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Effect of boxing exergame addition on brain-derived neurotrophic factor of elderly women

Nadia Rizki Rahmawati[1,2], Damayanti Tinduh[1,3], Ditaruni Asrina Utami[1,4], Budi Utomo[5]

[1]Faculty of Medicine Airlangga University, Surabaya, Indonesia
[2]Department of Physical Medicine and Rehabilitation, "Dr. Soetomo" General Academic Hospital, Surabaya, Indonesia
[3]Sport Injury Rehabilitation Division, Department of Physical Medicine and Rehabilitation, "Dr. Soetomo" General Academic Hospital, Surabaya, Indonesia
[4]Musculoskeletal Rehabilitation Division, Department of Physical Medicine and Rehabilitation, Airlangga University Hospital, Surabaya, Indonesia
[5]Department of Epidemiology, Biostatistics, Population Studies and Health Promotion, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia

Nadia Rizki Rahmawati **ORCID ID:** 0009-0006-0482-325X
Damayanti Tinduh **ORCID ID:** 0000-0001-6604-8152

ABSTRACT

Background and objectives. The elderly population is growing rapidly. The aging process will result in the decline of cognitive functions. The frequency of cognitive impairment is higher in women than in men, resulting in a greater risk of decreased quality of life and dependence. Brain-derived neurotrophic growth factor (BDNF) is part of neurotrophins that play a key role in the cognitive process. Physical exercise can improve cognitive function in the normal aging process by triggering increased expression of neurotrophic factors such as BDNF, one type of which is exergame boxing. This study aims to analyze the effect of the exergame boxing addition on the brain-derived neurotrophic factor of elderly women.

Materials and methods. The study subjects were 30 elderly women, divided into treatment and control groups. Participants in the treatment group practiced exergame boxing three times per week for eight weeks. Participants in both groups were required to participate in light intensity aerobic exercise five times a week for ±15 minutes. Serum BDNF levels were assessed before and after eight weeks of exercise.

Results. There was a significant increase in serum BDNF levels after the addition of exergame boxing for eight weeks in the treatment group ($p = 0.002$) with an effect size of 0,62. There was no significant increase in serum BDNF levels after eight weeks of light intensity aerobic exercise in the control group (p-value = 0.480). There was a significant difference in the treatment group who received the addition of exergame boxing training for eight weeks compared to the control group who only received light intensity aerobic exercise ($p = 0.038$).

Conclusion. The addition of boxing exergame to light intensity aerobic exercise for eight weeks can improve the BDNF serum of elderly women compared to the use of light intensity aerobic exercise alone.

Keywords: elderly women, exergame boxing, cognitive, brain-derived neurotrophic growth factor, BDNF

Abbreviations (in alphabetical order):

BDNF	– Brain Derived Nerve Factor
MET	– Metabolic Equivalent of Task
MoCA-Ina	– Montreal Cognitive Assessment Score Indonesia Version
PASE	– Physical Activity Scale for the Elderly
RPE	– Rating of Perceived Exertion
VO_2	– Oxygen consumption

Corresponding author:
Nadia Rizki Rahmawati, Damayanti Tinduh
E-mail: nadiarizkir@gmail.com, damayanti.tinduh@fkunair.ac.id

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INTRODUCTION

The number of elderly in the global population is growing rapidly. By 2050, individuals aged 60 or over will make up 22% of the world's population, with women over 65 making up 54% of the population [1]. In the aging process there will be a deterioration in cognitive functions [2]. The frequency of cognitive impairment is higher in women than in men [3]. Cognitive impairment will cause a decrease in the quality of life of the elderly and have greater risk of dementia and mortality. Cognitive impairment can also have an impact on social consequences, including loss of independence and leading to a permanent need for caregivers and health care assistant [4]. Brain-derived neurotrophic factor (BDNF) is part of a neurotrophin that plays a key role in neuronal growth and survival, supports neural plasticity, and plays an important role for synapse plasticity associated with cognitive processes [5].

Recent alternative rehabilitation approaches that target training with various physical and cognitive components in the form of interactive game-based exercises (exergames) has become available along with the rapid development of technology. These game-based interactive exercises use technology-based platforms that require users to move their bodies to complete tasks presented via video game display elements. Studies have shown that exergames are quite interesting because they can provide real interaction and feedback to users, which can increase motivation and exercise compliance. This exercise can also be applied in rehabilitation centers and in communities or homes [6].

