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Research Article

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

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ABSTRACT

Introduction: Early post-stroke rehabilitation reduces disability and improves quality of life. However, limited access to rehabilitation facilities presents a significant challenge. Home-based telerehabilitation has emerged as a viable solution to reach distant stroke populations. Motor recovery relies on penumbral reorganization and restructuring. Brain-derived neurotrophic factor (BDNF) plays a crucial role in regulating synaptic plasticity. However, the impact of additional rehabilitation sessions on BDNF levels and motor function in post-stroke patients remains unexplored.

Materials and Methods: A randomized controlled trial was conducted from June to September 2023, involving 50 patients with stroke. A medical history was assessed using a questionnaire, and motor function was evaluated using the Fugl-Meyer assessment (FMA). Blood samples were collected to measure BDNF levels. The intervention included prescribing home-based exercises using a telerehabilitation application on cell phones for 12 weeks. BDNF levels and FMA scores were reassessed at the end of the study.

Results: Significant increases in BDNF and FMA scores were observed in the mobile-based telerehabilitation group. The increase in BDNF and FMA levels in the intervention group exceeded that of the control group.

Conclusion: Mobile-based telerehabilitation is superior to conventional home exercise programs for delivering home-based therapeutic exercises.

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Introduction

Numerous studies have underscored the efficacy of early rehabilitation interventions in mitigating disability and enhancing independence in post-stroke patients. However, challenges persist in ensuring equitable access to these programs after treatment has been completed. Factors, such as geographical proximity to rehabilitation facilities, scheduling complexities, and patient compliance, present barriers to achieving 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, has emerged as a promising solution to reach stroke populations that are distanced from traditional healthcare settings [1–5].

Neuroplasticity mechanisms are crucial for stroke recovery. Initially, neuronal polarization and synaptic 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 enhances blood supply, thereby promoting neuronal survival. Motor improvement relies on the reorganization of penumbral tissue, which is correlated with heightened stimuli resulting from long-term potentiation. Regular therapeutic exercise accelerates this process and promotes functional recovery [6].

Brain-derived neurotrophic factor (BDNF) is a key neurotrophic protein and a central member of the neurotrophin family, alongside nerve growth factor (NGF), neurotrophin-3 (NT-3), and NT-4. While NGF and NT-3 have more peripheral or restricted neural targets, BDNF is broadly distributed throughout the central nervous system. Regionally, BDNF is abundantly expressed in the brain, including the hippocampus, cerebral cortex, amygdala, and cerebellum. BDNF primarily exerts its effects via the tropomyosin receptor kinase B receptor, activating downstream signaling pathways, such as phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), mitogen-activated protein kinase/extracellular signal-regulated kinase, and phospholipase C-gamma. 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, including increased neuronal activity, improved cerebral blood flow, and 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 our knowledge, no prior studies have examined the addition of telerehabilitation sessions using Bobath exercises to improve BDNF levels and functional motor status. This study aimed 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, as assessed using the Fugl-Meyer assessment (FMA), and changes in 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 to optimize stroke rehabilitation outcomes.

Materials and 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 was performed using consecutive sampling with sequence randomization. The inclusion criteria included patients aged 35-65 years, diagnosed with either non-hemorrhagic or hemorrhagic stroke in the sub-acute or chronic phase, with a history of first stroke occurrence, exhibiting unilateral neurological deficits while maintaining full consciousness (compos mentis), and demonstrating a minimum manual muscle testing scale score. The 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.

The study withdrawal conditions included failure to adhere to the physician-prescribed program for three consecutive days, incomplete execution of at least 50% of the 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 the inclusion criteria without triggering the 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 into 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 trials.

Data measurements

Participants who provided voluntary written informed consent underwent comprehensive assessments, including a motor function evaluation using the FMA score, and physical, radiological, and laboratory examinations, including measurements of BDNF levels. Motor function was assessed using the FMA, a standardized and validated tool for evaluating post-stroke motor recovery, focusing on total motor function scores. To minimize assessment bias, all evaluations were conducted by trained physicians who were blinded to the group assignments throughout the study.

