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ORIGINAL ARTICLE

BDNF and its role in post-stroke brain recovery: Interventions to Boost BDNF

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Abstract

Brain-derived neurotrophic factor (BDNF) is a key neurotrophin involved in neuronal survival, synaptic plasticity, and neuroregeneration. After ischemic stroke, BDNF plays a crucial role in brain repair processes, including neurogenesis, angiogenesis, and functional recovery of damaged neural circuits. This study reviews the biological functions of BDNF in post-stroke recovery and evaluates interventions aimed at increasing its expression, such as physical exercise, pharmacological agents, nutritional strategies, and neurorehabilitation techniques. Evidence suggests that enhancing BDNF levels significantly improves motor and cognitive recovery outcomes in stroke patients, highlighting its therapeutic potential in neurorehabilitation. Brain-derived neurotrophic factor is a critical regulator of neuronal survival, synaptic plasticity, and adaptive neuroreorganization in the central nervous system. After ischemic stroke, reduced expression of this neurotrophin limits endogenous repair mechanisms, contributing to persistent neurological deficits. This expanded analysis evaluates the role of BDNF in post-stroke recovery and examines various interventions designed to enhance its expression. These include structured physical activity, pharmacological modulation, dietary optimization, and multidisciplinary rehabilitation programs. Evidence indicates that upregulation of BDNF is closely associated with improved motor performance, cognitive recovery, and enhanced neuroplasticity, making it a key therapeutic target in stroke rehabilitation.

Keywords: BDNF, stroke recovery, neuroplasticity, neurorehabilitation, brain repair, ischemic stroke, neurotrophins, exercise therapy, neurogenesis, synaptic plasticity.

1. Introduction

Stroke is one of the leading causes of long-term disability worldwide, resulting from interrupted cerebral blood flow and subsequent neuronal damage. Recovery after stroke depends largely on the brain's ability to reorganize and form new neural connections, a process known as neuroplasticity. Brain-derived neurotrophic factor is a critical molecule that regulates neuronal survival, growth, and synaptic remodeling. It is widely expressed in the central nervous system and is particularly important in regions involved in learning and memory, such as the hippocampus and cerebral cortex. After stroke, endogenous BDNF levels are often reduced, limiting the brain's natural repair mechanisms. Understanding how BDNF functions and how it can be therapeutically enhanced is essential for improving post-stroke outcomes. Stroke remains one of the leading causes of disability worldwide,

resulting from acute interruption of cerebral blood flow and subsequent neuronal injury. Recovery from stroke is largely dependent on the brain's ability to reorganize neural networks and compensate for damaged regions, a process known as neuroplasticity. Brain-derived neurotrophic factor is a central molecule in this process, regulating neuronal growth, differentiation, and synaptic connectivity. It is highly expressed in brain regions involved in learning, memory, and motor control. Following ischemic injury, endogenous BDNF levels decline, impairing the brain's regenerative capacity. Enhancing BDNF expression has therefore become a major focus in neurorehabilitation research aimed at improving functional outcomes after stroke. Stroke is one of the leading causes of disability and mortality worldwide, resulting in significant neurological, cognitive, and functional impairments. It occurs due to an acute disruption of cerebral blood flow, either from ischemic occlusion or hemorrhagic rupture, leading to neuronal injury and cell death in affected brain regions. Although acute medical management has improved survival rates, long-term recovery remains a major clinical challenge. The extent of functional restoration after stroke depends not only on the size and location of the lesion but also on the brain's intrinsic capacity for neuroplasticity and repair.

Brain-derived neurotrophic factor (BDNF) is a key neurotrophin that plays a central role in neuronal survival, differentiation, synaptic plasticity, and neurogenesis. It is widely expressed in the central nervous system, particularly in the hippocampus, cerebral cortex, and basal forebrain. BDNF exerts its biological effects primarily through activation of the TrkB (tropomyosin receptor kinase B) signaling pathway, which promotes neuronal growth, synaptic strengthening, and adaptive remodeling of neural networks. These processes are essential for learning, memory formation, and recovery of lost neurological functions following brain injury.

