Research Article

Correlation of Brain-Derived Neurotrophic Factor and Fugl-Meyer Score Changes after Telerehabilitation in Stroke

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Running Title: BDNF and Fugl-Meyer Score Changes after Telerehabilitation

Abstract

Background: Early post-stroke rehabilitation reduces disability and improves quality of life. However, limited access to rehabilitation facilities can be challenging. Home-based telerehabilitation emerges as a viable solution to reach distant stroke populations. Motoric recovery

relies on penumbral reorganization and restructuring. Brain-Derived Neurotrophic Factor (BDNF) plays a crucial role in synaptic plasticity regulation. Yet, the impact of additional rehabilitation sessions on BDNF levels and motoric function in post-stroke patients remains unexplored.
Method: A randomized controlled trial was conducted, involving 50 stroke patients from June to September 2023. Medical history was assessed via a questionnaire, and motoric function was evaluated using the Fugl-Meyer Assessment (FMA). Blood samples were drawn to measure BDNF levels. The intervention included prescribing home-based exercises using a telerehabilitation application on cellphones for 12 weeks. BDNF levels and FMA scores were reassessed at the study's conclusion.
Result: Significant increases in BDNF and FMA scores were observed in the mobile-based telerehabilitation group. The increment of BDNF and FMA in the intervention group exceeded that of the control group.
Conclusion: Mobile-based telerehabilitation proves superior to conventional home exercise programs for delivering home-based therapeutic exercises.
Keywords: Stroke; brain-derived neurotrophic factor; telerehabilitation; recovery of function

Introduction

Numerous studies have underscored the efficacy of early rehabilitation interventions in mitigating disability and enhancing independence among post-stroke patients. However, challenges persist in ensuring equitable access to these programs post-treatment. Factors such as geographical proximity to rehabilitation facilities, scheduling complexities, and patient compliance present barriers to optimal rehabilitation outcomes. Notably, the emergence of the Coronavirus Disease 2019 (COVID-19) pandemic has exacerbated these challenges, imposing social restrictions that hinder patient access to hospital-based rehabilitation services. Given the potential recurrence of pandemic-related restrictions, innovative care models are imperative to bridge the gap in rehabilitation services. Health institutions must pivot toward facilitating home-based rehabilitation programs to ensure continuity of care. Telemedicine, or telerehabilitation, emerges as a promising solution to reach stroke populations distanced from traditional healthcare settings (1–5).

Neuroplasticity mechanisms post-stroke are crucial for recovery. Initially, neuronal polarization and synapse pruning refine neural connections, enhancing signal transmission. Subsequently, neurite growth and neurogenesis form new pathways, aiding in functional restoration. Myelin repair ensures efficient impulse conduction, while synaptic reconnection and brain remodeling facilitate adaptive responses. Additionally, vascular regeneration improves blood supply, fostering neuronal survival. Motor improvement relies on penumbral tissue reorganization, which is correlated with heightened stimuli from long-term potentiation. Regular therapeutic exercises accelerate this process, promoting functional recovery (6).

Brain-Derived Neurotrophic Factor (BDNF) serves as a key neurotrophic protein and is a central member of the neurotrophin family—alongside Nerve Growth Factor (NGF), Neurotrophin-3 (NT-3), and Neurotrophin-4 (NT-4). While NGF and NT-3 have more peripheral or restricted neural targets, BDNF is broadly distributed throughout the central nervous system (CNS). Regionally, BDNF is abundantly expressed in brain areas, including the hippocampus, cerebral cortex, amygdala, and cerebellum. BDNF primarily exerts its effects via the tropomyosin receptor kinase B (TrkB) receptor, activating downstream signaling pathways such as phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK), and phospholipase C-gamma (PLC-γ). These cascades support neuronal survival, differentiation, and synaptic plasticity—key processes for learning, memory, and post-injury recovery (7–12). Physical exercise is a powerful stimulator of BDNF expression. It enhances BDNF production through multiple mechanisms: (1) increased neuronal activity, (2) improved cerebral blood flow, and (3) the release of exerkines (8). Thus, BDNF acts as a central hub integrating signals from both central neuronal activity and peripheral metabolic changes, making it a key mediator of exercise-induced brain plasticity.

To the best of the researchers' knowledge, no prior studies have examined the addition of telerehabilitation sessions using Bobath exercises to improve BDNF levels and functional motor status. This study aims to investigate the efficacy of integrating home exercise sessions utilizing Telerehabilitasi Hasanuddin, a mobile-application telerehabilitation tool. The primary objective is to evaluate whether post-stroke patients participating in this rehabilitation program experience improvements in motor function—assessed using the Fugl-Meyer Assessment (FMA)—and BDNF levels following regular use of the application. Through rigorous assessment, this study seeks to provide valuable insights into the potential benefits of incorporating innovative telerehabilitation solutions in optimizing stroke rehabilitation outcomes.

Methods

Study Design and Recruitment

This study employed a randomized controlled trial design to evaluate the efficacy of a therapeutic intervention for stroke patients, conducted between June and September 2023 at Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital. Participant selection followed consecutive sampling with sequence randomization. The inclusion criteria comprised patients diagnosed with either non-hemorrhagic or hemorrhagic stroke in the sub-acute or chronic phase, aged between 35-65 years, with a history of first stroke occurrence, exhibiting unilateral neurological deficits while maintaining full consciousness (compos mentis), and demonstrating a minimum Manual Muscle Testing (MMT) scale score of 2. Exclusion criteria eliminated patients with musculoskeletal complications, cognitive impairment or global sensory aphasia, psychotic symptoms and/or severe depression, severe balance disorders or transfer disabilities, history of percutaneous coronary intervention or coronary artery bypass grafting surgery, active tuberculosis, severe respiratory disease, or recent digital subtraction angiography, as well as those presenting large hemispheric infarction on non-contrast computed tomography scans.