Exergames require body movement for control during gameplay. Existing game systems (e.g., Nintendo Wii®, Dance Dance Revolution, PlayStation Eye Toys®, and Xbox® Kinect) have been shown to have the potential to increase activity, especially in less active individuals, including elderly. Exergames can be used to increase physiological responses such as energy expenditure, heart rate, oxygen consumption (VO_2), rating of perceived exertion (RPE), and metabolic equivalent of task (MET) in participants when playing [7]. Exergames can be sports simulations consisting of hand-eye coordination, flexibility and balance activities. The sports games can be boxing, tennis, bowling, golf, table tennis and so on. In these games, players can hold the remote or with a movement detector, then move their arms and legs to punch, block or swing [8]. In contrast to stationary videogames, exergames, especially boxing, detect various body movements such as jumping, kicking and punching, which encourages players to get more involved in the game and win it. This is supported by studies that indicate boxing exergaming as an exercise with adequate dose and response, in accordance with the American College of Sports Medicine exercise guidelines [7].

High-intensity exercise by listening to the music with fast tempo significantly increases BDNF expression and the number of hippocampal neurons [9,10]. Exergame boxing has elements of rhythm and group activities, flexibility, strength, and aerobics, which stimulate the release of the Brain Derived Neurotropic Factor (BDNF), which is contained in the human nervous system [11]. Game-based exercise using Nintendo Wii-Fit®, and Microsoft Kinect® sensors, effectively improves physical abilities, improving cognitive abilities (e.g. executive function, processing speed) in the elderly [6]. This study aims to analyze the effect of the exergame boxing addition on BDNF in elderly women.

MATERIALS AND METHODS

This study is a randomized controlled trial with pre-test and post-test group study design. This study was conducted at Griya Wredha Kalijudan Elderly Nursing home, Surabaya, Indonesia, from June to July 2023. The subjects of this study were 30 elderly women.

Inclusion criteria for this study were: 1) Elderly woman aged more than or equal to 60 years, 2) Ambulate independently without a walking aid, 3) Body mass index 18.5-24.9 kg/m^2, 4) Normal hearing and visual function, and 5) Willing to participate in this study by signing an informed consent.

The exclusion criteria were: 1) Cardiorespiratory disease that affects physical performance during exercise, 2) Neuromusculoskeletal disease that can hinder exercise, 3) Moderate-severe cognitive impairment (MoCA-Ina score <18), 4) Inability to stand >30 minutes, 5) Unstable hemodynamics, 6) Uncontrolled comorbidities (hypertension, heart disease, diabetes, respiratory disease, smoking, alcohol consumption, etc), and 7) Afraid of needle, 8) Consumption of drugs that can affect blood analysis.

Criteria for drop out were: 1) Research subjects are not willing to continue the research for any reason, 2) Attendance is less than 75% of the total training sessions, 3) Unable to complete the training according to the research protocol, 2 consecutive training sessions in one week from the total number of training sessions during 8 weeks of training, 4) Sick condition so unable to continue training, and 5) Subject dies.

Simple randomization performed to divide subjects into treatment and control groups with 15 subjects in each group.

Exercise intervention

The treatment group was asked to take part in a boxing exergame using an Xbox 360® Kinect. The subject is explained about game consoles, video games, examples of movements, equipment used and how to play by watching videos, demonstrations that will be carried out in a standing position. The subject is introduced first through a familiarization period which is carried out in three sessions a week where the game is played for 10-15 minutes. The familiarization period was carried out until reaching a certain level of familiarization (obtaining a hitting accuracy score of at least 80% from the game mode used in the study). The exergame boxing intervention was carried out for 25 minutes (5 minutes warm-up, 15 minutes exergame boxing and 5 minutes cool-down) per session 3 times a week for 8 weeks according to the training protocol. The core duration (exergame boxing) is added 5 minutes gradually every week until it reaches 30 minutes. Before starting the exercise, the subject was first introduced to the training protocol in the first meeting. Three doctors (researchers) and three nursing home staff were responsible for supervising the safety of participants during the intervention. During the program, subjects were asked to fill out an exercise monitoring card each time the intervention was performed to assist with monitoring.