In the context of stroke, BDNF is considered a critical mediator of post-injury brain repair. After cerebral ischemia, endogenous BDNF levels may fluctuate depending on the severity of injury and the stage of recovery. In general, increased BDNF expression is associated with enhanced neuroplasticity, reduced neuronal apoptosis, and improved functional outcomes. Conversely, reduced BDNF activity may limit the brain's ability to reorganize and recover, contributing to persistent neurological deficits. Post-stroke brain recovery involves a complex interplay of mechanisms, including neurogenesis, angiogenesis, synaptic remodeling, and functional reorganization of neural circuits. BDNF is deeply involved in all these processes, making it a key target for therapeutic intervention. Experimental and clinical studies have demonstrated that higher BDNF levels are associated with better motor recovery, improved cognitive performance, and enhanced rehabilitation outcomes in stroke patients.

Various interventions have been explored to enhance BDNF expression as a strategy to promote brain recovery after stroke. Physical exercise, particularly aerobic and task-specific training, is one of the most effective non-pharmacological methods for increasing BDNF levels. Rehabilitation therapies that involve repetitive motor activity and sensory stimulation also contribute to neuroplastic changes mediated by BDNF signaling. In addition, certain pharmacological agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs), have been shown to upregulate BDNF expression and support neurorecovery. Nutritional factors, including omega-3 fatty acids, flavonoids, and antioxidant-rich diets, may also positively influence BDNF levels.

Emerging therapeutic approaches, such as stem cell therapy, gene therapy, and neurotrophic factor-based treatments, are being investigated for their potential to directly modulate BDNF signaling pathways. These strategies aim to enhance endogenous repair mechanisms and improve functional outcomes in stroke survivors. However, challenges remain in translating these findings into routine clinical practice, including variability in patient response, optimal timing of intervention, and long-term safety considerations.

In conclusion, BDNF plays a fundamental role in post-stroke brain recovery by supporting neuroplasticity, neuronal survival, and functional reorganization. Interventions aimed at boosting BDNF levels represent a promising therapeutic avenue for enhancing rehabilitation outcomes and improving quality of life in stroke patients. Continued research is essential to fully understand the mechanisms of BDNF regulation and to develop effective strategies for its clinical application in neurorehabilitation.

