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ORIGINAL ARTICLE

Effect of brain endurance training on fatigue and physical endurance among stroke survivors: a non-blinded randomized controlled trial

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ABSTRACT

BACKGROUND

Post-stroke fatigue (PSF) is a multifactorial impairment characterized by persistent tiredness not relieved by rest, and affects nearly half of stroke survivors, leading to poor physical endurance which limits recovery and overall quality of life. Limited evidence suggests that combining cognitive and physical training might help in reducing fatigue. Brain endurance training (BET) involves both cognitive training and physical training, targeting PSF. The study aimed to evaluate the effect of BET on fatigue and physical endurance among stroke survivors.

METHODS

A parallel group pilot randomized controlled trial was carried out in a private setting with 30 stroke survivors. Patients were randomized into two groups. Group A (n=15) received BET and group B (n=15) received conventional physiotherapy. Both groups underwent training for 65 minutes per day, thrice a week for eight weeks. Primary outcomes were Fatigue Severity Scale (FSS) and Six-Minute Walk Test (6MWT). Statistical analysis was performed using the chi-square test and independent t-test.

RESULTS

At baseline, no significant differences were observed between groups for FSS and 6MWT ($p>0.05$). The BET group reported better reduction in fatigue (FSS: 5.39 ± 0.18 to 3.48 ± 0.16, $p<0.001$) and improvement in physical endurance (6MWT: 202.03 ± 4.35 to 273.35 ± 6.26, $p<0.001$) than the control group (FSS: 5.25 ± 0.10 to 4.19 ± 0.06) (6MWT: 200.53 ± 2.72 to 222.70 ± 3.64).

CONCLUSION

Brain endurance training is a feasible and safe approach for reducing fatigue and improving physical endurance among stroke survivors.

Keywords: Stroke, fatigue, physical endurance, cognitive training, physical exercises, quality of life

INTRODUCTION

Stroke ranks as the fourth leading cause of death and the fifth leading cause of disability, serving as a major public health concern in India.[1,2] Though motor impairments have been given more importance and attention during rehabilitation, post-stroke fatigue (PSF) emerges as a common non-motor impairment experienced by most stroke survivors. Post-stroke fatigue is not just normal tiredness; it involves various factors such as physical, emotional, cognitive and perceptual, which are rarely eased by rest.[3] The onset of fatigue ranges from 10 days to as late as 2 years after stroke. Around 50% of stroke survivors feel fatigue within the first two years after stroke. The worldwide prevalence of PSF is 46.79%.[4] The PSF significantly impairs rehabilitation outcomes, quality of life and participation in daily activities. Despite its prevalence, PSF remains under-recognized and poorly understood.[5,6]

The etiology of post-stroke fatigue involves many factors. It is associated with predisposing factors (e.g. pre-stroke fatigue/depression), triggers (e.g., inflammation, brain injuries) and perpetuating factors (e.g., cognitive decline, affective disorders).[7] The strongest model to explain post-stroke fatigue is the sensory attenuation model. This model conceptualizes fatigue as a result of increased perceived effort due to inadequate attenuation of sensory inputs, which includes exteroceptive, interoceptive and proprioceptive inputs resulting from altered attentional mechanisms. Impaired attentional control results in multiple regions firing together due to neural network dysfunction.[8]

In addition to the sensory attenuation model, other proposed mechanisms include dopamine pathway disruptions and neuroinflammation. Damage to dopaminergic pathways can potentially lead to impaired motivation, arousal, movement and immunity. Chronic inflammation may impair mitochondrial function, reduce adenosine triphosphate (ATP) production and affect the neurotransmitter systems, resulting in persistent fatigue.[9,10] These overlapping mechanisms suggest that post-stroke fatigue stems from both cognitive and physiological factors rather than being merely a consequence of reduced physical activity. Fatigue after a stroke limits physical activity, leading to reduced physical endurance and vice versa. This creates a vicious cycle of fatigue and inactivity.[11]

