits notable face validity and acceptance, demonstrating its suitability for research and clinical settings. Moreover, it is straightforward to administer and does not require much evaluation time. The JBI's evaluation criteria include:

- A representative sample
- An appropriate apparatus
- An adequate sample size
- An appropriate description of study reports, subjects, and setting;
- Adequate data coverage
- Validity of condition measurement
- Reliability of condition measurement
- Appropriate statistical analysis
- The adequacy of the response rate

The evaluation of eligible research was conducted by two reviewers, with any discrepancies resolved through consensus discussion or by consulting a third reviewer.

Results

Study search results

The search yielded 2,928 studies: 29 from PubMed, 1,560 from Medline, 16 from CENTRAL, 1,322 from Wiley Online Library, and 1 from a bibliographic search. After eliminating 328 duplicates, 2,600 studies remained for review. The titles of 2,549 studies were evaluated for eligibility, resulting in 127 potentially eligible studies. The abstracts of the 127 studies were then reviewed according to the inclusion criteria, and 122 studies were excluded, leaving five articles that met the inclusion criteria. These five studies were subsequently analyzed, and the necessary data were extracted. Figure 1 illustrates the flowchart of the search strategy and selection process, adhering to PRISMA guidelines.

Study Methodological Quality

Overall, the studies demonstrated moderate methodological quality. Many studies had low methodological quality, primarily due to small sample sizes, which increased the risk of bias and exaggerated results [1-6]. Most studies employed suitable sampling techniques when selecting research participants [1, 3-6]; however, one study raised concerns about the reliability of its sampling procedures [2]. None of the included studies met the criteria for an acceptable sample size [1-6]. Additionally, the eligible studies did not provide an accurate representation of the participants or the specific environments in which the studies took place [1-6]. The condition identification methods utilized in all studies were deemed valid, with consistent and dependable measurements across participants in many investigations [1-6]. All studies employed appropriate statistical analyses [1-6]. Moreover, all eligible studies had sufficient response rates, and instances of low response rates were adequately addressed [1-6]. Please refer to Table 2 for the quality assessment of all included studies.

Characteristics of the Participants

Participants' average age ranged from 35 to 56 years [1-6]. The years since injury (YSI) among participants ranged from eight to 31 years [1-6]; however, two studies did not report YSI [3, 5]. Male participants predominated in these studies [1-3], though two studies did not specify the number of male and female participants [5, 6]. One study reported an equal number of male and female participants [4]. Most participants were tetraplegic rather than paraplegic [1-3, 6]. Two studies included seven participants with complete injuries [4], while two studies reported 19 participants with incomplete injuries [1, 2, 4]. The remaining two studies did not specify the number of participants based on injury level [5, 6]. Table 3 displays the characteristics of the participants.

Characteristics of the Studies

The six included papers used various study designs, including prospective observational [1], repeated measure [2], cross-sectional [3], and prospective cohort designs [4], while two studies did not specify their design [5, 6]. All studies had small sample sizes, ranging from 10 to 16 participants, with a total of 74 participants across all studies [1, 2, 4, 6]. The types of exercise and physical activity varied, including wheelchair marathons [1], wheelchair rugby training [4], gait training on a treadmill [3], single-bout gait training, graded exercise gait training using a treadmill with body weight support (BWST) [2, 5], and hand bike incremental exercise [6]. The summary of the study characteristics is tabulated in Table 4.

The Relationship of Exercise and Physical Activity on The Level of BDNF Concentration

As previously indicated, the exercises and physical activities used in the included studies varied. Two studies reported significant immediate effects on BDNF levels after a 1-hour half marathon ($p < 0.05$) and 10 minutes of hand bike incremental exercise (60 rpm, 20W/5 minutes) [1-3]. Tetraplegic participants showed

higher BDNF levels ($p = 0.0055$) compared to paraplegic participants ($p = 0.0312$) after the 1-hour half marathon [1]. Two studies reported no significant changes in BDNF levels following exercise: one after BWST gait training and a treadmill run ($p > 0.05$) [4], and another after wheelchair rugby training at rest, during training, and cooldown ($p > 0.05$) (5). One study found that BDNF levels were nearly regulated after high-intensity exercise (HIE) compared to moderate and low-intensity activities ($p = 0.05$) [3].