For BDNF measurement, venous blood samples were collected following the World Health Organization (WHO) 2010 protocol using venous aspiration. 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 Hasanuddin University Medical Research Center (HUMRC) laboratory freezer at −80 ˚C, as recommended by IARC protocols. BDNF levels were quantified using the enzyme-linked immunosorbent assay (ELISA) technique by the manufacturer's instructions provided in the Human BDNF 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 at the post-intervention time point. Any adverse events were systematically documented based on patient-reported experiences and clinical observations. This rigorous monitoring protocol ensured comprehensive data collection while maintaining the participants' safety and the integrity of the study.

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 motor abilities 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. In contrast, lower extremity tasks included sit-to-stand training and 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 features several integrated components, such as an exercise planner that enables patients to schedule daily sessions according to 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 who were unable to complete the full session were instructed to perform at least 8 minutes of exercise, with their completion time 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 by the attending physician.

To prevent exercise-related side effects during the home-based intervention, all participants received clear guidance on maintaining adequate hydration and rest before exercising. To ensure safety during the home program, participants were given direct access to the study team for communication and instructed to report any symptoms or complaints. Symptomatic patients 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 and managed.

Data analysis

Baseline data were descriptively summarized and cross-tabulated for analysis. For normally distributed data, a paired t-test was employed to assess changes in BDNF levels and FMA scores before and after the intervention, using a comparative analysis. The Wilcoxon test was utilized for non-normally distributed data. To compare BDNF and FMA levels between the intervention and control groups, an independent t-test was applied for normally distributed data. In contrast, the Mann-Whitney test was used for non-normally distributed data. The 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.

Results

Demographic data of research participants

In this study, comprising 50 participants, the mean age was 61.2±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/m2. Upon initial assessment, the mean 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		Mean±SD/No. (%)			P
		Entire Population (n=50)	Telerehabilitation (n=25)	Control (n=25)	
Age (y)		61.2±6.68	61.64±6.54	60.76±6.78	0.774
Gender	Male	24(48)	13(52)	11(44)	0.283
	Female	26(52)	12(48)	14(56)	
BMI (kg/m^2)		23.8±2.42	24.28±2.25	23.32±2.48	
≥25 kg/m^2		18(36)	11(44)	7(28)	0.912
<25 kg/m^2		32(64)	14(56)	18(72)	
Stroke type	Hemorrhagic	27(54)	14(56)	13(52)	0.141
	Non-hemorrhagic	23(46)	11(44)	12(48)	
Stroke Onset	Subacute	17(34)	9(36)	8(32)	0.141
	Chronic	33(66)	16(64)	17(68)	
BDNF (ng/mL)		12.21±8.84	15.97±9.5	8.45±6.14	0.673
FMA		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.

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).

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, 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).

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 one-minute increase in exercise duration, the FMA score increased by 0.01, a statistically significant difference (P<0.05) (Figure 1). Additionally, analysis showed that each additional exercise session resulted in a 0.4-point increase in the FMA score, which was statistically significant (P<0.05) (Figure 2).

Linear regression analysis revealed that each additional minute of exercise duration was associated with a statistically significant increase in BDNF levels of 0.004 ng/mL (P<0.05) (Figure 3). Furthermore, each additional exercise session was correlated with a statistically significant increase in BDNF levels of 0.17 ng/mL (P<0.05) (Figure 4).

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 2. Duration and frequency of home therapeutic exercises

Variables	Mean±SD			P
	Entire Population	Telerehabilitation	Control	
Exercise duration (minutes)	1819.34±516.71	2333.56±31.82	1305.12±64.2	0.012[a+]
Exercise frequency (n)	153.06±9.62	160.2±2.24	145.92±8.83	0.003[a+]

[a]Mann Whitney test, [+]Significant with P<0.05.