Considering the multifactorial nature of PSF, a wide range of interventions have been identified, which aim at reducing post-stroke fatigue. The interventions are classified into ten categories, which include pharmacological, physical, cognitive and traditional therapies. These approaches reflect conventional and alternative therapies tailored to patient needs.[12]

Among the existing interventions, energy conservation techniques, motor training and drug management are widely used for managing PSF. Evidence has shown that structured physical activity, cognitive behavioral therapy and a combination of both interventions are effective for managing PSF.[13]

Anguera et al.[14] reported that a two-month intervention combining cognitive tasks with physical training led to improvements in both physical fitness and attention in older adults compared with an active control group. These improvements were sustained for up to one year. However, fatigue was not examined as a primary outcome and the participants did not include individuals with stroke. Furthermore, a systematic review and meta-analysis showed moderate-certainty evidence of an association between higher PSF and impaired fitness. These results indicate that fitness might protect against PSF, but the findings were largely correlational and did not evaluate combined cognitive training and physical training protocols.[11]

Similarly, another systematic review reported that interventions combining cognitive and physical training improve cognitive and balance outcomes compared with control groups. However, these findings are also mainly correlational, and fatigue or physical endurance were not considered as primary outcomes.[15]

Unlike previous studies, the present study directly targets central fatigue mechanisms using a structured brain endurance training (BET) protocol in stroke survivors, translating BET from sports science into stroke rehabilitation. Furthermore, fatigue severity and physical endurance were considered as primary outcomes rather than secondary observations.

To address the limitations of existing interventions, BET emerges as an innovative and novel strategy for PSF. Brain endurance training was originally developed in the field of sports science by Marcora and colleagues. They proposed that combining mental tasks with physical training will enhance performance by improving resilience against mental fatigue and thereby improving the overall performance.[16,17]

The key mechanism underlying BET lies in its influence on the prefrontal cortex. The prefrontal cortex helps in regulating endurance performance by combining the physical signals with the mental signals to manage motor output and exertion.[18] Research studies have found that after BET, the oxygen levels in the brain are maintained at a steady level with demanding physical tasks, suggesting the adaptability of the brain to resist fatigue.[19]

Although BET has demonstrated efficacy in improving resilience to fatigue and enhancing endurance in older adults and athletes, the feasibility of the intervention is yet to be investigated among stroke survivors, thus leaving a translational gap.[20,21]

Given this gap, a study is required to assess the feasibility of implementing BET among stroke survivors. Hence, this research study aims to evaluate the effect of BET on fatigue and physical endurance among stroke survivors.

METHODS

Research design

A pillot randomized controlled trial was conducted among stroke patients in a private setting in Chennai. The participants were recruited from May 2025 to July 2025. Follow-up assessments were completed by October 2025 using telephonic communication.

Study subjects

Thirty patients were recruited for the study after a thorough explanation of the study and obtaining informed consent. This randomized pilot study used a parallel group framework with an allocation ratio of 1:1. Random allocation was done by an independent statistician using a computer-generated block randomization sequence with a block size of four in the study. The eligible participants were enrolled and assigned to two groups by the primary investigator using the sealed envelope method. The participants were randomly divided into Group A- brain endurance training (BET)(n=15) and Group B- conventional physiotherapy (CP) (n=15). The outcome assessors were blinded to group allotment. Participants and the therapist were not blinded in the study. The participants enrolled in the study were those meeting the inclusion criteria, namely patients with ischemic or hemorrhagic stroke confirmed by MRI/CT scan, aged 30- 70 years, duration of stroke more than 1 month, National Institutes of Health Stroke Scale (NIHSS) score of 3-5, fatigue score of 4 and above according to Fatigue Severity Score (FSS), Functional Ambulation Classification (FAC) of 3 or above, Mini- Mental State Examination (MMSE) of 24 or more and being medically stable. Participants with severe cognitive impairment, global aphasia, history of neurodegenerative or psychiatric conditions, serious cardiopulmonary disorders or musculoskeletal conditions along with uncontrolled hypertension or diabetes were excluded from the study.

