

Research Gaps in the Relationship Between Serum Brain-derived Neurotrophic Factor (BDNF) and Trunk Control After Stroke: A Scoping Review of the Last Decade (2014–2024)

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ABSTRACT

Brain-derived neurotrophic factor (BDNF) plays a crucial role in neuroprotection and neuroplasticity, positioning it as a key target for enhancing rehabilitation outcomes in stroke survivors. This scoping review aimed to explore the relevance of serum BDNF levels in improving trunk control and balance performance among this population. Using the PICO framework, the review focused on stroke patients (Population), undergoing rehabilitation (Intervention), compared to healthy individuals (Comparison), with outcomes including trunk control, balance, and serum BDNF levels (Outcome). A systematic search was conducted across five major databases: MEDLINE, PsycINFO, Embase, CINAHL Plus, and Cochrane Central, targeting full-text English studies published between 2014 and 2024. Studies meeting the inclusion criteria were analysed to identify patterns and research gaps. Five studies met the inclusion criteria. The findings suggest that serum BDNF levels increase following rehabilitation interventions and correlate with the duration of mobilisation. However, none of the included studies directly assessed trunk control, highlighting significant research gaps in understanding the direct impact of BDNF on trunk recovery after stroke. Further research is needed to elucidate how BDNF may facilitate trunk recovery, enhance early ambulation, and improve functional outcomes in individuals with stroke. This review highlights the absence of direct evidence linking serum BDNF to trunk-specific recovery and emphasises the need for targeted research in this area. Most research focuses on gait and balance, which serve as surrogate measures for trunk control, and emphasises spasticity in the extremities. Addressing these gaps through targeted research could optimize rehabilitation strategies and improve outcomes for stroke survivors.

Keywords

cerebrovascular accident, neurorehabilitation, neurotrophins, synaptic plasticity, stroke survivors

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INTRODUCTION

Brain plasticity is a key area in neurorehabilitation, particularly in stroke recovery.¹⁻³ Research has highlighted the significance of neurotrophins in stroke

recovery, identifying them as valuable prognostic biomarkers. Among these, brain-derived neurotrophic factor (BDNF) stands out for its essential role in supporting neural plasticity and its frequent use as a

prognostic indicator in post-stroke rehabilitation. BDNF is widely distributed throughout the healthy human brain, where it induces anti-apoptotic mechanisms and reduces lesion size, promoting neuronal survival.⁴ Additionally, BDNF supports neuronal differentiation and maturation,^{4,6} essential for maintaining neural health and function.

Following brain injury, BDNF is pivotal in promoting neuronal growth and healing. It facilitates the formation of new neuronal connections, strengthens protective mechanisms in nerve cells, and enhances overall neuronal health and vitality.⁷ Rising BDNF levels in the cortex have been linked to the brain's ability to reorganize itself, creating new connections through synaptogenesis, strengthening dendritic structures, and ramification. These adaptations are essential for motor learning and recovery after a stroke.^{6,8,9} Moreover, BDNF has been shown to reduce the degree of cerebral infarction and aid the natural salvage of damaged nerve cells.¹⁰

Stroke patients typically present with multiple motor impairments, including deficits in the trunk, upper, and lower limbs, which significantly hinder their ability to perform activities of daily living. Poor trunk control is a major concern, as it affects patients' ability to shift weight appropriately due to trunk muscle weakness and reduced proprioception on the paretic side.¹¹⁻¹⁴ This impairment in trunk control can lead to balance disorders, gait abnormalities, limited stability in both sitting and standing positions, and dysfunctions in speech and respiratory functions.^{15,16} Effective trunk control is therefore crucial for overall functional recovery, particularly in the early phase of stroke rehabilitation.^{14,17}

Despite the recognised role of BDNF in stroke recovery, most literature has concentrated on upper limb motor function, with comparatively few studies addressing lower limb or trunk control. The impact of stroke on BDNF production and its relevance to trunk-specific

recovery and balance remain underexplored, and to our knowledge, no published study to date has directly

evaluated trunk-specific outcomes in relation to serum BDNF following rehabilitation. Existing studies have primarily assessed balance and overall functional performance, which may only indirectly reflect trunk stability, leaving their relationship with serum BDNF uncertain. This scoping review maps the available literature from the past decade (2014–2024) to define the extent and nature of current evidence, identifies significant research gaps in the literature, and highlights research priorities to inform more targeted, evidence-based rehabilitation strategies.