Study withdrawal conditions included failure to adhere to the physician-prescribed program for three consecutive days, incomplete execution of at least 50% of planned rehabilitation exercises within one week, voluntary withdrawal from the study, development of significant hemodynamic symptoms requiring therapy discontinuation in three consecutive or five separate sessions, or patient mortality. Eligible participants who met inclusion criteria without triggering exclusion parameters were enrolled and sequentially numbered according to their arrival order.

Participants were allocated to either the intervention or control group through a concealed randomization process conducted by an independent physician using Microsoft Excel. The randomization procedure involved creating two spreadsheet columns: one listing patient identification numbers and another generating random values between 0 and 1 for each subject using the "=RAND" function. These random values were converted to static data to prevent subsequent recalculation changes. The complete list was then sorted in ascending order based on the random numbers, with the first half assigned to the mobile-based telerehabilitation intervention group and the remaining participants allocated to the conventional rehabilitation control group. This methodology ensured unbiased group assignment while maintaining allocation concealment throughout the trial.

Data measurements

Participants who provided voluntary written informed consent underwent comprehensive assessments, including motor function evaluation using the Fugl-Meyer Assessment (FMA) score, along with physical, radiological, and laboratory examinations, including Brain-Derived Neurotrophic Factor (BDNF) level measurements. Motor function was assessed using the FMA, a standardized and validated tool for evaluating post-stroke motor recovery, with a focus on total motor function scores. To minimize assessment bias, all evaluations were conducted by trained physicians who remained blinded to group assignments throughout the study.

For BDNF measurement, venous blood samples were collected following the World Health Organization (WHO) 2010 protocol using the venous aspiration technique. The collected specimens were immediately transported to the Biomolecular Laboratory of Hasanuddin University Medical Research Center (HUMRC) for processing and analysis. Sample handling adhered to the UK Biobank standards for blood collection, processing, and transport, while storage procedures followed the International Agency for Research on Cancer (IARC) guidelines for sample preservation. Serum samples were stored in the HUMRC laboratory freezer at −80°C, as recommended by IARC protocols. BDNF levels were quantified using the Enzyme-Linked Immunosorbent Assay (ELISA) technique in accordance with the manufacturer's instructions provided in the Human Brain-Derived Neurotrophic Factor ELISA Kit (Elabscience Biotechnology Inc.).

Throughout the 12-week study period, participants were closely monitored, with FMA scores and serum BDNF levels assessed at baseline and post-intervention. Any adverse events were systematically documented based on patient-reported experiences and clinical observations. This rigorous monitoring protocol ensured comprehensive data collection while maintaining participant safety and study integrity.

Intervention

Both the intervention and control groups received standard post-stroke conventional rehabilitation at the hospital, incorporating Bobath principles to enhance postural control, balance, movement patterns, speed, accuracy, strength, and endurance. Both groups were instructed to perform home therapeutic exercises consisting of assistive active exercises aligned with the Bobath principle, prescribed twice daily for 15 minutes. Each participant was assigned two specific Bobath-based exercises. One for the upper extremity and one for the lower extremity, based on their individual motor ability and functional status. For example, upper extremity tasks often included weight-bearing in a sitting or quadruped position to enhance proximal stability and scapular control, while lower extremity tasks included sit-to-stand training or bridging exercises that emphasized trunk alignment and weight transfer.

Patients in the telerehabilitation group received additional education on using the "Telerehabilitasi Hasanuddin" application, including registration and exercise scheduling. The application includes several integrated features such as an exercise planner that allows patients to schedule daily sessions based on physician recommendations, and a reminder system that sends automated notifications to prompt timely exercise. It also features an exercise timer to guide session duration, and tutorial videos demonstrating each assigned Bobath-based movement to ensure correct execution. Additionally, a compliance tracker logs completed sessions and monitors adherence, allowing clinicians to review the frequency and consistency of patient engagement.

Participants unable to complete the full session were instructed to perform at least 8 minutes of exercise, with completion recorded accordingly. Exercise intensity followed the Borg Rating of Perceived Exertion scale, targeting a level between Light and Somewhat Hard (Borg Scale 11–13). Participants were advised to discontinue exercise if they experienced severe headaches, vomiting, shortness of breath, palpitations, or chest pain. Any reported symptoms were managed with appropriate medical treatment provided by the attending physician.

To prevent exercise-related side effects during the home-based intervention, all participants were provided with clear guidance on maintaining hydration and adequate rest before exercising. To ensure safety during the home program, participants were given direct communication access to the study team and were instructed to report any symptoms or complaints. Symptomatic cases were followed up via phone or in-person visits, and appropriate treatment was provided by the attending physician based on the reported symptoms. This protocol ensured that any side effects experienced during home exercise sessions were promptly addressed.

Data Analysis

Baseline data underwent descriptive summarization and cross-tabulation. For normally distributed data, the comparative analysis employed the paired t-test to assess changes in BDNF levels and FMA scores pre- and post-intervention. Conversely, the Wilcoxon test was utilized for non-normally distributed data. To compare BDNF and FMA levels between the intervention and control groups, the independent t-test was applied for normally distributed data, while the Mann-Whitney test was used for non-normally distributed data. Correlation between BDNF levels and FMA scores was evaluated using the Pearson correlation test for normally distributed data and the Spearman correlation test for non-normally distributed data.

Ethical clearance

This study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki. This study was approved by the Research Ethics Commission of the Faculty of Medicine, Hasanuddin University (No: 387/UN4.6.4.5.31/PP36/2023).

Result

Demographic Data of Research Participants

In this study, comprising 50 participants, the mean age was 61.20 ± 6.68 years, with a predominant representation of females (52%). Notably, individuals with a body mass index (BMI) <25.0 kg/m^2 constituted the majority (64%), exhibiting an average BMI of 23.80 ± 2.42 kg/m^2. Upon initial assessment, the mean levels of BDNF and FMA scores were 13.19 ± 10.96 and 64.14 ± 26.16, respectively. Statistical analysis revealed no significant differences in baseline characteristics between the study groups ($p > 0.05$) (**Table 1**).