Both groups are required to take part in light intensity aerobic exercise programmed by the nursing home itself in the form of a combination of light intensity aerobic activities and physical stretching five times a week for 10-15 minutes which is divided into components of five minutes of warm-up, five minutes of core and five minutes of cool-down.

BDNF Assessment

Brain-derived neurotrophic factor assessment session was scheduled for each participant at the same time of day (08:00-09.00 a.m.) at both pre and post-test to avoid variability due to individual diurnal fluctuations in BDNF levels. For both pre and post-test, each session started with a catheter being inserted into the participant's antecubital vein by a medical professional. Thereafter, the blood sample were drawn. Approximately 5 mL blood was collected into a clot activator tube for serum analysis. After the blood was drawn, the tube was left to clot at room temperature for at least 10-20 min, after which it was centrifuged at 2,000-3,000 rpm for 20 min to separate the serum. All centrifuging was performed at 4°C. Thereafter, samples were stored at -80°C until analysis. For the quantification of BDNF concentrations, samples were analyzed in duplicate using the Bioassay Human Free BDNF Immunoassay kit (ELISA) and the manufacturer's instructions. The BDNF concentrations measured and used for analysis were expressed in ng/mL.

The BDNF serum value was measured before the intervention and after 8 weeks of the intervention in both groups. A comparison of BDNF serum value was carried out in each group and in both groups before and after 8 weeks of intervention, 1 day after the last training session.

Statistical analysis

Data was analyzed using SPSS version 26. Wilcoxon signed ranks was used to compare the BDNF serum within each group before and after intervention. Mann Whitney U test was used to compare BDNF serum value in the two groups before and after intervention. The effect size was observed using Cohen's formula to elaborate on the statistical effect of changes. The p value is considered significant if $p < 0.05$.

RESULTS

The subjects of this research were 30 women, divided into two groups (treatment and control) with 15 subjects in each group. Six subjects were dropped out, 3 subjects from each group. At the end of the study, data analysis was carried out on 12 subject from the treatment and control group. The characteristics of subjects are shown in Table 1.

TABLE 1. Characteristics of subjects

Characteristics	Treatment Group (n=15) Means ± SD	Control Group (n=15) Means ± SD	p. value
Age (years)	69.53 ± 5.77	71.27 ± 7.32	0.477[a]
Body Weight (kg)	49.48 ± 6.48	47.60 ± 7.02	0.452[a]
Body Height (cm)	146.63 ± 6.42	145.23 ± 8.08	0.603[a]
Body Mass Index (kg/m^2)	23.69 (19.46-25.21)*	23.69 (14.73-25.19)*	0.836[b]
Physical Activity Scale for The Elderly (PASE) Score	113.40 ± 9.29	111.27 ± 15.42	0.650[a]
Mini Nutritional Assessment Score	12 (8-13)*	12 (10-13)*	0.650[b]
Perceived Stress Scale Score	11.53 ± 4.85	9.40 ± 2.95	0.157[a]
Insomnia Severity Index Score	10 ± 4,21	10.53 ± 5.05	0.756[a]
MoCA-Ina score	21.73 ± 3.33	21.20 ± 2.78	0.638[a]
BDNF serum (ng/mL)	3.83 ± 3.72	3.45 ± 2.99	0.431[a]

**)median (minimum score-maximal score) a)Independent T Test. Significant if p < 0.05. b)Mann Whitney U Test. Significant if p < 0.05*

Table 2 shows the effect of exergame training for 8 weeks on BDNF serum values in the treatment group and control group before the first exercise and after 8 weeks of training. There was a significant difference between the results of the BDNF serum value in the treatment group before and after being given exergame training with a medium effect size (p = 0.002; Cohen's d = 0.62). There was no significant difference between the BDNF serum value in the control group before and after training (p = 0.480).