MATERIALS AND METHODS

Protocol and registration

The review protocol was developed based on the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) guidelines.¹⁸⁻²⁰ The protocol was not registered but adhered to the principles of transparency and reproducibility in the scoping review methodology.

Eligibility criteria

Studies were selected based on predefined eligibility criteria using a PICO (Population, Intervention, Comparison, and Outcome) model framework. The population of interest included human participants diagnosed with stroke in acute, sub-acute, or chronic phases. Interventions considered were rehabilitation programs focusing on task-specific training and neuroplasticity-based therapies. Comparisons included studies contrasting stroke patients with healthy individuals or those receiving alternative or standard care. The outcomes of interest were trunk control, balance, and serum BDNF levels. Eligible study designs included randomized controlled trials, cohort studies, cross-sectional studies, and case-control studies. Only articles published in English were included. Studies were excluded if they were investigating induced stroke in animals, focused on infantile or paediatric stroke, or

other neurodegenerative diseases, or were non-original articles such as reviews or conference abstracts.

Information sources

The literature search used five major electronic databases: MEDLINE, PsycINFO, Embase, CINAHL Plus, and Cochrane Central. Additional references were identified through manual searches of reference lists from included studies.

Search strategies

The search strategy was developed collaboratively with the study authors to ensure relevance and comprehensiveness. Keywords and Medical Subject Headings (MeSH) terms were tailored to each database and combined using Boolean operators (AND, OR). The search terms included: "stroke," "trunk control," "balance," "neurotrophins," "brain-derived neurotrophic factor (BDNF)," and "rehabilitation." The complete search strategy is detailed in Table I. The search was limited to studies published between 2014 and 2024 based on three key scientific developments that established modern standards in stroke rehabilitation research: (1) standardization of BDNF measurement protocols,²¹⁻²³ (2) widespread PRISMA guideline adoption,^{20,24,25} and (3) validation of trunk-specific assessment tools.²⁶⁻²⁹ It captures the period when neurorehabilitation research achieved sufficient methodological consistency for reliable evidence synthesis, while excluding earlier studies that used heterogeneous assays or lacked consensus on outcome measures. The selected timeframe ensures our review reflects current clinical practices and technological advances without compromising comprehensiveness, particularly for studies examining BDNF's role in post-stroke recovery.

Selection of sources of evidence

Three reviewers (AMU, AAA, and MAS) independently screened the titles and abstracts retrieved from the searches. Full-text articles were assessed for eligibility, and disagreements were resolved through discussion

with a fourth reviewer (NBR). The selection process was systematically documented using a PRISMA-ScR flow diagram.

Data extraction and synthesis of results

Data from the included studies were extracted using a predefined charting form in Microsoft Excel. The form