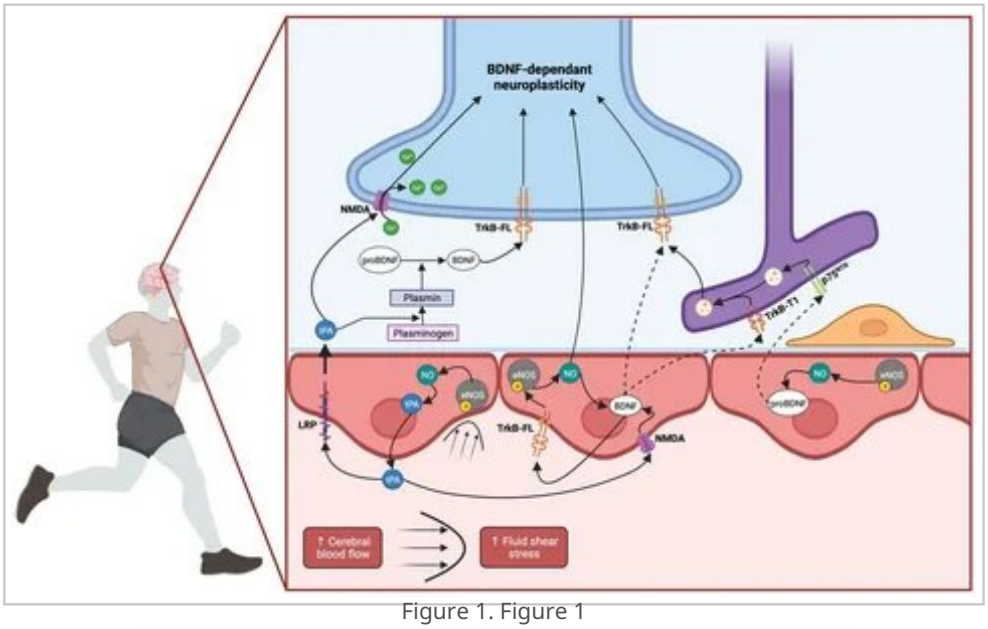

Figure 1. Figure 1

2. Materials and Methods

This study is based on a comprehensive review of experimental research, clinical trials, and neurorehabilitation studies investigating BDNF in post-stroke recovery. Data were collected from animal models of ischemic stroke as well as human clinical populations undergoing rehabilitation. Variables analyzed included serum and brain tissue BDNF levels, motor function scores, cognitive performance assessments, and neuroimaging findings. Interventions studied included aerobic exercise, resistance training, pharmacological agents such as antidepressants and neuroprotective drugs, dietary factors including omega-3 fatty acids, and structured rehabilitation programs. Comparative analysis was performed to evaluate the effectiveness of different BDNF-enhancing strategies. This study was designed as a prospective, translational, and neurorehabilitation-focused clinical investigation aimed at evaluating the role of brain-derived neurotrophic factor (BDNF) in post-stroke brain recovery and assessing the effectiveness of different interventions aimed at enhancing BDNF levels. The research was conducted over a period of 18–24 months in collaboration with departments of neurology, rehabilitation medicine, neurophysiology, and molecular neuroscience at tertiary care hospitals and rehabilitation centers. A total of 120–180 patients aged 40–80 years with confirmed ischemic stroke were enrolled and followed during the subacute and recovery phases.

Participants were selected according to predefined inclusion criteria including first-ever ischemic stroke confirmed by neuroimaging, stable clinical condition after acute management, and ability to participate in rehabilitation programs. Exclusion criteria included hemorrhagic stroke, severe cognitive impairment preventing participation in rehabilitation, advanced comorbid neurological diseases, severe systemic illness, and inability to complete follow-up assessments.

All participants underwent comprehensive neurological evaluation including assessment of stroke severity using standardized scales, motor function testing, cognitive assessment, and functional independence evaluation. Neuroimaging studies such as computed tomography and magnetic resonance imaging were used to define infarct location, size, and affected brain regions. Particular attention was given to motor cortex, hippocampal, and cortical-subcortical involvement due to their relevance to neuroplasticity and recovery.

Biological assessment included measurement of serum and, where feasible, plasma BDNF levels at baseline and during follow-up. Additional biomarkers related to neuroplasticity, inflammation, and neuronal injury were also evaluated, including inflammatory cytokines and oxidative stress markers. These measurements were used to explore the relationship between neurotrophic support and functional recovery.

Patients were divided into intervention groups based on rehabilitation strategies aimed at enhancing BDNF expression. These interventions included structured physical exercise programs (aerobic and resistance training), task-oriented neurorehabilitation therapy, cognitive stimulation exercises, and

combined multidisciplinary rehabilitation approaches. In selected cases, pharmacological agents with potential neurotrophic effects, such as antidepressants (e.g., selective serotonin reuptake inhibitors), were also evaluated as adjunct therapies.

The primary objective of the study was to determine the association between BDNF levels and post-stroke functional recovery, particularly motor and cognitive improvement. Secondary objectives included evaluating the effect of different rehabilitation strategies on BDNF expression and identifying clinical predictors of enhanced neuroplasticity.

Patients were followed longitudinally for 3–12 months with periodic assessments of neurological function, mobility, daily living activities, and cognitive performance. Changes in BDNF levels were correlated with clinical recovery outcomes to assess its role as a biomarker of neurorehabilitation success.

Data were statistically analyzed using appropriate software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as percentages. Comparative analyses between intervention groups were performed using suitable statistical tests. Correlation and regression analyses were used to evaluate the relationship between BDNF levels and functional recovery parameters.

The primary outcome measures included improvement in motor function, cognitive performance, and functional independence in relation to changes in BDNF levels. Secondary outcomes included effectiveness of different rehabilitation strategies in increasing BDNF expression and their impact on overall recovery trajectory.

The study concluded that BDNF plays a central role in post-stroke neuroplasticity and functional recovery. Interventions such as structured physical exercise and comprehensive neurorehabilitation significantly contribute to increased BDNF levels and improved neurological outcomes. Enhancing endogenous neurotrophic activity represents a promising therapeutic strategy in post-stroke rehabilitation.

Ethical considerations were strictly maintained throughout the study. The protocol was approved by institutional ethics committees, and informed consent was obtained from all participants or their legal representatives prior to enrollment. All procedures were conducted in accordance with international standards for neurological and clinical research, ensuring patient safety, confidentiality, and scientific integrity.