Table 1. Demographic Data of Research participants

Variables	Entire population (n = 50)	Telerehabilitation (n = 25)	Control (n = 25)	p-value
Age (years); mean ± SD	61.20 ± 6.68	61.64 ± 6.54	60.76 ± 6.78	0.774
Gender				0.283

Male; n (%)	24 (48)	13 (52)	11 (44)	
Female; n (%)	26 (52)	12 (48)	14 (56)	
BMI (kg/m²); mean ± SD	23.80 ± 2.42	24.28 ± 2.25	23.32 ± 2.48	0.912
≥25,0 kg/m²; n (%)	18 (36)	11 (44)	7 (28)	
<25,0 kg/m²; n (%)	32 (64)	14 (56)	18 (72)	
Stroke type				0.141
Hemorrhagic; n (%)	27 (54)	14 (56)	13 (52)	
Non-hemorrhagic; n (%)	23 (46)	11 (44)	12 (48)	
Stroke Onset				0.141
Subacute; n (%)	17 (34)	9 (36)	8 (32)	
Chronic; n (%)	33 (66)	16 (64)	17 (68)	
BDNF (ng/mL); mean ± SD	12.21 ± 8.84	15.97 ± 9.50	8.45 ± 6.14	0.673
FMA; mean ± SD	64.14 ± 26.16	61.36 ± 27.85	66.92 ± 24.03	0.168

Abbreviations: BMI, body mass index; BDNF, brain-derived neurotrophic factor; FMA, Fugl-Meyer Assessment; SD, standard deviation.

Duration and Frequency of Home Therapeutic Exercise

The study revealed that the mean exercise duration for the entire population was 1819.34 ± 516.71 minutes, with an average exercise frequency of 153.06 ± 9.62 times throughout the study period. Notably, statistical analysis demonstrated significant disparities in both exercise duration and frequency between the two groups ($p < 0.05$) (**Table 2**).

Table 2. Duration and Frequency of Home Therapeutic Exercises

	Entire Population	Telerehabilitation	Control	p-value
Exercise duration (minutes); mean ± SD	1819.34 ± 516.71	2333.56 ± 31.82	1305.12 ± 64.20	0.012[a+]
Exercise frequency (n); mean ± SD	153.06 ± 9.62	160.20 ± 2.24	145.92 ± 8.83	0.003[a+]

[a] = Mann Whitney test, [+]significant with p-value < 0.05

Comparison of BDNF Levels and FMA Scores Before and After Intervention

Based on the Wilcoxon test analysis, both the telerehabilitation and control groups exhibited significant increases in FMA and BDNF scores post-treatment ($p < 0.05$). Additionally, employing the Mann Whitney test revealed a significant disparity in the enhancement of BDNF and FMA levels between the intervention and control groups ($p < 0.05$) (**Table 3**).

Table 3. Statistical analysis of BDNF levels and FMA scores

Variables	Control		Telerehabilitation		ΔPre-Post	
	Before	After	Before	After	Control	Telerehabilitation
FMA; (mean±SD)	66.92 ± 24.03	76.56 ± 23.45[a+]	61.36 ± 27.86	81.12 ± 21.75[a+]	9.64 ± 5.04	19.76 ± 9.42[b+]
BDNF (ng/ml) (mean±SD)	8.45 ± 6.14	12.80 ± 8.10[a+]	15.97 ± 9.50	24.32 ± 12.84[a+]	4.35 ± 3.34	8.34 ± 5.87[b+]

Abbreviations: FMA: Fugl Meyer Assessment, BDNF: Brain-Derived Neurotrophic Factor
[a] = Wilcoxon test, [b] = Mann Whitney test, [+]significant with p-value < 0.05

Correlation of BDNF Levels and FMA Scores

Based on the analysis using the Spearman correlation test (**Table 4**), a moderate positive correlation was observed between the duration and frequency of exercise and changes in FMA scores. Additionally, a weak positive correlation was found between the duration and frequency of exercise and changes in BDNF levels, both of which were statistically significant ($p < 0.05$).
Linear regression analysis revealed that for every 1-minute increase in exercise duration, the FMA score increased by 0.01, which was statistically significant ($p < 0.05$) (**Figure 1**). Additionally, analysis showed that each additional exercise session resulted in a 0.4 increase in the FMA score, also statistically significant ($p < 0.05$) (**Figure 2**).

Table 4. Correlation of Duration and Frequency of Exercise on Changes in BDNF Levels and FMA Scores

		Duration	Frequency
ΔFMA	ρ	0,49[a+]	0,52[a+]
ΔBDNF	ρ	0,39[a+]	0,36[a+]