Table I: Search strategy for BDNF, trunk control, and balance in stroke care

Query	Search
Medline via Ovid	1: stroke/ 2: stroke.ab,kw,ti. 3: Sub-acute stroke.ab,kw,ti. 4: acute stroke.ab,kw,ti. 5: chronic stroke.ab,kw,ti. 6: cerebrovascular accident.ab,kw,ti. 7: cerebrovascular diseases/ 8: cerebrovascular diseases.ab,kw,ti. 9: cerebrovascular attack.ab,kw,ti. 10: 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 11: Trunk control.ab,kw,ti. 12: balance.ab,kw,ti. 13: 11 OR 12 14: Brain derived neurotrophic factor/ 15: Brain derived neurotrophic factor.ab,kw,ti. 16: BDNF.ab,kw,ti. 17: Neurotrophin.ab,kw,ti. 18: peripheral BDNF.ab,kw,ti. 19: 14 OR 15 OR 16 OR 17 OR 18 20: 10 AND 13 AND 20
PsycINFO via Ovid	1: stroke.ab,ti. 2: sub-acute stroke.ab,ti. 3: acute stroke.ab,ti. 4: chronic stroke.ab,ti. 5: cerebrovascular diseases.ab,ti. 6: cerebrovascular accident/ 7: cerebrovascular accident.ab,ti. 8: cerebrovascular attack.ab,ti. 9: 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 10: Trunk control.ab,ti. 11: balance.ab,ti. 12: 10 OR 11 13: Brain derived neurotrophic factor / 14: Brain derived neurotrophic factor.ab,ti. 15: BDNF.ab,ti. 16: Neurotrophin.ab,ti. 17: peripheral BDNF.ab,ti. 19: 13 OR 14 OR 15 OR 16 OR 17 OR 18 20: 9 AND 12 AND 19
Embase via Ovid	1: stroke.ab,kw,ti. 2: sub-acute stroke.ab,kw,ti. 3: acute stroke.ab,kw,ti. 4: chronic stroke.ab,kw,ti. 5: cerebrovascular diseases/ 6: cerebrovascular diseases.ab,kw,ti. 7: cerebrovascular accident/ 8: cerebrovascular accident.ab,kw,ti. 9: cerebrovascular attack.ab,kw,ti. 10: 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 11: Trunk control.ab,kw,ti. 12: balance.ab,kw,ti. 13: 11 OR 12 14: Brain derived neurotrophic factor / 15: Brain derived neurotrophic factor.ab,kw,ti. 16: BDNF.ab,kw,ti. 17: Neurotrophin/ 18: Neurotrophin.ab,kw,ti. 19: peripheral BDNF. ab,kw,ti. 20: 14 OR 15 OR 16 OR 17 OR 18 OR 19 21: 10 AND 13 AND 20
CINAHL Plus	S1: (MH "stroke") S2: TI "stroke" OR AB "stroke" S3: TI "sub-acute stroke" OR AB "sub-acute stroke" S4: TI "acute stroke" OR AB "acute stroke" S5: TI "chronic stroke" OR AB "chronic stroke"

S6: TI "cerebrovascular disease" OR AB "cerebrovascular disease"
 S7: TI "cerebrovascular accident" OR AB "cerebrovascular accident"
 S8: TI "cerebrovascular attack" OR AB "cerebrovascular attack"
 S9: S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
 S10: (MH "balance")
 S11: TI "balance" OR AB "balance"
 S12: TI "trunk control" OR AB "trunk control"
 S13: S10 OR S11 OR S12
 S14: (MH "Brain derived neurotrophic factor")
 S15: TI "Brain derived neurotrophic factor" OR AB "Brain derived neurotrophic factor"
 S16: TI "BDNF" OR AB "BDNF"
 S17: TI "Neurotrophin" OR AB "Neurotrophin"
 S18: TI "peripheral BDNF" OR AB "peripheral BDNF"
 S20: S14 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19
 S21: S9 AND S13 AND S20
 1: stroke.sh.
 2: stroke.ab,kw,ti.
 3: sub-acute stroke.ab,kw,ti.
 4: acute stroke.ab,kw,ti.
 5: chronic stroke.ab,kw,ti.
 6: cerebrovascular accident.ab,kw,ti.
 7: cerebrovascular disease.ab,kw,ti.
 8: cerebrovascular attack.ab,kw,ti.
 9: 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8
 10: Trunk control.ab,kw,ti.
 11: balance.ab,kw,ti.
 12: 10 OR 11
 13: Brain derived neurotrophic factor.sh.
 14: Brain derived neurotrophic factor.ab,kw,ti.
 15: BDNF.ab,kw,ti.
 16: Neurotrophin.ab,kw,ti.
 17: peripheral BDNF.ab,kw,ti.
 19: 13 OR 14 OR 15 OR 16 OR 17 OR 18
 20: 9 AND 12 AND 19

Cochrane Central

captured the author(s) and year of publication, sample characteristics, inclusion and exclusion criteria, intervention specifics (type, duration, and intensity), outcome measures, results, and conclusions. The three independent reviewers piloted the charting process on a subset of studies to ensure consistency.