Sample size determination

Sample size was calculated using G*Power software (version 3.1.9.7) considering an independent t-test, with effect size of 0.8, α error probability of 0.05 and statistical power of 80%. The results indicated 15 participants per group for the study. Considering possible dropouts, 37 participants were initially recruited. Based on the inclusion and exclusion criteria, 30 eligible participants were finally included in the study.

Intervention

Group A (BET): The participants assigned to the intervention group took part in BET. Brain endurance training involves cognitive training, resistance training and endurance training. Each session began with 20 minutes of cognitive training, followed by 20 minutes of resistance training and 25 minutes of aerobic training. The duration of training was 65 minutes per day, thrice a week for a period of eight weeks. Therapist assistance was provided as required during each training. Assistive devices were given to the patient if required during walking.

Cognitive training: Participants in the BET group performed a 20-minute Stroop task using the Stroop effect mobile phone application.

Resistance training: The participants after completing the cognitive task were asked to perform resistance training for 20 minutes. The training consisted of squats and biceps curls. Every exercise was performed for four one-minute repetitions with 1.5-minute resting period. For biceps curls, 50-80% of the estimated 1-repetition maximum (1-RM) was used as training intensity, performed in a seated position.

Endurance training: The final component involved 25 minutes of overground walking with walking intensity of 55–80% of estimated maximal heart rate (HRmax) under the supervision of a therapist. [21]

Group B (CP): The control group received conventional physiotherapy (CP) which involved breathing exercises, mainly pursed lip breathing and diaphragmatic breathing, strengthening exercises for upper and lower extremities using TheraBand, energy conservation techniques and health education on stroke recovery and sleep hygiene. Each session was performed for 65 minutes per day, three times a week for eight weeks.

Measurements

Primary outcome measures

Fatigue severity scale: The fatigue severity scale is used for measuring fatigue in chronic conditions and neurological conditions such as stroke. The tool involves 9 statements and each statement is rated from 1 (strongly disagree) to 7 (strongly agree) on the Likert scale. The overall fatigue score is given by the average scores of nine items. Among the stroke population the scale has strong internal consistency with Cronbach's $\alpha=0.928$ and good test–retest reliability with intraclass correlation coefficient (ICC) of 0.742. Further, the scale also showed inverse correlation with short form health survey (SF-36v) ($r=-0.498$, $p<0.001$) and weak positive correlations with hospital anxiety and depression scale (HADS) anxiety ($r=0.310$) and depression ($r=0.334$), showing its validity and reliability in stroke.[22,23]

Six-minute walk test (6MWT): The six-minute walk test assesses exercise capacity, mostly used for neurological patients with functional limitations. For the stroke population, the test showed excellent test–retest reliability, even when administered with aphasia-friendly pictorial instructions, showing ICC values of 0.97 for a 15 m path and 0.94 for a 30 m path. Besides that, 6MWT also showed strong concurrent validity in the incremental cycle test with r value of 0.55 to 0.83 and predictive validity for community ambulation with area under the curve (AUC) between 0.759 and 0.795.[24,25]

Secondary outcome measures: In addition to outcome measures, feasibility outcomes such as recruitment percentage and adherence rate were included in the study.

Statistical analysis

Statistical analysis was done using IBM SPSS version 25 in the study. Descriptive statistics were used to summarize the participant demographics. Normality of data was evaluated using Shapiro-Wilk test. After assessing for normality of data, paired and independent T- tests were used for within and between group analysis. Significance was set at $p<0.001$.

Ethical clearance

Approval for the study was granted by the institutional ethical committee on human experimentation with ISRB No:017/05/2025/ISRB/PGSR/SCPT in accordance with the WMA Declaration of Helsinki.