[a] = Spearman test, [+]significant with p-value < 0.05

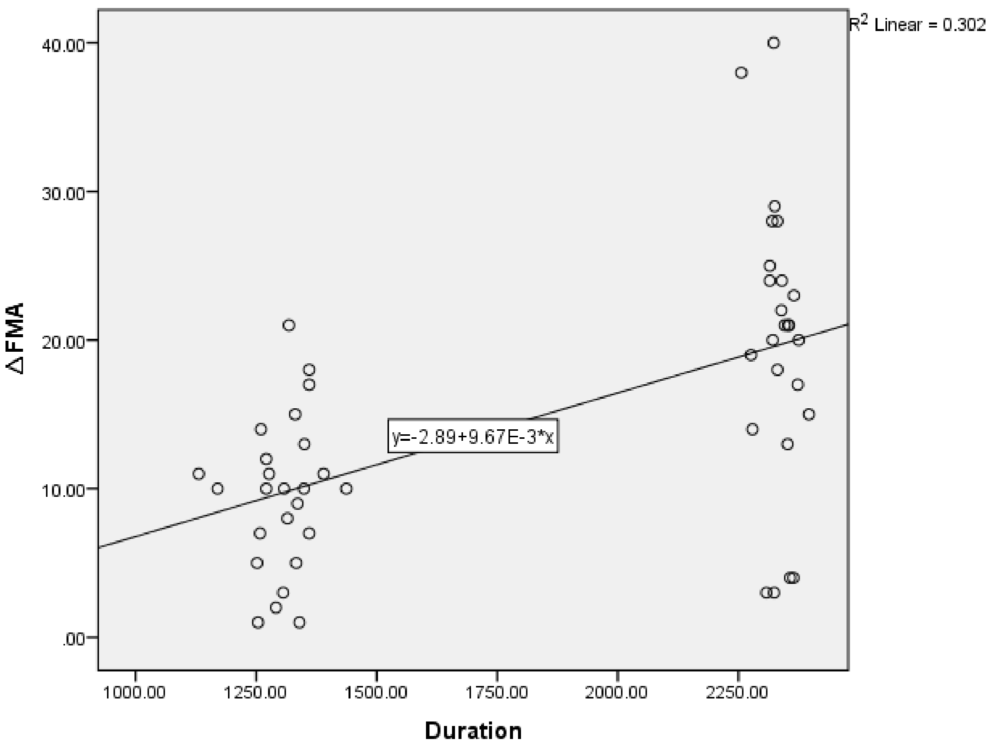

Figure 1. Linear Regression of Exercise Duration on Changes in FMA Scores

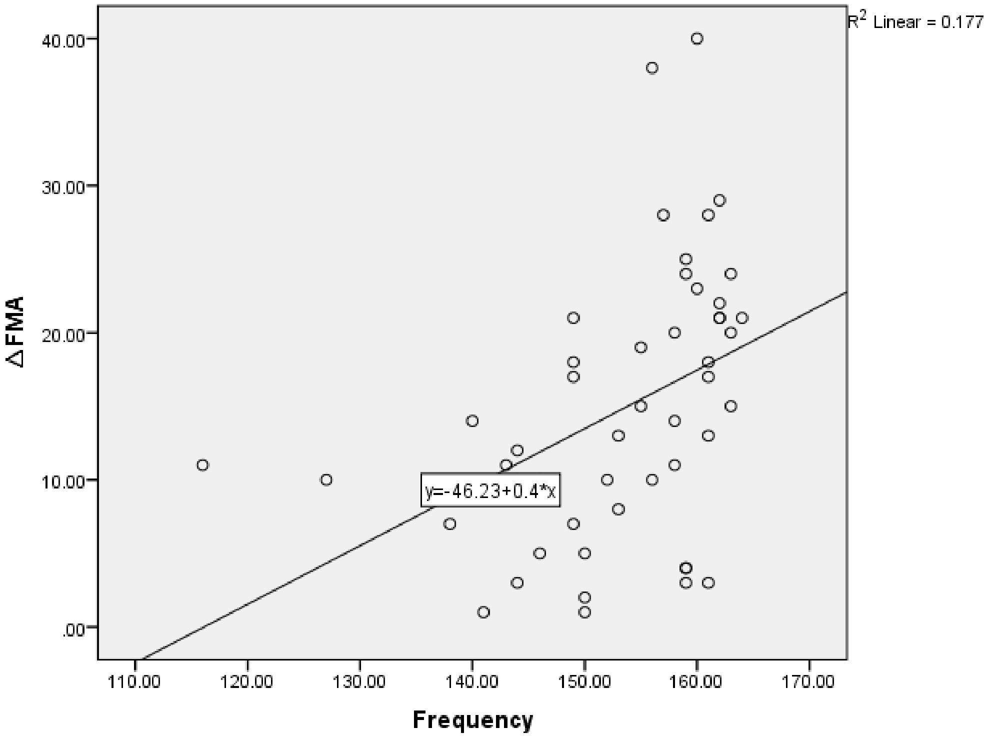

Figure 2. Linear Regression of Exercise Frequency on Changes in FMA Score

Linear regression analysis demonstrated that each additional minute of exercise duration was associated with an increase in BDNF levels of 0.004 ng/mL, which was statistically significant ($p<0.05$) (**Figure 3**). Furthermore, each additional exercise session was correlated with an increase in BDNF levels of 0.17 ng/mL, also statistically significant ($p< 0.05$) (**Figure 4**).