Discussion

Quality of the included studies

This review examines the correlation between exercise, physical activity, and BDNF levels in individuals with SCI. Despite an exhaustive search of studies published between 1993 and 2023, only six studies met the criteria for inclusion [29-34]. This scarcity highlights a significant gap in research on how exercise and physical activity influence BDNF levels in this population. The moderate methodological quality of these studies points to several challenges specific to SCI research, such as variability in study design, demographic characteristics, injury severity and levels, functional limitations, health considerations, and rehabilitation intervention which contribute to methodological issues.

Key limitations observed in the included studies encompass the type of study design, small sample sizes, recruitment challenges, and the complexity of exercise interventions. These constraints may have affected the reliability, introduced bias, and limited the generalizability of the reported findings. To enhance future research, it is imperative to prioritize rigorous study designs such as randomized controlled trials (RCTs) and prospective cohort studies [43]. These designs offer better control over confounding variables and enable the identification of causal relationships between exercise, physical activity, and BDNF levels.

The heterogeneity among the included studies further complicates the synthesis of results and the formulation of robust conclusions. Variations in study designs, exercise interventions, and outcome measures contribute to inconsistent findings, making it challenging to establish clear patterns or causal relationships. Exercise modalities, intensity levels, and outcome measures differed across studies, leading to diverse and sometimes conflicting results. The decision to include a range of study designs and interventions was made to provide a comprehensive overview of existing evidence on BDNF responses to exercise in the SCI population. However, this diversity also highlights the need for standardized protocols in future research. Standardization would improve the consistency and comparability of findings, facilitating more accurate assessments of the impact of different exercise interventions on BDNF levels.

Personalized exercise programs are crucial given the variability in BDNF responses to different interventions. Future research should aim to develop and implement standardized protocols for exercise interventions and outcome assessments. Additionally, a thorough examination of participant characteristics, including the extent, intensity, and duration of SCI, as well as demographic factors such as age, gender, and length of injury, would provide a more nuanced understanding of BDNF responses. Such data would enable more precise subgroup analyses and enhance the contextual understanding of results.

Most studies on BDNF have been conducted on animals, likely due to ethical and safety considerations in human research [44]. While animal studies have shown positive effects of exercise on BDNF levels, these findings may not always translate reliably to humans [45]. Therefore, emphasizing human studies with larger sample sizes is essential for making reliable recommendations regarding exercise and physical activity for individuals with SCI. The findings from this review underscore the need for more rigorous, standardized research to better understand the relationship between exercise,

physical activity, and BDNF levels in the SCI population, ultimately informing more effective rehabilitation strategies.

The Influence of SCI Individual Characteristics on the level of BDNF

Several factors could have impacted the BDNF responses to exercise in the included studies. One significant factor is age. Age-related changes in neurobiology, such as decreased neuroplasticity and altered BDNF regulation [46, 47], can influence how individuals respond to exercise. Older adults may experience different BDNF responses compared to younger individuals, potentially affecting the generalizability of findings across different age groups.

Gender is another critical factor [47]. Research suggests that gender differences may affect BDNF levels and neuroplasticity. Hormonal variations and sex-specific biological mechanisms might lead to differential responses to exercise between males and females. The studies reviewed often had limited gender diversity, which could impact the overall findings and their applicability to both sexes.

Injury severity also plays a crucial role in determining BDNF responses [48]. Individuals with more severe injuries may experience greater challenges in neuroplasticity and functional recovery. Variations in injury severity among study participants could contribute to inconsistencies in BDNF levels and their response to exercise interventions. A more granular analysis of injury severity in future research could provide insights into how different levels of injury affect BDNF responses.

Time since injury is another important factor [48]. The stage of injury recovery can influence BDNF levels and the effectiveness of exercise interventions. Early post-injury periods may see different BDNF dynamics compared to later stages of recovery. Thus, including a range of time since injury in studies is crucial for understanding how BDNF responses to exercise evolve over time.