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Table 3. Statistical analysis of BDNF levels and FMA scores

Variables	Mean±SD					
	Control		Telerehabilitation		ΔPre-post	
	Before	After	Before	After	Control	Telerehabilitation
FMA	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)	8.45±6.14	12.80±8.1[a+]	15.97±9.5	24.32±12.84[a+]	4.35±3.34	8.34±5.87[b+]

FMA: Fugl Meyer assessment; BDNF: Brain-derived neurotrophic factor.

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[a]Wilcoxon test, [b]Mann Whitney test, [+]Significant with P<0.05.

Table 4. Correlation of duration and frequency of exercise on changes in BDNF levels and FMA scores

Variables		Duration	Frequency
ΔFMA	ρ	0.49[a+]	0.52[a+]
ΔBDNF	ρ	0.39[a+]	0.36[a+]

[a]Spearman test, [+]Significant with P<0.05.

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Table 5. Reported side effects

Variables	No. (%)			P
	Entire Population	Telerehabilitation	Control	
Side effects	9(18)	5(20)	4(16)	0.141
Fatigue	3(6)	2(8)	1(4)	-
Cephalgia	2(4)	1(4)	1(4)	-
Migraine	3(6)	1(4)	2(8)	-
Nausea	1(2)	1(4)	-	-

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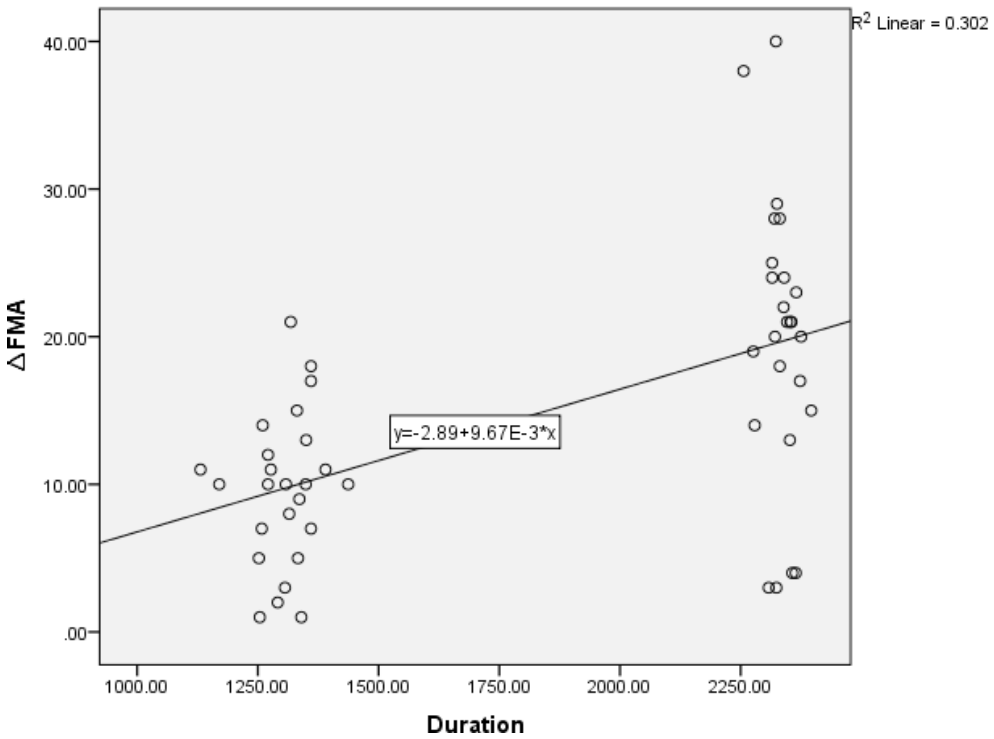