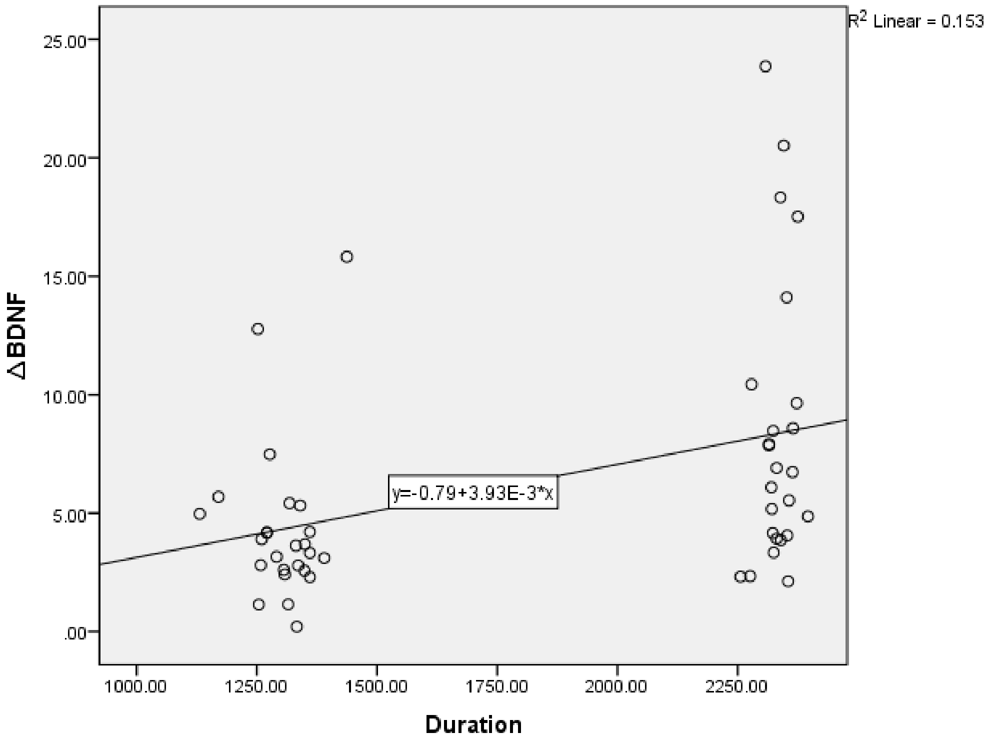

Figure 3. Linear Regression of Exercise Duration on Changes in BDNF Levels

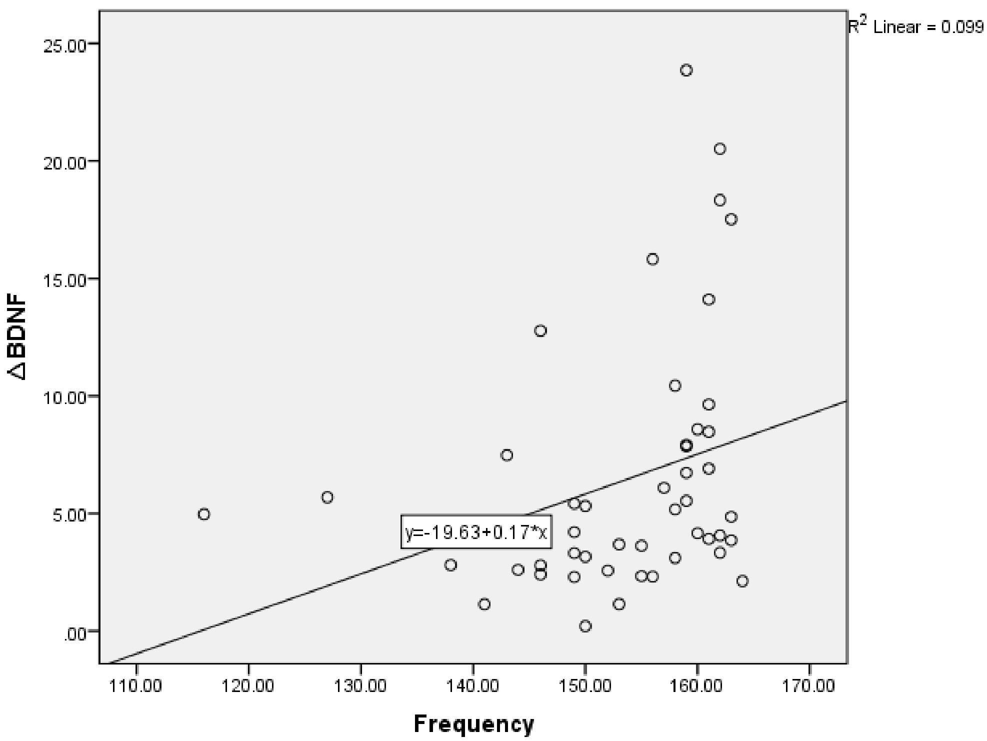

Figure 4. Linear Regression of Exercise Frequency on Changes in BDNF Levels

Reported side effects

Following the completion of the 12-week program, participants in both the intervention and control groups reported mild side effects. These included fatigue in 3 individuals (6%), and single cases of cephalgia, migraine, and nausea (2% each). Notably, no participants experienced recurring side effects three times consecutively or five times separately, leading to no dropouts during the study. Statistical analysis revealed no significant difference between the intervention and control groups (**Table 5**)

Table 5. Reported Side Effects

	Entire population	**Telerehabilitation**	**Control**	**p-value**
Side effects; n (%)	9 (18)	5 (20)	4 (16)	0,141
Fatigue; n (%)	3 (6)	2 (8)	1 (4)	
Cephalgia; n (%)	2 (4)	1 (4)	1 (4)	
Migraine; n (%)	3 (6)	1 (4)	2 (8)	
Nausea; n (%)	1 (2)	1 (4)	-	

Discussion

The sample in this study consisted of 50 post-stroke patients with a mean age of 61.20 ± 6.68 years, which aligns with global stroke demographics. Age is a well-established risk factor for stroke, with incidence doubling every decade after 55 years (14,15). The gender distribution was relatively balanced, with a slight predominance of females (52%). Although stroke risk varies by sex and age, overall incidence tends to be higher in women, partly due to longer life expectancy (15). The average BMI was 23.80 ± 2.42 kg/m², which is categorized as overweight in Asian populations, a known risk factor for stroke due to its association with metabolic syndromes (16). Importantly, there were no significant baseline differences between the telerehabilitation and control groups in terms of demographics, stroke characteristics, or outcome variables ($p > 0.05$), indicating that both groups were comparable prior to the intervention. This baseline homogeneity strengthens the internal validity of the study and supports the conclusion that observed post-intervention improvements were due to the intervention itself.

Adherence to the intervention protocol was good across both groups. All 50 participants met the minimum adherence criteria and remained in the study until completion. However, minor challenges were noted. Some participants occasionally missed sessions or reported low motivation, and many completed only the minimum required 8 minutes of exercise rather than the recommended 15 minutes. These issues did not exceed the predefined thresholds for exclusion. To support adherence, attending physicians were also asked to reinforce the importance of home exercise during routine clinical visits.

Duration and Frequency of Home Therapeutic Exercise

Significant disparities in exercise duration and frequency were noted between the study groups, favoring the application-based telerehabilitation group. Telerehabilitation's inherent flexibility encourages patients to engage in rehabilitation regardless of their geographical location, eradicating accessibility barriers. Existing research underscores telerehabilitation's efficacy in supporting patient adherence and reducing dropout rates. Tailored guided exercise sessions are readily accessible to patients, promoting convenience and adherence to individual schedules. Telerehabilitation interventions incorporate timely exercise prompts, fostering regular engagement and enhancing exercise consistency, thereby impacting exercise duration and frequency positively. Moreover, employing video platforms in telerehabilitation enables precise exercise execution, mitigating injury risks and optimizing therapeutic outcomes (17–21).