The results of the included studies were synthesized narratively, focusing on the interventions and their outcomes. Data were organized thematically and presented in an evidence table to enhance clarity and accessibility.

RESULTS

Study selection

The flow of studies through the selection process is illustrated in Figure 1. A total of 163 articles were identified through database searches and manual reference checks. After removing 39 duplicates, 124 articles were screened for relevance based on titles and abstracts. Most of the studies screened, primarily

conducted by physiotherapists, were considered unrelated to the particular emphasis of this review concerning the function of serum BDNF in enhancing trunk control in stroke patients following rehabilitation. Subsequently, eight full-text articles were assessed for eligibility, with three excluded due to not meeting the inclusion criteria. After a thorough evaluation, only five studies were included in the review, as detailed in Table I.

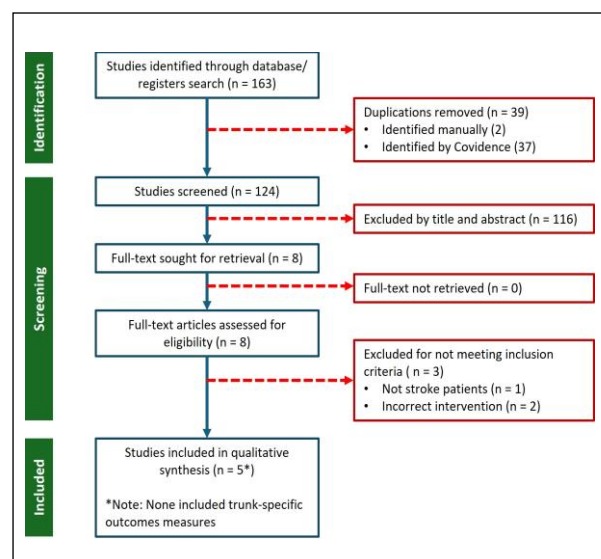


Figure 1: PRISMA-ScR flow chart of the study

Table II: Evidence table of included studies

First author	Sample	Inclusion criteria	Interventions	Outcomes	Results*	Conclusion
Rahayu et al. ³⁰	40 patients recruited based on specific inclusion criteria, randomly divided into two groups: (1) treatment group (n=20) receiving early mobilisation (EM) at 24 hours and (2) control group (n=20) receiving EM at 48 hours post-ischemic stroke diagnosis via CT scan.	1. Ischemic stroke diagnosis with motor control reduction. 2. Sensory and proprioceptive deficits with a muscle strength score of at least 2+. 3. First-stage stroke confirmed unilateral hemiparesis without neurological deterioration. 4. No aphasia or severe cognitive impairment (MMSE >19)	Mobilization lasted 30-60 minutes, focusing on exercise progression from cognitive to associative stages; the control group did not have graded exercises.	No specific trunk control outcome measured via the Berg Balance Scale. Functional ability via the Barthel Index on days 5 and 7.	Significant differences were noted on day 7 for both balance (p=0.038) and functional ability (p=0.021); on day 5, only functional ability showed a significant difference (p=0.002), with no significant difference in balance (p=0.147).	Early mobilisation at 24 hours post-ischemic stroke showed better outcomes in balance and functional ability compared to 48 hours.