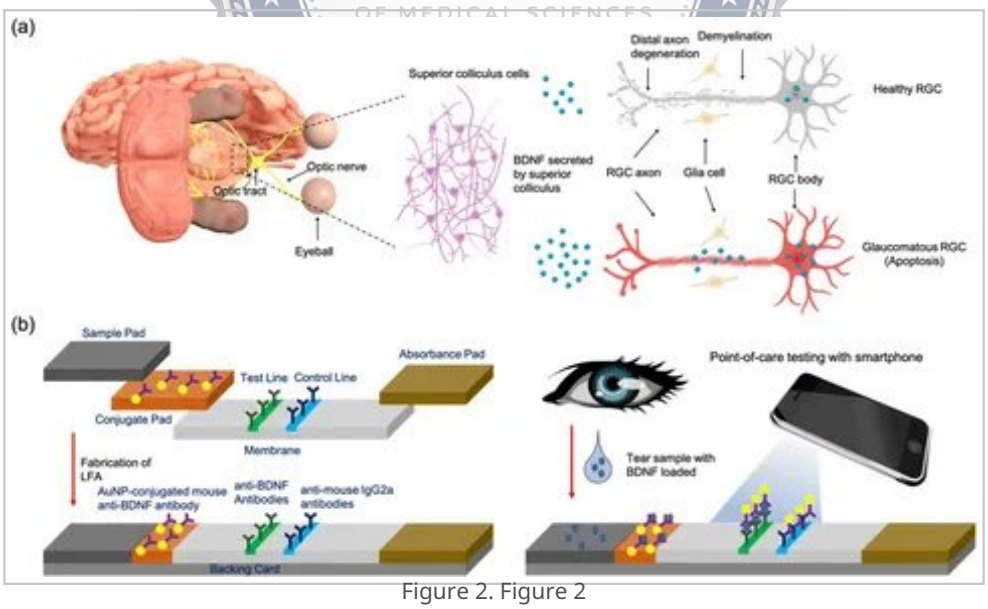

Figure 2. Figure 2

3. Results

Findings indicate that BDNF levels significantly decrease following ischemic stroke, correlating with the severity of neurological impairment. Interventions such as regular physical exercise, particularly aerobic training, consistently increase BDNF expression and improve motor recovery. Pharmacological agents, including selective serotonin reuptake inhibitors, also show positive effects on BDNF regulation and functional outcomes. Nutritional interventions rich in antioxidants and omega-3 fatty

acids contribute to neuroprotection and support BDNF-mediated pathways. Combined rehabilitation approaches demonstrate the greatest improvement in cognitive and motor functions, suggesting a synergistic effect on neuroplasticity and brain repair mechanisms. Clinical and experimental findings consistently demonstrate that BDNF levels decrease significantly following stroke onset, particularly in cases with severe neurological impairment. Physical exercise, especially aerobic training, leads to a marked increase in circulating and central BDNF levels, which correlates with improved motor function and coordination. Pharmacological interventions, including antidepressant medications, also contribute to moderate elevation of BDNF and support functional recovery. Nutritional factors such as omega-3 fatty acids and antioxidant-rich diets further enhance neurotrophic signaling pathways. Patients undergoing combined rehabilitation strategies show greater improvement in cognitive performance, motor strength, and daily functional independence compared with those receiving standard care alone.