Increase in FMA Score and BDNF Levels Before and After Intervention

This study's data analysis revealed a significant rise in FMA scores and BDNF levels post-application of mobile-based telerehabilitation, observed in both telerehabilitation and control groups. The Bobath concept, a staple in post-stroke rehabilitation, enhances movement patterns and functional outcomes via targeted exercises and sensory stimulation. It likely enhances neuroplasticity through various mechanisms: (1) promoting synaptic plasticity and neuronal connections via task-specific movements, and (2) promoting neurogenesis and dendritic growth through sensory stimulation. Moreover, by emphasizing normal movement patterns, Bobath therapy aids in motor control and coordination restoration, yielding functional enhancements (22). Rehabilitative exercises employing the Bobath concept show a notable positive correlation with enhanced FMA scores in individuals recovering from stroke. FMA scores serve as key indicators of post-stroke motor function recovery, where Bobath therapy's emphasis on task-specific exercises notably contributes to heightened motor function and elevated FMA scores. Furthermore, BDNF, crucial for neuronal viability and adaptability, exhibits increased levels following rehabilitative exercise, including Bobath therapy, among stroke patients. This elevation in BDNF levels underscores the role of rehabilitative interventions in promoting neuroplasticity, enabling the brain to effectively adapt and recover from injury, thus enhancing functional recovery post-stroke. The integrative impact of Bobath therapy on both FMA scores and BDNF levels underscores its comprehensive approach to stroke rehabilitation, concurrently addressing motor deficits and promoting neuroplastic mechanisms for optimal functional restoration (22,23).

In this study, a notable disparity was observed in the increase of BDNF levels and FMA scores between the telerehabilitation and control groups. Telerehabilitation via mobile applications is strategically designed to support the frequency, duration, and efficacy of rehabilitation regimens. Utilizing reminders and instructional videos as visual aids, telerehabilitation enhances patient adherence, thereby amplifying exercise frequency and duration while optimizing their effectiveness. Moreover, this approach mitigates the likelihood of injury (20,22).

Rehabilitation exercises have demonstrated efficacy in enhancing FMA scores, yet the impact of intensified exercise frequency and duration on FMA outcomes remains unclear. Variables such as motor impairment severity and individual patient traits may influence exercise effectiveness, necessitating personalized treatment approaches. Further investigation is warranted to explain the isolated effects of exercise frequency and duration increase (24,25). Our study addresses this gap by demonstrating that increased frequency and duration of app-based telerehabilitation sessions are significantly associated with greater FMA improvements in post-stroke patients.

Several studies have explored the efficacy of telerehabilitation in improving motor function after stroke. A randomized controlled trial conducted in Brazil investigated the effects of virtual reality (VR)-based telerehabilitation versus conventional therapy in chronic hemiparetic stroke patients.

The results showed significantly greater improvement in FMA scores in the VR group compared to conventional group (26). Another relevant study by Junata et al. evaluated the impact of a structured telerehabilitation program in 30 patients with chronic stroke, utilizing an app-based intervention that incorporated game-like, sensor-driven training. The study reported a significant improvement in FMA scores only in the intervention group, while no such change was observed in the control group that received standard care (27).

Wu et al. conducted a randomized controlled trial involving 61 chronic post-stroke patients, comparing an app-assisted, remotely supervised rehabilitation program to a control group that received routine rehabilitation guidance and weekly telephone follow-ups. Both groups exhibited significant improvements in FMA scores, with the intervention group achieving greater gains. Their telerehabilitation model incorporated a collaborative care team, delivering personalized rehabilitation via a video conferencing system with real-time therapist interaction twice weekly (28). Chen et al. conducted a randomized controlled trial involving 52 hemiplegic stroke patients to compare telemedicine-based rehabilitation with conventional face-to-face therapy. Patients in the telerehabilitation group performed these exercises at home using a dedicated Telemedicine Rehabilitation System (TRS) under real-time supervision by therapists via live video conferencing, while the control group received identical treatment in a conventional outpatient setting. The telerehabilitation group demonstrated significantly greater improvements in FMA scores compared to the control group (29).

Importantly, our results suggest that doing rehabilitation exercises more often and for a longer duration, even when using a simple mobile app without direct therapist involvement nor advanced technologies, can still lead to meaningful improvements in motor function. This supports the potential of accessible, app-based programs as a practical option for stroke rehabilitation, especially in settings with limited healthcare resources.

Tailoring rehabilitation strategies to individual patient needs and therapy responses is essential for optimal outcomes. It is important to acknowledge that while our study employed a standardized exercise protocol for remote telerehabilitation, this uniform approach may not fully capture the potential for optimized recovery in every patient. Standardized protocols ensure feasibility and consistency but may not adequately address individual differences in baseline motor function, motivation, and recovery capacity (30). Recent evidence, such as that reported by Pelosi et al., demonstrates that adaptive rehabilitation approaches, which dynamically tailor therapy to individual performance via reinforcement learning algorithms, can effectively adjust task difficulty in real time. Such personalized treatment strategies have the potential to maximize functional gains by accommodating individual variability, particularly for patients with severe impairments or complex clinical profiles (31). Moreover, while Bobath training remains important to stroke rehabilitation, decisions regarding its frequency and duration should be individualized, and incorporating supplementary interventions may enhance the potential for greater improvement in FMA scores (25,32).

Rehabilitation exercises also have demonstrated the capacity to elevate BDNF. While direct studies on the effect of Bobath therapy on BDNF levels are lacking, the exercise-based structure of Bobath provides a plausible rationale for such an impact. Bobath interventions involve active, repetitive, and task-specific movement training—core components shared with exercise strategies shown to enhance neuroplasticity and increase BDNF expression. Studies have demonstrated that physical activity promotes BDNF synthesis through increased neuronal activity, improved cerebral blood flow, and the release of peripheral factors known as exerkines, which influence brain function (8,33,34). Given that Bobath therapy incorporates these movement features, it is reasonable to hypothesize that it may engage similar mechanisms to support neuroplastic recovery and BDNF elevation.