Cont.						
Rahayu et al. ³¹	69 participants were recruited, with 64 completing the study.	Patients diagnosed with ischemic stroke 24 hours post-attack without neurological deterioration, experiencing decreased motor control, sensory and proprioceptive deficits, muscle strength of at least 2+ by manual testing, no aphasia, and agreed to participate	Neurorestoration intervention involved three stages: cognitive, associative, and automation, with intensity varying by participant performance. Standard protocols, tailored daily to patients' needs, included: Bobath PNF Rood approach Carr & Shepherd model CIMT.	No specific trunk control outcome measured BI evaluated ADL, Berg Balance Scale test BDNF analysis	Both groups showed improvements in all areas, but only balance and functional performance had statistically significant outcomes.	The neurorestoration protocol, combining various physiotherapy interventions, effectively improved balance and functional ability in stroke patients within seven days.
He et al. ³²	200 post-stroke hemiplegic patients were admitted from March 2022 to February 2023, evenly and randomly divided into control (C) and observation (O) groups.	Adherence to diagnostic criteria of the Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke via CT or MR imaging. First onset. Unilateral limb dysfunction post-onset. No progression in mild or moderate cases within 24 hours, stable vital signs, and no worsening neurological function in severe cases. Normal swallowing function.	MDT writing collaboration group established and provided functional rehabilitation training, psychological counselling, and nutritional support for the observation group, while the control group followed a routine rehabilitation protocol. Functional limb exercises were conducted daily in two groups with 10 repetitions each and a rest period of 1 minute, over a 4-week intervention.	No specific trunk control outcome measured Neurotrophin levels (NGF, BDNF, IGF-1). Nutritional status. Neurological impairment assessed via NIHSS. Quality of life via SS-QOL. The Fugl-Meyer (FM) scale used for motor function assessment (upper and lower limbs). BDNF analysis	No statistically significant differences ($p>0.05$) in NGF, BDNF, IGF-1, haemoglobin (HGB), albumin (ALB), transferrin (TRF), limb motor function, balance, neurological deficits, or quality of life scores between groups; however, post-intervention, NGF, BDNF, IGF-1, HGB, ALB, and TRF levels in the observation group were significantly higher ($p<0.05$). BDNF levels increased significantly during AR rehabilitation; treated patients showed similar patterns in BDNF levels, whereas untreated patients had lower levels at the endpoint.	MDT collaboration significantly enhances neurotrophin levels, mitigates nerve defects, and fosters recovery in limb function, balance, and quality of life for stroke patients with hemiplegia.
Koroleva et al. ³³	50 patients after acute recovery from ischemic stroke: 21 received classical rehabilitation on followed by motor rehabilitation on with motion sensors and augmented reality (AR), 14 only received AR rehabilitation on, and 15 were observed	Ages between 18 and 80 years. Mild-to-moderate upper limb hemiparesis (NIHSS <12 , mRS score <4 , MAS score ≤ 2). Absence of cognitive impairment (MMSE ≥ 22) or behavioural dysfunction	Classical rehabilitation and motor rehabilitation using motion sensors and augmented reality (AR) rehabilitation	No specific trunk control outcome measured Motor impairment quantified via Fugl-Meyer (FM) scale Functional disability and (ADL) measured with mRS. BDNF analysis	BDNF levels increased significantly during AR rehabilitation; treated patients showed similar patterns in BDNF levels, whereas untreated patients had lower levels at the endpoint.	BDNF changes do not consistently correlate with motor improvement but respond to active treatment.
Astuti et al. ³⁴	87 patients with suspected acute ischemic stroke were recruited on admission; 68 completed the study, categorised into dependent ($n=22$) and independent ($n=46$) groups based on BI scores on day 30 post-stroke.	First-time acute ischemic stroke. Ability to participate until the following month. Cooperative. No history of other CNS damage (tumour, trauma, encephalitis). Parkinson's disease, previous stroke, or previous physical disability.	Routine physiotherapy intervention	No specific trunk control outcome measured BI used for functional assessment BDNF analysis	Mean serum BDNF level in the acute phase was significantly higher in the independent group (27,152.28 vs 23,143.41; $p=0.044$), consistent in chronic phase measurements (27,526.48 vs 22,818.91; $p=0.036$).	Serum BDNF levels in both acute and chronic phases potentially predict functional outcomes in patients with acute ischemic stroke.