Figure 1. Linear regression of exercise duration on changes in FMA scores

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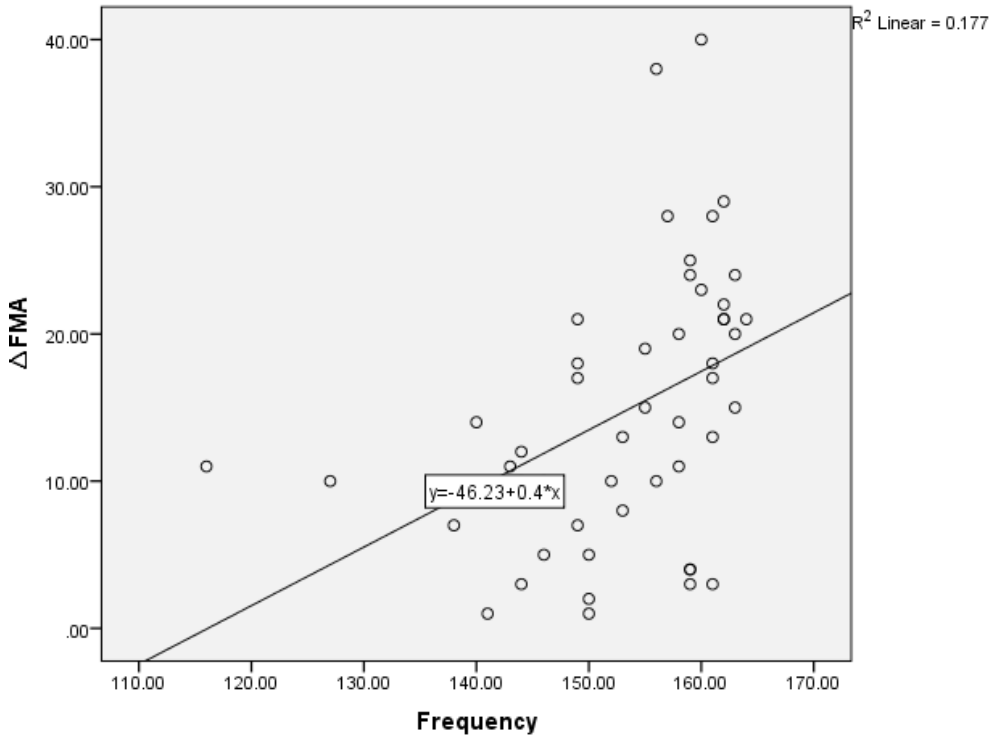