The precise correlation between the frequency and duration of Bobath exercises and BDNF elevation necessitates further investigation. Aerobic exercise has been shown to increase BDNF levels in a frequency-dependent manner (35), and a similar phenomenon is likely with Bobath training. Our study supports this hypothesis, demonstrating a significant rise in BDNF levels with increased frequency and duration of Bobath-based exercises delivered via mobile telerehabilitation, as confirmed by correlation and linear regression analyses. Nonetheless, further research is needed to clarify the dose-response relationship. Moreover, we found no prior studies directly examining the impact of telerehabilitation on BDNF, highlighting the novelty of our findings and the need for continued exploration in this area.

Side Effects of Home Therapeutic Exercise in Telerehabilitation and Control Groups

This study observed various side effects among patients engaging in physical exercise, including fatigue, cephalgia, migraine, and nausea, commonly associated with exercise. Fatigue may arise naturally depending on exercise type and intensity, exacerbated by prolonged or intense activity without sufficient rest intervals. Exercise-induced headaches stem from blood vessel dilation, termed primary exercise headaches. Nausea post-exercise can result from factors like dehydration, adrenergic receptor activation, and arginine vasopressin secretion stimulation. Individual factors such as fitness level, hydration status, nutrition, sleep quality, and comorbidities modulate side effect occurrence during rehabilitation (36–39). Importantly, despite these side effects, their incidence lacked statistical significance, suggesting the safety of home telerehabilitation implementation.

Limitations

This study's findings should be interpreted within the context of its limitations. A research duration of 12 weeks, albeit valuable, may be considered relatively short for capturing the entirety of post-stroke recovery dynamics. Individual trajectories of recovery vary, with significant improvements often manifesting months post-stroke onset. Moreover, the potential for long-term recovery underscores the necessity for extended observation periods beyond the study's timeframe. Post-stroke rehabilitation outcomes are multifaceted, influenced by stroke severity, comorbidities, and individual responsiveness to intervention. Consequently, the 12-week duration may not fully encapsulate the rehabilitation's full effect. Notably, while many stroke rehabilitation studies span 12 weeks to evaluate sustained enhancements and long-term consequences, longer observation periods afford a more thorough comprehension of rehabilitation effects.

Conclusions

This study demonstrates the significant efficacy of integrating mobile-based telerehabilitation into hospital-based rehabilitation programs to augment home therapeutic exercise regimens for post-stroke patients over a 12-week period. The intervention notably enhances the duration and frequency of home exercises, leading to tangible benefits for patients.

Moreover, the observed increase in BDNF values underscores the neuroplasticity-inducing potential of mobile-based telerehabilitation, aligning with prior research on telerehabilitation's efficacy. Additionally, improvements in FMA scores highlight enhanced motor function among participants compared to conventional home exercise programs.

Importantly, the intervention exhibits minimal side effects, ensuring its safety and suitability for clinical implementation. This study marks a pioneering effort, being the first to utilize application-based telerehabilitation alongside Bobath exercises, utilizing BDNF and FMA as outcome measures. Overall, the findings support the use of mobile-based telerehabilitation as a valuable adjunct to traditional rehabilitation strategies for post-stroke patients.

Conflicts of Interest

The authors declare no conflict of interest.

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Authors' Contributions:

All authors have contributed to all processes in this research, including preparation, data gathering, analysis, drafting, and approval for publication of this manuscript.

References

1. Chen J, Liu M, Sun D, Jin Y, Wang T, Ren C. Effectiveness and neural mechanisms of home-based telerehabilitation in patients with stroke based on fMRI and DTI: A study protocol for a randomized controlled trial. Medicine. 2018;
2. Dodakian L, McKenzie AL, Le V, See J, Pearson-Fuhrhop K, Burke Quinlan E, et al. A Home-Based Telerehabilitation Program for Patients With Stroke. Neurorehabil Neural Repair. 2017;
3. Markus HS, Brainin M. COVID-19 and stroke—A global World Stroke Organization perspective. International Journal of Stroke. 2020;
4. Sarfo FS, Ulasavets U, Opare-Sem OK, Ovbiagele B. Tele-Rehabilitation after Stroke: An Updated Systematic Review of the Literature. Journal of Stroke and Cerebrovascular Diseases. 2018 Sep;27(9):2306–18.
5. Khan F, Amatya B. Medical Rehabilitation in Pandemics: Towards a New Perspective. J Rehabil Med. 2020;52(4):jrm00043.
6. Jiao Y, Liu YW, Chen WG, Liu J. Neuroregeneration and functional recovery after stroke: Advancing neural stem cell therapy toward clinical application. Neural Regeneration Research. 2021.
7. Singh AA, Katiyar S, Song M. Phytochemicals Targeting BDNF Signaling for Treating Neurological Disorders. Brain Sci. 2025 Feb 27;15(3):252.
8. Cefis M, Chaney R, Wirtz J, Méloux A, Quirié A, Leger C, et al. Molecular mechanisms underlying physical exercise-induced brain BDNF overproduction. Front Mol Neurosci. 2023 Oct 5;16.
9. Adachi N. New insight in expression, transport, and secretion of brain-derived neurotrophic factor: Implications in brain-related diseases. World J Biol Chem. 2014;5(4):409.
10. Sasi M, Vignoli B, Canossa M, Blum R. Neurobiology of local and intercellular BDNF signaling. Pflugers Arch. 2017 Jun 9;469(5–6):593–610.
11. Ashcroft SK, Ironside DD, Johnson L, Kuys SS, Thompson-Butel AG. Effect of Exercise on Brain-Derived Neurotrophic Factor in Stroke Survivors: A Systematic Review and Meta-Analysis. Stroke. 2022 Dec;53(12):3706–16.
12. Mitre M, Mariga A, Chao MV. Neurotrophin signalling: novel insights into mechanisms and pathophysiology. Clin Sci. 2017 Jan 1;131(1):13–23.