*Findings are reported as described by the authors of the individual studies.

ADL: activities of daily living; BDNF: brain-derived neurotrophic factors; BI: Barthel Index; CIMT: Constraint-Induced Movement Therapy; CNS: central nervous system; CT: computed tomography; IGF: insulin-like growth factor; MAS: Modified Ashworth Scale; MDT: multidisciplinary team; MMSE: Mini-Mental State Examination; MR: magnetic resonance; mRS: Modified Rankin Scale; NGF: nerve growth factor; NIHSS: National Institutes of Health Stroke Scale; PNF: proprioceptive neuromuscular facilitation; SS-QOL: Specialized Stroke Quality of Life Scale.

Characteristics of included studies

All five studies focused on stroke rehabilitation and examined the effects of various interventions. The study designs included randomised controlled trials and cohort studies, reflecting a robust methodological approach. Sample sizes varied between 40 and 200 participants, with diverse demographic characteristics. The interventions differed across studies, with strategies such as early mobilisation, neurorestorative protocols, and augmented reality-based rehabilitation being implemented. Commonly reported outcome measures included serum BDNF levels, balance metrics (e.g., Berg Balance Scale), and functional assessments (e.g., Barthel Index), underscoring a consistent focus on evaluating functional recovery and biomarker relevance in stroke rehabilitation.

Population sample and inclusion criteria

The population in this review consisted of adult ischemic stroke patients who had experienced their first stroke, characterised by an acute onset affecting one hemisphere. Eligibility criteria across the studies required participants to have mild complications, a muscle strength score of at least 2+, and the ability to ambulate without severe cognitive impairment.³⁰⁻³² Most studies included had sample sizes greater than 30 participants, which is often considered a minimum

threshold for achieving adequate statistical power in clinical research. However, the actual power of each study depends on factors such as effect size and data variability, highlighting the importance of context in interpreting results. One study reported the largest cohort, with 200 participants randomised into experimental and control groups.³² Despite the relatively rigorous inclusion criteria, a notable limitation was the lack of direct assessments targeting trunk impairments after stroke, which highlights a significant research gap. These limitations, coupled with small sample sizes in certain studies,^{30,33} emphasise the need for further exploration in this domain.

Rehabilitation interventions and trunk stabilisation

The reviewed studies collectively highlighted the significance of rehabilitation interventions in enhancing functional recovery in stroke patients, although none explicitly focused on trunk muscle control. Mobilisation exercises, implemented in both early and late phases, emerged as a crucial component of stroke rehabilitation. Most interventions were administered for a duration of 30 minutes to one hour per day, three to five days a week, over four weeks. One study emphasised the role of early mobilisation in improving overall balance, indirectly benefiting trunk stabilisation.³⁰ These findings align with another study that demonstrated the efficacy of neurorestorative interventions in enhancing balance and functional impairments.³¹

Another study further highlighted the positive effects of augmented reality-based rehabilitation on motor impairments and neurotrophic factor levels, pointing to its potential for promoting trunk-related recovery.³³ Despite these promising results, most studies did not specifically address trunk muscle stabilisation or establish a direct correlation between serum BDNF levels and balance performance. This gap highlights the need for future research to elucidate the mechanisms through which rehabilitation interventions influence trunk-specific recovery outcomes. These findings collectively emphasise the importance of tailored

rehabilitation strategies to optimise functional outcomes in stroke survivors.

Balance and trunk stability outcomes

The included studies consistently demonstrated improvements in balance, overall functional ability, and quality of life following rehabilitation interventions,^{31,33,34} even though trunk muscle control was not explicitly assessed. Some studies highlighted the effectiveness of early mobilisation and neurorestorative protocols in improving balance metrics within seven days, emphasising their potential indirect benefits for trunk stabilisation.^{30,31} Similarly, augmented reality-based rehabilitation was associated with enhanced balance and motor function compared to standard rehabilitation approaches.³³ These findings illustrate the role of innovative rehabilitation strategies in achieving better balance outcomes in stroke survivors. However, while the studies collectively underscore the significance of balance function following a stroke, the absence of direct assessments of trunk control creates a gap in our understanding of how serum BDNF levels and trunk control rehabilitation influence trunk-related recovery.