RESULTS

Thirty seven patients were assessed, out of which 30 patients were included with no dropouts during the intervention (Figure 1). Baseline assessment was conducted before performing the intervention. There was no statistically significant difference between the groups at baseline ($p>0.05$), indicating that both groups were comparable prior to the intervention (Table 1). The pilot trial was completed after an eight-week intervention period with thirty participants. No adverse events or harms were reported during the treatment period. All the participants were analyzed for outcome measures in the study.

Primary outcomes

Both groups demonstrated significant improvements in fatigue and physical endurance with group BET showing superior improvement. Post-test comparisons between groups showed lower fatigue and longer six-minute walking distances in group BET compared to group CP. Although both interventions were statistically significant ($p<0.001$) (Table 2), group BET showed greater mean differences in FSS and 6MWT, proving that BET is superior in reducing fatigue and improving physical endurance.

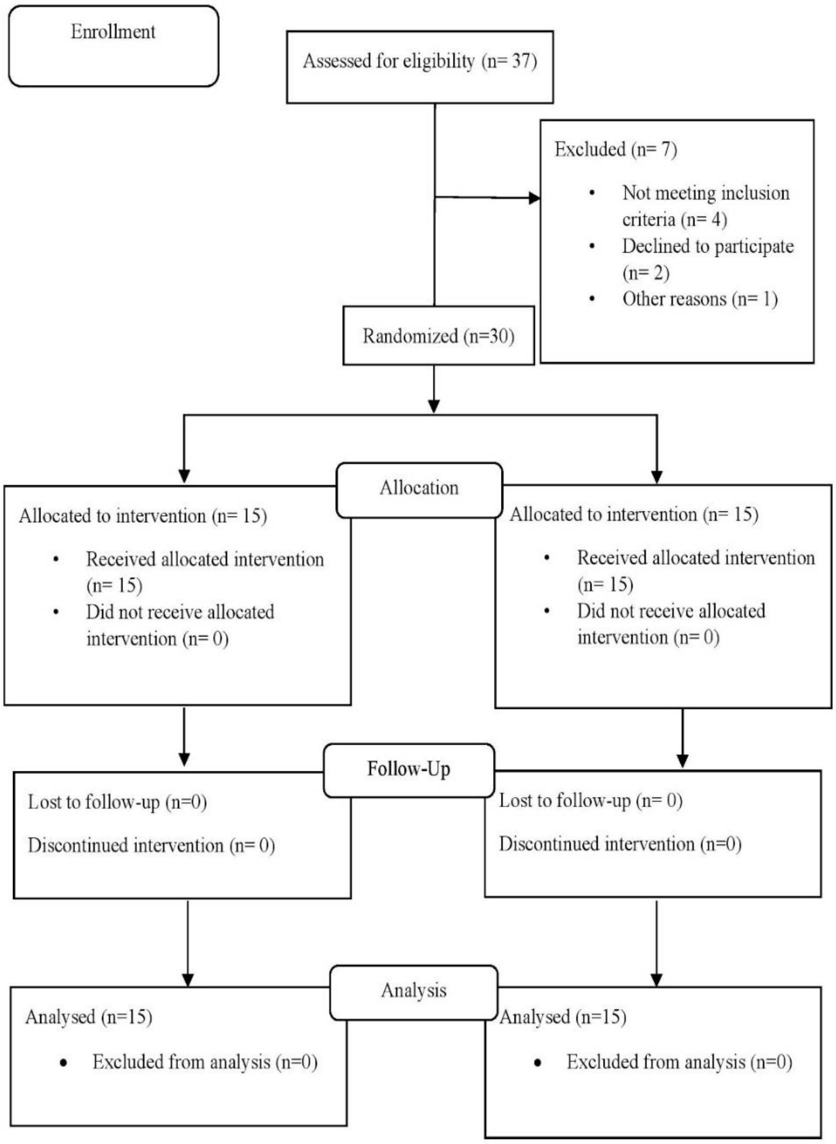

Figure 1. Consort flowchart of participants

Table 1. Baseline assessment of groups BET and CP

Variable	Group BET (n=15)	Group CP (n=15)	p value
Gender (Male/Female)	8 / 7	9/6	0.711
Age (years)	57.00 ± 4.08	57.07 ± 4.18	0.972
Stroke Type			0.701
Ischemic	9	10	
Hemorrhagic	6	5	
Diabetes mellitus	7/15	5/15	0.453
Hypertension	5/15	6/15	0.702
NIHSS	4.13 ± 0.83	3.60 ± 0.73	0.071
MMSE	26.47 ± 0.64	26.60 ± 0.63	0.583
Duration (months)	3.93 ± 0.79	3.87 ± 0.83	0.841

Note: Data presented as mean ± SD, except for gender, age, stroke type, diabetes mellitus and hypertension n (%); NIHSS: National Institutes of Health Stroke Scale, MMSE: Mini- Mental State Examination; BET: Brain endurance training; CP: Conventional physiotherapy

Table 2. Comparison of FSS and 6MWT score between the intervention groups after eight weeks intervention

Outcome Measures	Group BET (n=15)	Group CP (n=15)	p value
FSS	3.48 ± 0.16	4.19 ± 0.06	<0.001
6MWT	273.35 ± 6.26	222.70 ± 3.64	<0.001

Note: Data presented as mean ± SD. FSS: Fatigue Severity Scale, 6MWT: Six- Minute Walk Test, SD: Standard Deviation; p value< 0.001 shows statistical significance

Secondary outcomes

Feasibility metrics showed 81% recruitment rate. Adherence rate for BET was 91.6% with no attrition and adverse events reported.