The Influence of Exercise and Physical Activity on BDNF Levels in Individuals with SCI

The review highlights the complex and varied relationship between exercise, physical activity, and BDNF levels in individuals with SCI. BDNF is a crucial protein involved in neuroplasticity, neuronal survival, and cognitive function, making it a key target in SCI rehabilitation [50, 51]. BDNF is a key player in neuroplasticity and functional recovery after SCI [49, 51]. It promotes neuronal survival, growth, and differentiation, which are essential for repairing and regenerating damaged neural circuits [49, 51, 52]. Exercise and physical activity have been shown to elevate BDNF levels, potentially enhancing neuroplasticity and aiding functional recovery [50, 52].

Current understanding indicates that BDNF contributes to functional recovery by supporting the growth of new neuronal connections and improving synaptic plasticity [49, 51, 52]. In the context of SCI, elevated BDNF levels may facilitate the reorganization of neural pathways and enhance motor and sensory function [49, 52]. However, the precise mechanisms through which exercise-induced BDNF increases translate into functional improvements remain an area of ongoing research.

However, the evidence regarding the optimal exercise types and intensities for enhancing BDNF levels in this population remains inconclusive. One of the most significant findings from this review is the variability in BDNF responses to different exercise types and intensities among individuals with SCI. High-intensity exercises, such as half-marathons, graded intensity protocols, and High-Intensity Interval Training (HIIT), have shown more promise in increasing BDNF levels than low-intensity or short-duration exercises [29-34]. These high-intensity activities seem to create a more substantial physiological stimulus, which may be necessary for the upregulation of BDNF production in the central nervous system [52]. This observation suggests that exercise intensity

plays a critical role in modulating BDNF levels and highlights the limitations of a one-size-fits-all approach to exercise prescription in SCI rehabilitation.

The variability in BDNF responses can be attributed to several factors, including the type of exercise, its intensity, and the duration of the intervention. For example, endurance activities like wheelchair marathons [34] or graded exercise [30] protocols appear to encourage greater BDNF production compared to lower-intensity exercises. The mechanistic basis for this may lie in the physiological demands these exercises place on the body, leading to increased neurotrophic support [49, 51]. However, the review also points out that not all individuals with SCI may be capable of participating in high-intensity exercises due to their physical limitations, health status, or injury severity. Therefore, while high-intensity exercises may be beneficial for some, they may not be suitable for all, emphasizing the need for personalized rehabilitation programs.

In addition to intensity, the duration and consistency of exercise play crucial roles in influencing BDNF levels. The review indicates that short-term or sporadic exercise interventions may not be sufficient to sustain elevated BDNF levels over time. None of the included studies demonstrated that exercise and physical activity could stimulate sustained BDNF production over prolonged periods [29-34]. This finding suggests that while exercise can acutely boost BDNF levels, maintaining these benefits may require ongoing, long-term engagement in physical activity. Therefore, future research should prioritize long-term interventions with multiple follow-ups to better understand the lasting effects of various exercise modalities on BDNF levels in individuals with SCI.

Moreover, the relationship between exercise, BDNF levels, and broader rehabilitation outcomes remains underexplored. While BDNF is a marker of neuroplasticity [51, 52], its role in functional recovery after SCI is not fully understood. The review suggests that future studies should include broader outcome measures to evaluate the potential associations between BDNF levels and cognitive function, physical fitness, mobility, and pain. These measures would provide a more comprehensive understanding of how BDNF modulation through exercise influences overall rehabilitation outcomes in SCI patients.

Therefore, the review underscores the importance of exercise intensity in modulating BDNF levels in individuals with SCI but also highlights the variability in responses based on the type and duration of exercise. This variability suggests that a one-size-fits-all approach to exercise prescription may not be effective for BDNF enhancement in SCI patients. Instead, personalized rehabilitation programs should be developed, taking into account the specific type and intensity of exercise most likely to induce BDNF production while also considering the physical capabilities and safety of each individual. High-intensity exercises, particularly those used in HIIT protocols, appear promising for BDNF elevation and could be prioritized in rehabilitation settings. However, further research is needed to confirm these findings and to explore the long-term effects of various exercise modalities on BDNF levels, as well as their broader impact on functional recovery in SCI patients.