While these studies collectively demonstrated the importance of balance improvements, they lacked direct assessments of trunk muscle stabilisation, leaving a gap in understanding the specific mechanisms linking rehabilitation to trunk-related recovery. This highlights the need for future research targeting trunk-specific interventions and their effects on balance and functional outcomes.

Serum BDNF levels

Rehabilitation interventions were consistently associated with increased serum BDNF levels across the included studies. One study observed significant elevations in serum BDNF and other neurotrophic factors following multidisciplinary team-based interventions.³² Similarly, another study found a positive relationship between early mobilisation and serum BDNF levels in acute ischemic stroke patients.³⁰ Higher serum BDNF levels

in both acute and chronic phases were also correlated with better functional independence, further supporting the role of neurotrophic factors in post-stroke recovery.³⁴

However, one study noted variability in the relationship between serum BDNF levels and motor improvements, suggesting that additional factors may influence these outcomes.³³ Despite these variations, the findings highlight the potential of serum BDNF as a biomarker for recovery, particularly in enhancing balance and motor function. However, the impact of BDNF on trunk control following a stroke remains uncertain, as none of the studies included in the review directly assessed trunk control.

DISCUSSION

This scoping review reveals a critical gap in the literature: despite extensive research on BDNF's role in stroke recovery, no studies have directly investigated its relationship with trunk-specific rehabilitation outcomes. While included studies examined balance and functional measures, often used as proxies for trunk control, none employed validated trunk assessment tools, highlighting a significant research need.

The restorative processes of neural repair after stroke or brain injury, such as neurogenesis, gliogenesis, and axonal sprouting, are critical for balance and functional recovery. Neurotrophic factors such as BDNF, nerve growth factor (NGF), neurotrophin-3 (NT-3), and neurotrophin-4/5 (NT-4/5) are a group of secreted proteins that play pivotal roles in the development, growth, survival, and differentiation of the nervous system.³⁵ As the most abundant neurotrophin in the nervous system,³⁶ BDNF has been identified as a key marker in these processes.^{2,8,14} It facilitates the generation of epigenetic mechanisms by signalling through excitatory neurotransmitters like glutamate and its inhibitory counterpart, gamma-aminobutyric acid (GABA). These epigenetic changes alter BDNF activity, promoting positive stroke outcomes.⁸ Studies

have identified that BDNF release is activity-dependent. Research has shown significantly lower BDNF concentrations in acute stroke patients, attributing this reduction to altered neuronal excitability and downstream signalling in excitatory neurotransmitters.^{8,37}

Several neuroplasticity techniques were conducted to stimulate the release of BDNF post-neurological deficit, including stroke. Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) are non-invasive techniques that are widely used to enhance BDNF release.³⁸ tDCS is a widely used technique compared to rTMS as it has lower cost, portability, and ease of use. tDCS protocols typically target lesional (anodal) and contralesional (cathodal) motor cortex to promote perilesional recovery while reducing transcallosal inhibition.³⁸ Epidural cortical stimulation (ECS) is another invasive technique with a potential effect on cortical excitability and BDNF release.³⁸ Additionally, various neuroplasticity physical interventions, including aerobic training, task-specific exercises, and proprioceptive neuromuscular facilitation, have been proven to effectively elevate BDNF levels after stroke.³⁹

BDNF levels have been found to correlate with infarct volume. Larger infarct volumes have been associated with lower acute-phase BDNF levels.^{5,40-43} This relationship suggests BDNF's potential as a biomarker for stroke severity.⁴⁴ Spontaneous motor recovery often occurs after ischemic events, with significant progress seen in the first 30 days, continuing over the next 30 to 90 days.³³ BDNF plays a crucial role in this early motor recovery by resolving acute metabolic depression, enabling other muscle groups to execute motor tasks, and facilitating local and distant rewiring of the central nervous system.⁴³⁻⁴⁵ Additionally, BDNF helps adapt the activity of intracortical and corticofugal excitatory pathways necessary for motor task execution, regulating long-term potentiation (LTP) at glutamatergic synapses.^{46,47}