DISCUSSION

This randomized controlled study demonstrated that BET is more effective than CP in reducing fatigue and enhancing physical endurance among stroke survivors. The decline in fatigue supports the hypothesis that combining cognitive tasks along with motor tasks can modulate central fatigue mechanisms, thereby improving fatigue resistance as described by Marcora's model, originally developed for endurance athletes. Their foundational study demonstrated that introducing cognitive load during physical training significantly extended time to exhaustion compared to traditional endurance exercise.(26) The current study translates this framework into stroke rehabilitation, suggesting that brain endurance training may accelerate recovery in stroke survivors.

The present findings align with the cognitive graded activity training (COGRAT) model, which involves both cognitive and motor training. Cognitive graded activity training demonstrated a significant reduction in fatigue, but had its own limitations. Each training in the model was performed for 2 hours which led to reduced exercise adherence. In contrast, BET used in the study, addresses these barriers through more interactive and time-efficient session of 65 minutes, thus improving patient adherence.(27)

A systematic review and meta-analysis on dual task training in stroke patients which combined cognitive and physical training, reported that prefrontal oxygenation and cortical activation were improved in stroke patients who underwent dual-task walking which was verified using functional near-infrared spectroscopy studies (fNIRS). These findings align with the findings of the study, suggesting that cognitive engagement facilitates improved endurance capacity.(28,29)

Previous studies in stroke survivors showed that aerobic exercise improves 6MWT performance and reduces perceived exertion, aligning with the present findings in the study showing that inclusion of endurance training in BET not only improves physical performance but also improves fatigue resilience.(30) A systematic review has shown that combining aerobic with cognitive training improves endurance (6MWT), adherence and confidence in stroke patients. Some studies in the review have also shown improvement in serum brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF-1) after the intervention, thus improving neuroplasticity and central fatigue resilience.(31)