Table 3 shows that there is a significant difference between the BDNF serum value between the treatment and control groups with a small effect size (p =

TABLE 2. Comparison of BDNF serum value within group

	Pre-intervention median (min-max)	Post-intervention median (min-max)	p[a]	Effect size
Treatment Group	1.66 (1.25-11.78)	2.52 (1.8-12.54)	0.002	0.62
Control Group	2.27 (1.17-3.97)	1.81 (1.42-3.28)	0.480	-

a) Wilcoxon Signed Ranks. Significant if p < 0.05

TABLE 3. Comparison of BDNF sierum value between group post intervention

	Treatment group median (min-max)	Control group median (min-max)	p[a]	Effect size
BDNF serum value	2.52 (1.80-12.54)	1.81 (1.42-3.28)	0.038	0.42
ΔBDNF serum value	0.58 (0.21-1.72)	-0.03 (-2.09-0.78)	0.004	0.59

a) Mann Whitney U Test. Significant if p < 0.05

0.038; Cohen's d = 0.42). There was also a significant difference between the ΔBDNF serum value between groups with a medium effect size (p = 0.004; Cohen's d = 0.59).

DISCUSSION

The results of this study showed that light intensity aerobic exercise with the addition of exergame boxing for 8 weeks resulted in a significant increase in BDNF serum value and a small effect size in the treatment group compared to the control group.

The results of this study are in line with a study conducted by Jeon et al. (2017) which assessed the effects of light, moderate or vigorous intensity exercise using treadmill on serum BDNF. The result of this study showed significant increase in moderate-to-vigorous intensity exercise and no significant difference in light intensity exercise group [11].

A meta-analysis study by Coelho et al. (2013) indicates that exercise can increase peripheral concentration of BDNF in healthy elderly. The same study also indicates that moderate intensity exercise is effective in improving BDNF values in the elderly [12]. Study by Feter et al. also recommend continuous moderate exercise to improve BDNF [13].

A meta-analysis study by Mohd Jai et al. (2021) indicates that exergame boxing can provide light to vigorous intensity exercise, which can be adjusted to the user's needs [7]. A study by Yu et al. (2020) also shows that exergames using Xbox 360® Kinect can provide moderate intensity exercise in middle-aged and older adults [14]. This may indicate that exergame boxing using Xbox 360® Kinect can provide moderate to vigorous intensity exercise, which is in accordance with previous studies which show that moderate intensity exercise is effective in improving BDNF concentration in elderly.

Exercise in the control group in this study was light-intensity aerobic exercise 5x/week, with a duration of 15 minutes (5 minutes of warming-up, 5 minutes of core and 5 minutes of cooling-down) for 8 weeks. In the control group, there was no significant increase in serum BDNF. This could be due to the use of light intensity exercise where that intensity is less impactful on increasing serum BDNF.

Increased BDNF levels have been associated with modulation of cognition, neuroplasticity, angiogenesis and neural connectivity. The role of BDNF in improving metabolic and cardiovascular function and delaying the onset of neurodegenerative diseases has also received increasing attention. Recent evidence suggests that BDNF levels influence structural and functional brain changes, including hippocampal neurogenesis, long-term potentiation, increased hippocampal volume, and resilience of new hippocampal neurons. Thus, increased levels of BDNF have been linked to cognitive performance, attention, and spatial memory. BDNF may work as a potential mediator of the effects of exercise on the brain because it can promote neuroplasticity through several pathways (e.g. neurogenesis, synaptogenesis, long-term potentiation, etc.). Thus, BDNF may be on the causal pathway between exercise and cognitive [15].

Boxing exergames are more engaging and the real time interaction increases player motivation during the intervention. Players can simultaneously practice movement and cognitive skills while performing the game. Exergame boxing emphasizes correct positioning for specific body movements so that players can focus on participating in the game and concentrate on the in-game interactions without paying attention to their movements. In addition, exergame boxing can be played alone at home or together with a small group, making exergame boxing more attractive to the elderly [16].