Our review highlights the established role of BDNF in neurorehabilitation, while also revealing a critical gap: the scarcity of studies examining its direct impact on trunk control following stroke. Although the reviewed studies consistently demonstrated improvements in balance and functional independence following targeted rehabilitation interventions, the role of BDNF in trunk control recovery remains largely speculative. Improvements in balance and gait parameters, often used as surrogate measures for trunk stability, may suggest the importance of neuroplasticity interventions and BDNF-driven neuroplasticity;^{31,33} however, this connection remains unproven and requires direct validation. Additionally, the variability in neurotrophic responses indicates that factors such as intervention type, timing, and intensity could influence outcomes.³³ Another limitation of the reviewed studies is their focus on relatively stable and functionally capable patients, which restricts findings to those with moderate stroke impairments.

This gap in the literature highlights a critical area for future research, emphasising the need for targeted investigations exploring the direct relationship between serum BDNF and direct trunk control recovery outcomes. While BDNF is widely recognised for its role in neuroplasticity and motor recovery, its potential to facilitate early ambulation and enhance trunk recovery in stroke patients warrants further exploration.³ Integrating serum BDNF as a biomarker could aid in developing personalised rehabilitation strategies for stroke survivors. Additionally, other neurotrophic biomarkers, such as nerve growth factor (NGF) and insulin-like growth factor-1 (IGF-1), have shown associations with post-stroke recovery and may complement BDNF in a multimodal biomarker approach.³² Future studies could incorporate these biomarkers alongside trunk-specific assessments to better characterise neuroplastic potential.

LIMITATIONS

This review has several limitations that should be considered. First, the scarcity of studies directly investigating BDNF's role in post-stroke trunk control

restricts the generalisability of our findings. The available evidence is further limited by geographic underrepresentation, highlighting the need for more diverse, globally inclusive research. Second, our search strategy, which focused on major electronic national library databases, may have missed relevant studies in grey literature or less accessible sources, potentially omitting valuable insights. Additionally, this review specifically examined trunk control and excluded studies on BDNF's effects in upper or lower limb rehabilitation, which may have provided indirect evidence relevant to trunk recovery. Finally, newly published studies after our search cutoff were not included, possibly overlooking recent advancements in this field.

Implications for future work

Future research should prioritise direct investigations into the relationship between serum BDNF levels and trunk-specific recovery following stroke. Studies should integrate direct trunk control assessments such as the Trunk Impairment Scale, while simultaneously measuring BDNF concentrations to establish potential correlations. Standardised protocols are needed to examine how neurotrophic factors, including BDNF, NGF, and IGF-1, collectively influence trunk control mechanisms during rehabilitation. Future trials should also expand participant selection to include individuals with severe stroke impairments and complex comorbidities, as current evidence remains limited to moderately affected populations. Additionally, multicentre collaborations across diverse geographic regions would enhance the generalisability of findings and address current disparities in representation. Such studies should also explore the optimal timing, duration, and intensity of BDNF-modulating interventions, including both neuromodulation techniques and physical therapies, to maximize functional recovery. By addressing these gaps, researchers can better elucidate BDNF's potential as both a biomarker and therapeutic target, thus informing more personalised and effective rehabilitation strategies for stroke survivors with trunk control deficits.

CONCLUSION

The reviewed studies collectively highlight the relevance of serum BDNF in improving balance and functional outcomes after stroke. However, the lack of direct trunk control measures represents a significant gap. This review reveals the lack of available studies investigating the influence of serum BDNF levels on trunk control after stroke. Clinicians and researchers should prioritise exploring these areas to develop more effective interventions and enhance the quality of life for individuals recovering from stroke.

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