Extending beyond stroke, these principles are further supported by evidence from other neurological conditions. A recent randomized controlled trial (RCT) on dual task training in multiple sclerosis demonstrated a significant reduction in fatigue measured by functional status score (FSS).(32) A similar study in multiple sclerosis involving combined aerobic-cognitive training and aerobic training found improvement in 6MWT and modified fatigue impact scale (MFIS) in the aerobic-cognitive training group. The study also reported decreased interleukin-17 (IL-17) levels indicating that aerobic exercise with cognitive training could alter cytokine regulation, attenuating fatigue and neuroinflammation. These findings mirror findings of BET showing that combining cognitive tasks with physical training builds endurance and fatigue resilience.(33)

Research evidence on the use of digital applications such as iHealth and STARFISH has shown that technology-based approaches might reduce fatigue. Only 13.1% of the patients reported fatigue by using the iHealth app, whereas 40% of patients reported fatigue in the control group in a study involving intracerebral hemorrhage patients. Similarly in another study involving the STARFISH game, there was a reduction in fatigue and improvement in physical activity. Together these studies have shown that mobile application-based therapy can help patients to stay motivated, aligning with the current study, serving as a powerful approach for reducing fatigue and enhancing recovery in stroke patients.[34-36]

By integrating resistance and endurance training along with cognitive training, BET targets physical and mental aspects of fatigue in stroke patients. This study has shown that BET is a feasible and noble intervention in stroke rehabilitation. Methodological quality is further supported by the randomized controlled design and the application of validated outcome measures (FSS, 6MWT). There are limitations in this pilot study. Small sample size (n=30) restricts the ability to generalize the findings and reduces statistical power. Usage of telephonic communication for follow up assessment may offer less precision than direct evaluations. The study may have been biased due to the absence of double blinding. Moreover, the study did not investigate the variation in findings across the different age groups and types of strokes, which may influence the responsiveness to the intervention. Finally, the study was done in a single center which could restrict external validity and applicability of the study to a wider stroke population. However, the study met the feasibility metrics also supporting progression readiness criteria for future randomized controlled trials.

Brain endurance training can be used in routine stroke rehabilitation, as increased fatigue and reduced physical endurance can limit daily living of stroke survivors. This structured intervention pairs cognitive tasks with physical tasks, thereby addressing the central fatigue mechanism involved in post stroke fatigue rather than focusing solely on peripheral conditioning. Improvements in fatigue levels and endurance could lead to greater independence during daily tasks, thus enhancing functional recovery. Furthermore, BET is a cost effective and feasible strategy for improving long term rehabilitation outcomes.

In order to build on these findings, future studies should involve larger multicenter studies with different stroke patients. Studies can include neuroimaging tools such as functional magnetic resonance imaging (fMRI) or electroencephalogram (EEG) to get insights into the neural mechanisms involving BET-induced shifts in fatigue and physical endurance. Analyzing patients depending on age, severity or: lifestyle factors may guide in the development of precise intervention for maximizing the effect. Also, integrating BET with motivational interviewing and using wearable biosensors for tracking fatigue could improve engagement, research accuracy and clinical decisions. Comparing BET with other fatigue management strategies is needed to determine the most effective approach for managing fatigue and physical endurance in stroke survivors.

CONCLUSION

The brain endurance training group showed greater statistical and clinical improvement in fatigue than the control group. This training was found to be a feasible and safe intervention for fatigue and improving physical endurance among stroke survivors, thereby supporting daily functioning and productivity. Monitoring fatigue levels and physical endurance could guide and shape treatment plans and evaluate the progression of patients.

Conflict of Interest

Nil.

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Author Contributions

JS contributed to conception of study, designing the study, preparing the study proposal, analyzing the data and drafting the manuscript. PS contributed to study design and manuscript drafting. DS contributed in data analysis and provided guidance in interpreting statistical data. HV contributed to manuscript drafting and revision of the manuscript. All authors contributed to critical reviewing and final approval of the manuscript.

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Data Availability Statement

The data of the study will be available from the corresponding author upon reasonable request.

Declaration of AI Usage in Scientific Writing

AI was used only for minor grammatical corrections. All data presented in this study are original.

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