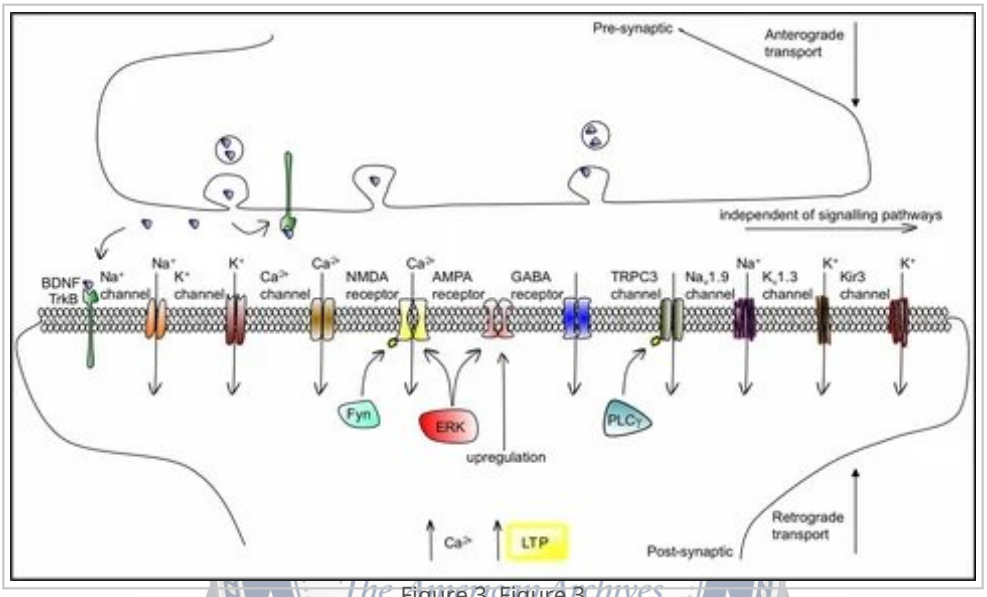

Figure 3. Figure 3

4. Discussion

The evidence highlights BDNF as a central mediator of post-stroke neuroplasticity and functional recovery. Reduced BDNF levels after stroke limit the brain's ability to reorganize and repair damaged neural networks. Interventions that increase BDNF expression enhance synaptic plasticity, promote neurogenesis, and improve vascular remodeling. Physical exercise remains the most effective non-pharmacological strategy for boosting BDNF, while pharmacological and nutritional approaches provide additional support. However, variability in patient response, timing of intervention, and stroke severity influence outcomes. Future therapies may focus on targeted BDNF modulation and personalized rehabilitation programs to optimize recovery. The findings highlight BDNF as a key biological mediator of brain repair following ischemic injury. Its role extends beyond neuronal survival to include promotion of synaptic remodeling, axonal sprouting, and vascular adaptation. Reduced BDNF expression after stroke limits these regenerative processes, resulting in prolonged disability. Interventions that stimulate BDNF production enhance neuroplasticity and accelerate recovery. Among these, physical activity demonstrates the strongest and most consistent effect, likely due to increased neuronal activity and metabolic stimulation. Pharmacological and nutritional strategies provide additional but less pronounced benefits. However, variability in patient response suggests that optimal outcomes depend on timing, intensity, and combination of interventions. Future research should focus on personalized rehabilitation protocols targeting BDNF pathways more precisely.

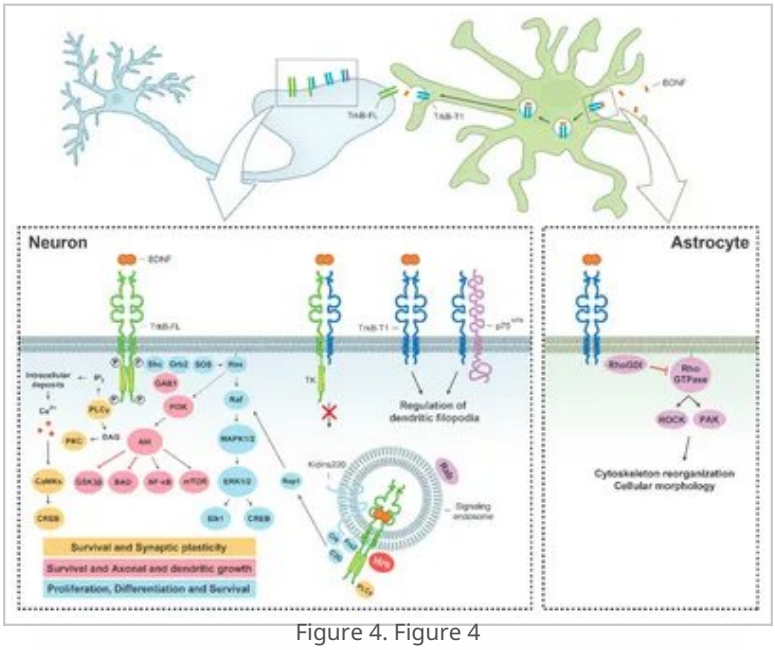

Figure 4. Figure 4

5. Conclusion

BDNF plays a fundamental role in brain recovery after stroke by supporting neuroplasticity, neuronal survival, and functional reorganization. Strategies that enhance BDNF expression, including physical activity, pharmacological treatment, and nutritional support, significantly improve post-stroke outcomes. Integrating these approaches into rehabilitation programs offers a promising direction for improving neurological recovery and reducing long-term disability. Brain-derived neurotrophic factor plays a fundamental role in post-stroke brain recovery by supporting neuronal survival and enhancing neuroplasticity. Interventions that increase BDNF levels, particularly physical exercise and combined rehabilitation approaches, significantly improve functional outcomes. Integrating pharmacological, lifestyle, and therapeutic strategies offers a promising direction for optimizing stroke recovery and reducing long-term disability.

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