Exergames have feedback, challenges, and rewards that are made by the game maker to increase user enjoyment. High levels of enjoyment can lead to better play and physical activity over time [17]. iEnjoyment is an important factor in adherence to engage in activities related to cognitive health including physical activity, cognitive stimulating activities, and other leisure activities. Enjoyment is also linked to brain health, which contributes to the point where older adults are eager to participate in activities that can stimulate cognition and improve brain health. Engagement in enjoyable activities can also counteract the negative impact of stress through neuroendocrine processes associated with pleasure and reward that can reduce the allostatic load. Engaging in enjoyable activities can also improve mood and reduce symptoms of depression. Studies show that improved mood may provide protection from the negative effects of emotional stress [18]. This suggests that the enjoyment found in exergames may contribute to brain health, stress reduction and mood improvement which are important in cognitive improvement. Anti-depressants show a positive increase in the concentration of BDNF, based on studies of depressed individuals [19]. Exercise has the same effect as anti-depressants, especially if the exercise is done in an engaging way. Optimal BDNF levels can be achieved through a combination of therapies that have anti-depressant effects and physical activity. This can optimize BDNF in key brain regions to improve neuronal health and functional recovery of these regions [20].

The results of this study are in line with a study conducted by Cavalcante et al. (2021), who gave exergames using Xbox Kinect to healthy elderly people 2x/week for 6 weeks. The study showed a significant increase in BDNF after the intervention [21]. Another similar study was conducted by Anderson-Hanley et al. (2012), who gave exergames using cybercycling to healthy elderly for 3 months. The study showed a more significant increase in BDNF in the cybercycling group with moderate intensity compared to the exercise group using a conventional bicycle[22]. Physical exercise will stimulate molecular and cellular processes, which can modulate the process of chemical messengers such as neurotransmitters and neurotrophins such as BDNF, which results in the potentiation of functional plasticity of the brain [23].

The results of this study are in line with research by Håkansson et al. (2017) who examined the acute effects of aerobic exercise using exergame (Xbox Kinect®) for 35 minutes in subjects aged 65-85 years. The results of this study showed a significant difference in BDNF levels in the exergame group (3.29±1.00 ng/mL) compared to the cognitive group (0.211 ng/mL) and the mindfulness group (-0.55±1.27 ng/mL). This is because the exercise used in the exergame group is moderate intensity aerobic exercise which effectively increases BDNF levels in the elderly [24].

The results of this study are not in line with research by Schaeffer et al. (2022) who examined the effects of providing moderate intensity aerobic exercise using Microsoft Kinect® for 6 weeks in subjects with Parkinson's disease. The results of this study showed significant improvements in BDNF results in the intervention group and control group. However, the analysis of serum BDNF levels between groups showed no significant difference at the beginning and end of the study. This may be due to the chosen exercise protocol; exergames exercise which has a combination of moderate-intensity aerobic exercise, coordination, and speed; is not adequate enough to trigger a significant increase in BDNF levels in participants with Parkinson's disease [25].

Increased age is associated with decreased serum BDNF levels [26]. This suggests that serum BDNF levels will decrease with age, which is associated with decreased hippocampus volume and cognitive function [27]. Exercise can increase BDNF levels in the blood by regulating BDNF gene expression in the hippocampus [28]. Thus, exercise can inhibit the decline in BDNF levels associated with decreased cognitive function in the elderly.

During the boxing exergame training, no side effect were found that could affect the security and safety of the subjects. A meta-analysis by Maroni et al. (2016) showed that only a few studies showed the presence of side effects during intervention [29]. Some of these reported side effects ranged from mild discomfort to musculoskeletal pain and no studies in the meta-analysis reported serious side effects during exergame play, meaning that exergame interventions may be quite safe for the elderly. Most of these studies are carried out in laboratories, rehabilitation or community centers and provide extra security such as supervision, walking frames or walking belts, so that safety is maintained.

Limitations

This study has several limitations. The study was conducted over a relatively short period of time so it did not assess the subsequent effiects of providing exergame training. This study also did not control for other things that could influence BDNF serum such as nutritional status, stress level and sleep disturbancie, espiecially on physical activity considering that increased physical activity can also trigger an increase in BDNF levels in the blood. Using exergame boxing tools also requires skills and understanding in operating the machine, which is difficult to be done by the elderly themselves.

CONCLUSION

Boxing exergames for eight weeks in addition to light intensity aerobic exercise can increase serum BDNF levels of elderly women compared to the use of light intensity aerobic exercise alone, as it could engage the elderly in a more enjoyable and motivating way of exercise to increase BDNF levels and result in improved cognition.

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