Figure 2. Linear regression of exercise frequency on changes in FMA score

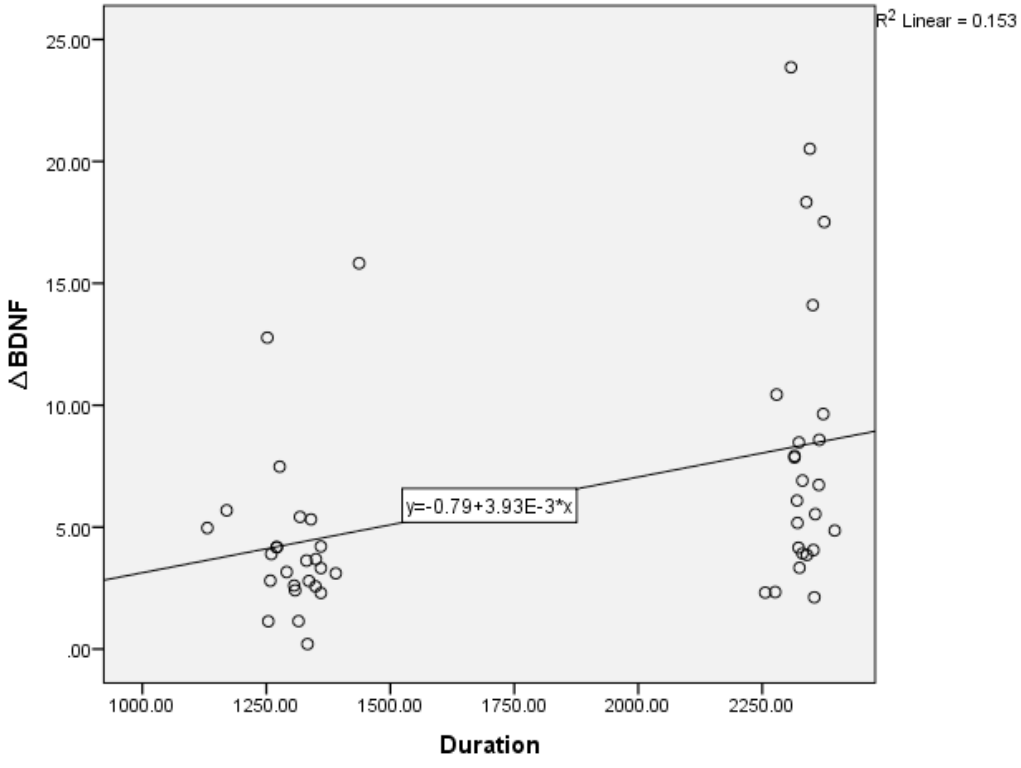


Figure 3. Linear regression of exercise duration on changes in BDNF levels

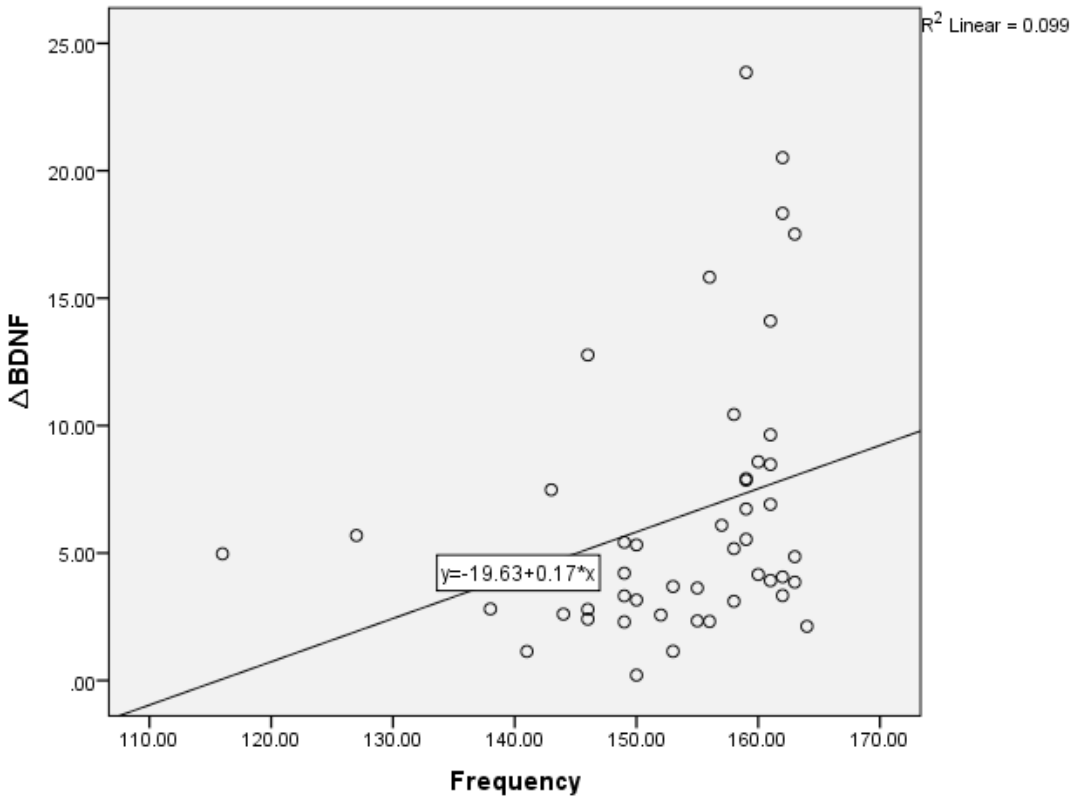


Figure 4. Linear regression of exercise frequency on changes in BDNF levels

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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 sex 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 syndrome [16]. No significant baseline differences were observed between the telerehabilitation and control groups in terms of demographics, stroke characteristics, or outcome variables (P>0.05), indicating that both groups were comparable before 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 in both groups. All 50 participants met the minimum adherence criteria and completed the study. However, minor challenges were observed. 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 exclusion thresholds. To support adherence, attending physicians were 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 highlights telerehabilitation's efficacy in promoting 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, which positively impacts exercise duration and frequency. Moreover, employing video platforms in telerehabilitation enables precise exercise execution, mitigates injury risks, and optimizes therapeutic outcomes [17–21].