13. Dhingra N, Diepart M, Dziekan G, Khamassi S, Otaiza F, Wilburn S, et al. WHO Guidelines on Drawing Blood: Best Practices in phlebotomy. Cadman H, editor. Geneva: World Health Organization; 2010.
14. Vijayan M, Reddy PH. Stroke, Vascular Dementia, and Alzheimer's Disease: Molecular Links. Journal of Alzheimer's Disease. 2016 Sep 6;54(2):427–43.
15. Boehme AK, Esenwa C, Elkind MSV. Stroke Risk Factors, Genetics, and Prevention. Circ Res. 2017 Feb 3;120(3):472–95.
16. Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1·8 million participants. The Lancet. 2014 Mar;383(9921):970–83.
17. Eichler S, Salzwedel A, Rabe S, Mueller S, Mayer F, Wochatz M, et al. The Effectiveness of Telerehabilitation as a Supplement to Rehabilitation in Patients After Total Knee or Hip Replacement: Randomized Controlled Trial. JMIR Rehabil Assist Technol. 2019 Nov 7;6(2):e14236.
18. Amirabadi N, Hessam M, Monjezi S, Molhemi F, Mehravar M, Hosseinpour P. Effectiveness of telerehabilitation intervention to improve pain and physical function in people with patellofemoral pain syndrome: study protocol for a randomized controlled trial. Trials. 2024 Mar 19;25(1):195.
19. Dias JF, Oliveira VC, Borges PRT, Dutra FCMS, Mancini MC, Kirkwood RN, et al. Effectiveness of exercises by telerehabilitation on pain, physical function and quality of life in people with physical disabilities: a systematic review of randomised controlled trials with GRADE recommendations. Br J Sports Med. 2021 Feb;55(3):155–62.
20. Pratama AD, Farelin AD, Karnadipa T, Pahlawi R, Noviana M, Abdullah F. The Application of Telerehabilitation for Pain Reduction and Improving Quality of Life in Workers with Work-Related Musculoskeletal Disorders: Systematic Review. In: ICVEAST. Basel Switzerland: MDPI; 2023. p. 45.
21. Sari F, Oskay D, Tufan A. Effects of a telerehabilitation-based exercise program in patients with systemic sclerosis. Z Rheumatol. 2024 Feb 25;83(S1):167–74.
22. Pathak A, Gyanpuri V, Dev P, Dhiman N. The Bobath Concept (NDT) as rehabilitation in stroke patients: A systematic review. J Family Med Prim Care. 2021;10(11):3983.
23. Geng H, Li M, Tang J, Lv Q, Li R, Wang L. Early Rehabilitation Exercise after Stroke Improves Neurological Recovery through Enhancing Angiogenesis in Patients and Cerebral Ischemia Rat Model. Int J Mol Sci. 2022 Sep 10;23(18):10508.
24. Pumprasart T, Pramodhyakul N, Piriyaprasarth P. The effect of the Bobath therapy programme on upper limb and hand function in chronic stroke individuals with moderate to severe deficits. Int J Ther Rehabil. 2019 Oct 2;26(10):1–12.
25. Kollen BJ, Lennon S, Lyons B, Wheatley-Smith L, Scheper M, Buurke JH, et al. The Effectiveness of the Bobath Concept in Stroke Rehabilitation. Stroke. 2009 Apr;40(4).
26. Alves SS, Ocamoto GN, de Camargo PS, Santos ATS, Terra AMSV. Effects of virtual reality and motor imagery techniques using Fugl Meyer Assessment scale in post-stroke patients. Int J Ther Rehabil. 2018 Nov 2;25(11):587–96.
27. Junata M, Cheng KCC, Man HS, Lai CWK, Soo YOY, Tong RKY. Kinect-based rapid movement training to improve balance recovery for stroke fall prevention: a randomized controlled trial. J Neuroeng Rehabil. 2021 Dec 11;18(1):150.
28. Wu Z, Xu J, Yue C, Li Y, Liang Y. Collaborative Care Model Based Telerehabilitation Exercise Training Program for Acute Stroke Patients in China: A Randomized Controlled

Trial. Journal of Stroke and Cerebrovascular Diseases. 2020 Dec;29(12):105328.
29. Chen J, Sun D, Zhang S, Shi Y, Qiao F, Zhou Y, et al. Effects of home-based telerehabilitation in patients with stroke. Neurology. 2020 Oct 27;95(17).
30. Federico S, Cacciante L, De Icco R, Gatti R, Jonsdottir J, Pagliari C, et al. Telerehabilitation for Stroke: A Personalized Multi-Domain Approach in a Pilot Study. J Pers Med. 2023 Dec 6;13(12):1692.
31. Pelosi AD, Roth N, Yehoshua T, Itah D, Braun Benyamin O, Dahan A. Personalized rehabilitation approach for reaching movement using reinforcement learning. Sci Rep. 2024 Jul 30;14(1):17675.
32. Scrivener K, Dorsch S, McCluskey A, Schurr K, Graham PL, Cao Z, et al. Bobath therapy is inferior to task-specific training and not superior to other interventions in improving lower limb activities after stroke: a systematic review. J Physiother. 2020 Oct;66(4):225–35.
33. Pathak A, Gyanpuri V, Dev P, Dhiman NR. The Bobath Concept (NDT) as rehabilitation in stroke patients. J Family Med Prim Care. 2021 Nov;10(11):3983–90.
34. Díaz-Arribas MJ, Martín-Casas P, Cano-de-la-Cuerda R, Plaza-Manzano G. Effectiveness of the Bobath concept in the treatment of stroke: a systematic review. Disabil Rehabil. 2020 Jun 4;42(12):1636–49.
35. Schmolesky MT, Webb DL, Hansen RA. The effects of aerobic exercise intensity and duration on levels of brain-derived neurotrophic factor in healthy men. J Sports Sci Med. 2013;12(3):502–11.
36. Ament W, Verkerke GJ. Exercise and Fatigue. Sports Medicine. 2009;39(5):389–422.
37. Upadhyaya P, Nandyala A, Ailani J. Primary Exercise Headache. Curr Neurol Neurosci Rep. 2020 May 15;20(5):9.
38. Sandoe CH, Kingston W. Exercise Headache: a Review. Curr Neurol Neurosci Rep. 2018 Jun 19;18(6):28.
39. Wilson PB. ‘I think I’m gonna hurl’: A Narrative Review of the Causes of Nausea and Vomiting in Sport. Sports. 2019 Jul 4;7(7):162.