Conclusions

In conclusion, this systematic review highlights the potential of exercise and physical activity to influence BDNF levels in individuals with SCI. Although findings suggest a possible link between specific exercise modalities and increased BDNF concentrations, the evidence remains limited due to moderate level of study quality, small sample sizes and heterogenenity of the included studies. Further research with larger, well-designed studies is needed to establish clear recommendations. Clinically, these findings support the integration of tailored, high-intensity exercise protocols in SCI rehabilitation to potentially enhance neuroplasticity and functional recovery.

Clinical implications

This review reveals that exercise may significantly elevate BDNF levels, enhancing neuroplasticity and neuronal regeneration in individuals with spinal cord injury (SCI) [49, 50, 51, 52]. Incorporating targeted exercises like aerobic training, resistance training, and high-intensity interval training (HIIT) into rehabilitation programs could improve outcomes in motor function, sensory recovery, and overall quality of life for SCI patients. Clinicians can personalize these exercises based on the patient's injury severity, health status, and specific functional goals, maximizing the benefits of rehabilitation. For instance, Paraplegia Fitness Integrated Training (PARAFiT), introduced by Hisham et al. [5], is an example of a regimen that may elevate BDNF levels, although further research is needed to confirm its effectiveness to elevate BDNF level. The variability in BDNF responses across different exercise types emphasizes the importance of individualized rehabilitation strategies. These findings provide a strong foundation for developing more effective, evidence-based rehabilitation protocols to enhance recovery in SCI patients.

Limitations of the study

The main constraint of this analysis is the small number of eligible studies, with only six studies meeting the inclusion criteria. Furthermore, the study also have moderate level of quality and demonstrated significant heterogeneity in terms of study designs, participant characteristics, interventions, and outcome measures. This heterogeneity complicates direct comparisons, impedes the feasibility of a meta-analysis, and potentially weakens the overall conclusions, introduce biases, impacting the accuracy and reliability of the findings.

Recommendations for future research

Future studies should focus on larger, well-designed clinical trials that can more definitively establish the long-term effects of exercise on BDNF levels and neuroplasticity in the SCI population. Such research will be crucial in refining exercise prescriptions and maximizing the therapeutic benefits of rehabilitation for individuals with SCI. Additionally, exploring the underlying mechanisms by which different exercises influence BDNF production could provide deeper insights into how these activities promote neuroplasticity and neuronal regeneration.

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Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Authors contributions

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Table 1. Search strategies

Criteria	Databases
Databases	PubMed, Medline, CENTRAL, Wiley Online Library
Keywords	'Spinal Cord Injury OR Paraplegia OR Tetraplegia' AND 'Exercise OR Physical Activity' AND 'Brain-Derived Neurotrophic Factor OR Neurotrophic'
Limiters	Full Text; English, 1993-2023, academic journals, spinal cord injury population
Search modes	Boolean/Phrase

*This table shows the search strategies in health-related databases for literature searching