Increase in FMA score and BDNF levels before and after intervention

Data analysis revealed a significant increase in FMA scores and BDNF levels following the application of mobile-based telerehabilitation, observed in both the 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 helps restore motor control and coordination, yielding functional improvements [22].

Rehabilitative exercises employing the Bobath concept showed 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, and 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 exercises, including Bobath therapy, among stroke patients. This elevation in BDNF levels highlights the role of rehabilitative interventions in promoting neuroplasticity, enabling the brain to adapt and recover effectively from injury, thereby enhancing functional recovery after 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. Utilizing reminders and instructional videos as visual aids, telerehabilitation enhances patient adherence, thereby amplifying exercise frequency and duration while optimizing its effectiveness. Moreover, this approach mitigates the likelihood of injury [20, 22].

Rehabilitation exercises are effective in enhancing FMA scores; however, 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 [24, 25]. Our study addresses this gap by demonstrating that increased frequency and duration of app-based telerehabilitation sessions are significantly associated with greater improvements in FMA 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 patients with chronic hemiparetic stroke. The results showed significantly greater improvement in FMA scores in the VR group compared to the 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, which 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 a week [28]. Chen et al. [1] 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 under real-time supervision by therapists via live videoconferencing. The control group received identical treatment in a conventional outpatient setting. The telerehabilitation group demonstrated significantly greater improvements in FMA scores than the control group [29].

Our results suggest that performing rehabilitation exercises more frequently and for a longer duration, even with a simple mobile application and without direct therapist involvement or advanced technologies, can

still lead to meaningful improvements in motor function. This supports the potential of accessible, app-based programs as practical options 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 crucial 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 all patients. Standardized protocols ensure feasibility and consistency but may not adequately address individual differences in baseline motor function, motivation, and recovery capacity [30]. Recent evidence 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 in patients with severe impairments or complex clinical profiles [31]. Moreover, while Bobath training remains important for 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 have also been shown to elevate BDNF levels. Although 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, which are core components shared with exercise strategies that 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, 22, 33]. 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 [34]; a similar phenomenon is likely to occur 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. However, 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 further 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, and can be exacerbated by prolonged or intense activity without sufficient rest intervals. Exercise-induced headaches, termed primary exercise headaches, stem from blood vessel dilation. Post-exercise nausea can result from various factors, such as dehydration, adrenergic receptor activation, and stimulation of arginine vasopressin secretion. Individual factors, such as fitness level, hydration status, nutrition, sleep quality, and comorbidities, modulate the occurrence of side effects during rehabilitation [35–38]. Despite these side effects, their incidence was not statistically significant, suggesting the safety of home telerehabilitation implementation.

Conclusion

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 12 weeks. The intervention notably enhances the duration and frequency of home exercises, leading to tangible benefits for patients.

Moreover, the observed increase in BDNF levels 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.

The intervention exhibits minimal side effects, ensuring its safety and suitability for clinical implementation. This study marks a pioneering effort, as it is 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 in post-stroke patients.

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. Individual recovery trajectories vary, with significant improvements often manifesting months after stroke onset. Moreover, the potential for long-term recovery underscores the necessity of extended observation periods beyond the study's timeframe. Post-stroke rehabilitation outcomes are multifaceted, influenced by stroke severity, comorbidities, and individual responsiveness to interventions. 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.

Ethical Considerations

Compliance with ethical guidelines

This study was conducted by the ethical principles outlined in the Declaration of Helsinki. This study was approved by the Ethics Committee of the Hasanuddin University, Makassar, Indonesia (Code: 387/UN4.6.4.5.31/PP36/2023).

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Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interpretation of the results, and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

Conflict of interest

The authors declared no conflict of interest.

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