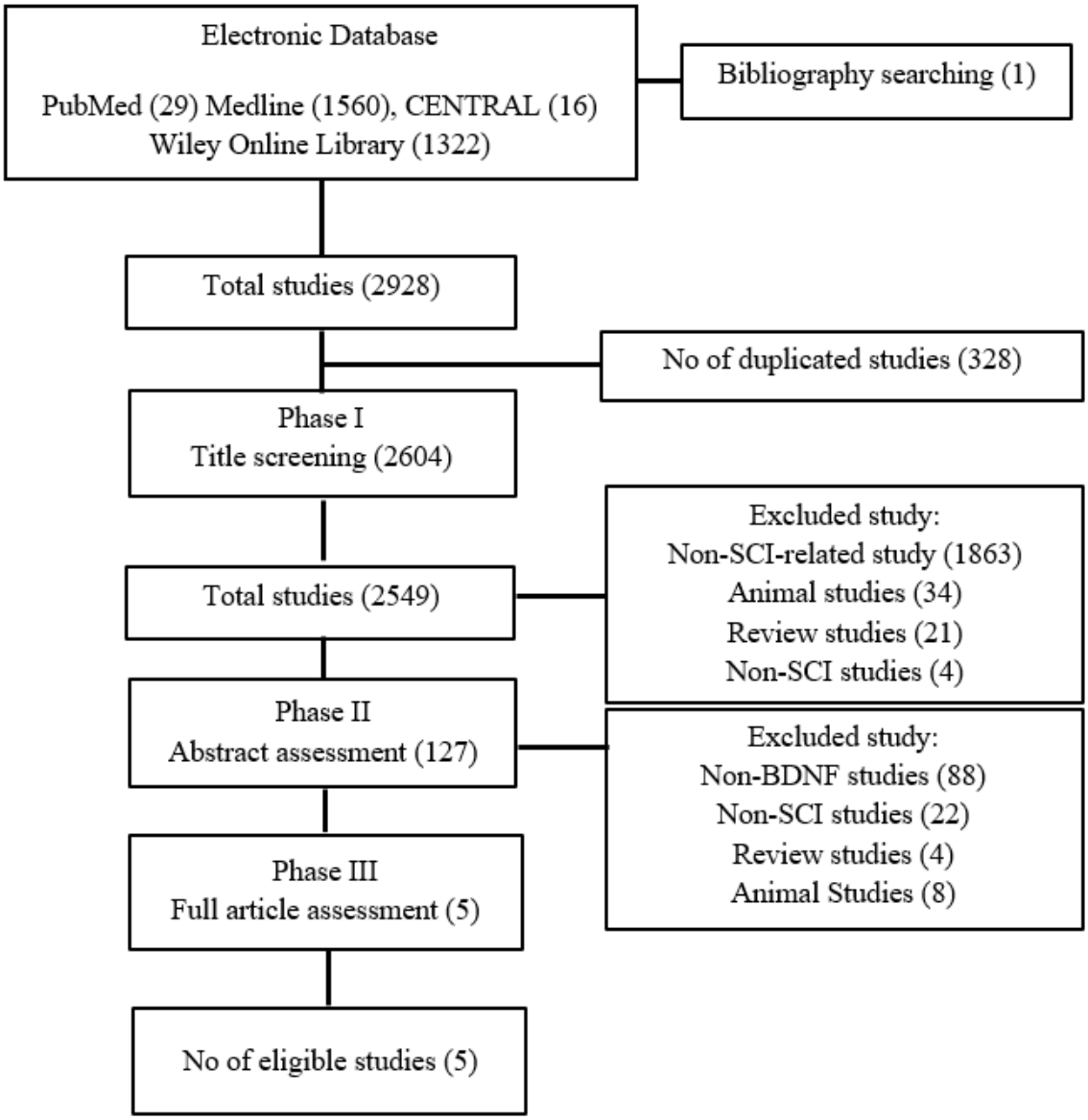

Figure 1. Search results

Table 2. JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data.

No.	Criteria	Studies					
		Nishimura et. al (2022)	**Goldhardt et al. (2019)**	**Leech and Hornby, (2017)**	**Zeller et al (2015)**	**Harness et al (2014)**	**Vega et. al (2008)**
1.	Was the sample frame appropriate to address the target population?	Yes	Yes	Yes	Yes	Yes	Yes
2.	Were study participants sampled appropriately?	Yes	Yes	Unclear	Yes	Unclear	Unclear
3.	Was the sample size adequate?	No	No	No	No	No	No
4.	Were the study subjects and the setting described in detail?	Yes	No	No	Yes	No	No
5.	Was the data analysis conducted with sufficient coverage of the identified sample?	Yes	Yes	Yes	Yes	Yes	Yes
6.	Were valid methods used for the identification of the condition?	Yes	Yes	Yes	Yes	Yes	Yes
7.	Was the condition measured in a standard, reliable way for all participants?	Yes	Yes	Yes	Yes	Yes	Yes
8.	Was there an appropriate statistical analysis?	Yes	Yes	Yes	Yes	Yes	Yes
9.	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Yes	Yes	Yes	Yes	Yes	Yes

Table 3. The participants' characteristics

Author	Sample size (n)	Age Mean (SD)	YSI Mean (SD)	Gender	Level of SCI	Severity of injury
Nishimura et. al (2022)	16	Para: 56 (4) y/o Tetra: 35 (4) y/o	Para: 381 (63) months (31 years) Tetra: 161 (35) months (13 years)		Para (n): 8 Tetra (n): 9	
Goldhardt et al. (2019)	10	40.6 (9.03) y/o	3.5 (1.27) years	Male (n): 5 Female (n): 5	C4 – C7 (n): 3 T1 - L5 (n): 7	Complete (n): 2 Incomplete (n): 8
Leech and Hornby, (2017)	11	41 (14) y/o	103 (85) months (8.5 years)	Male (n): 8 Female (n): 2	C4-C7 (n): 10 T4 (n): 1	Chronic incomplete (n): 11
Zeller et al (2015)	11	31.7 (5.9) y/o		Male (n): 11	C5-C7 (n): 11	Complete and incomplete
Harness et al (2014)	15	31.8 (10.9) y/o	63.9 (54.4) months	Male (n): 12 Female (n): 3	C4-C7 (n): 10 T2-L1 (n): 5	Complete (n): 5 Incomplete (n): 10
Vega et. al (2008)	11	40.6 (6.3) y/o			Para (n): 11	ASIA A and B

**YSI: Years Since Injury, y/o: Years old, Para: Paraplegia, Tetra: Tetraplegia, C: Cervical, T: Thoracic, L: Lumbar, ASIA: American Spinal Injury Association. This table shows the demographic data of the included participants.

Table 4. Characteristics of the included studies.

Author	Study design	Type of exercise and PA	Main result	Conclusion
Nishimura et. al (2022)	Prospective observational study	Half marathon wheelchair race and physical training before the race	Pre-race: No significant difference in BDNF level between the LSCI and CSCI After the race (1 hour): A significant difference between CSCI (P = 0.0055) and LSCI (P = 0.0312) After the injury: Returned to the baseline level (1 hour)	BDNF in LSCI and CSCI was increased immediately after the race
Goldhardt et al. (2019)	Cross-sectional (crossover design)	A single session of gait training with a treadmill and seven days later with a walker	No significant differences during pre- to post-intervention for TS and WS (p>0.05): TS, Pre: 434.02 (184.02) pg/mL Post: 341.31 (152.35) pg/mL WS, Pre: 261.22 (182.21) pg/mL Post: 277.96 (130.05) pg/mL	A single bout of gait training with a BWS treadmill or walker without BWS is not able to alter BDNF levels.
Leech and Hornby (2017)		Graded-intensity body weight supported treadmill	The BDNF was nearly increased with HIE (p = 0.05) whereas no significant increase in the low intensity of the exercise group (p = 0.56).	Serum BDNF concentrations were modulated by the exercise intensities
Zeller et al (2015)	A prospective cohort	Warm-up (10 min): Continuous pushing, 20-meter submaximal sprints (8 times), agility drills. UL stretching The main training (45 min): Ball handling, passing drills, scrimmage activity, tactical practice, game simulation Cool down: Moderate continuous pushing	No significant differences in BDNF concentration level during (p >0.05): At rest: 33.2 (21.6) $ngml^{-1}$ After warming up: 31.9 (18.9) $ngml^{-1}$ After training: 29.9 (11) $ngml^{-1}$	A typical wheelchair rugby training session does not affect basal serum BDNF concentration in elite SCI athletes
Harness et al (2014)		30 minutes of LB, BWSTT, WBV	No effect of exercise on BDNF, (p >0.05): F(4, 52) = 0.14, P = 0.97, with baseline levels of BDNF at 2.37 (1.41) $ngml^{-1}$	Acute changes in BDNF were not observed.
Vega et. al (2008)		Hand bike incremental exercise test until exhaustion (increased to 20 W every 5 minutes for 60 r.p.m	BDNF increase after 10 minutes of exercise at approximately 1.5-fold from basal level (P<0.05).	short moderate intensity hand biking increases the BDNF level immediately but in long-term effects.

**CSCI: Cervical Spinal Cord Injury, LSCI: Lumbar Spinal Cord Injury, HIE: High Intensities Exercises, OM: Outcome Measure, BWS: Body Weight Supported, BWSTT: Body Weight Supported Treadmill Training, TS: Treadmill Session, WS: Walker Session, WBV: Whole Body Vibration, FES: Functional Electrical Stimulation (FES), LB: Load Bearing, UL: Upper limb, ELISA: Enzyme-linked immunosorbent assay, W: Watts, pg/ml: Picogram/Mililiter, $ngml^{-1}$: Nanogram per Milliliter. This table shows the search strategies in health-related databases for literature searching.

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