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The Increase of Brain-Derived Neurotrophic Factor Expression after Moderate-Intensity Aerobic Exercise in Obese Women

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Abstract
Obesity is closely related to a decrease in brain-derived neurotrophic factor (BDNF) expression, which will pose a risk for metabolic disorders. Therefore, this study aims to prove the effect of moderate-intensity aerobic exercise on increasing BDNF expression in obese women. A total of sixteen obese women were selected based on predetermined criteria and were divided into 2 groups, namely the aerobic exercise group (AE) and the control group (CN). Aerobic exercise was carried out by running on a treadmill at moderate intensity (60-70 HRmax) for 40 minutes/session with a frequency of 5x/week for 2 weeks. Blood samples were taken twice before and after exercise intervention to see BDNF expression using the Enzyme-Linked Immunosorbent Assay (ELISA-kit) method. The results of the analysis showed differences in increase between the control group (1816.66 ± 689.48 vs. 1822.86 ± 467.87 pg/mL; p = 0.974) and the intervention group (2173.81 ± 705.89 vs. 3635.01 ± 699.71 pg/mL; p = 0.013). This shows that moderate-intensity aerobic exercise carried out for 2 weeks has proven effective in increasing BDNF expression in obese women.

Keywords: Aerobic exercise; BDNF expression; obesity; metabolic health

1. Introduction

Obesity is a very complex global health problem and continues to increase, causing higher morbidity and mortality and reducing life expectancy (Chen et al., 2021). The latest report states that currently, around 39% of the world's population is obese (Varela et al., 2017), making it a serious health problem as obesity is associated with many adverse health effects such as increased mortality risks, hypertension, cardiovascular diseases, and others (Maulana et al., 2021). Obesity is correlated with decreased BDNF expression, which can lead to metabolic disorders (Unamuno et al., 2018). Increasing BDNF expression can be done through increasing energy, which can be done by exercising (Jamka et al., 2021). However, appropriate and effective exercise for increasing BDNF expression is still controversial.

Several factors that influence obesity include an imbalance in energy intake and expenditure (Sholikhah & Tuah, 2021), as well as unhealthy lifestyles, which are factors that trigger a decrease in BDNF expression, which results in various diseases such as type 2 diabetes mellitus, heart disease, and other diseases (Jamka et al., 2021). Obesity is associated with metabolic disorders, including insulin resistance, high blood pressure, and inflammatory processes that play a role in the expression of cytokines and adipokines (Unamuno et al., 2018). BDNF expression plays a role in blood flow, which is correlated with metabolic disorders (Lee et al., 2016), and metabolic disorders are thought to have an excellent relationship with brain function (Uranga et al., 2019). BDNF is mainly secreted from nerve cells and plays a role in the survival ability of nerve cells, suppression of neuroinflammation, and protection of nerve damage involved in cognitive function (Lu et al., 2013). In addition, BDNF is expressed in platelets, leukocytes, and endothelial cells and plays a role in non-neuronal cells related to fat metabolism, insulin metabolism, and cardiovascular homeostasis (Amadio et al., 2017).

Previous studies revealed that regular exercise has many benefits on improving health, including boost immune system, increase muscle and bone strength, and help to maintain healthy bodyweight (Hariyanto et al., 2023). Physical exercise is also found to be an effective way to increase BDNF expression. Thus, physical activity and exercise are considered an appropriate therapy and method for obesity (Merawati et al., 2023; Pranoto et al., 2024). Exercise performed with appropriate intensity can increase muscle mass and reduce fat mass (Kolnes et al., 2021; Rejeki et al., 2023), which boosts metabolism and reduces inflammation in obesity (Pranoto et al., 2023). When the volume and intensity are also taken into account, researchers agree that exercise with moderate intensity gives more positive benefits to health (Sholikhah & Ridwan, 2021). Exercise done in a structured and regular manner can reduce fat accumulation throughout the body, although the exact mechanism is still not detailed (Zhao et al., 2017). Research conducted by Azevedo et al. (2020) reported an increase in BDNF expression in adolescents after moderate-intensity aerobic exercise intervention carried out with a frequency of 3-5 times a week with an exercise duration of 20 to 60 minutes. However, appropriate and adequate physical exercise is still a matter of debate. Therefore, this study aims to prove the effect of moderate-intensity aerobic exercise on increasing BDNF expression in obese women.

2. Method

This study was true experimental with a pretest-posttest control group design. A total of 16 obese women as subjects were selected using the following criteria: 20-30 years old, BMI ≥ 25 kg/m^2 with body fat percentage ≥ 30%, normal resting heart rate, and normal systolic and diastolic blood pressure. Subjects were randomly divided into 2 groups: the control group (CN) and the aerobic exercise (AE) group. Moderate-intensity aerobic exercise was performed by placing the subject on a treadmill, where the subject had to run at an intensity (60-70 HRmax; calculated using the 220-age formulation) for 40 minutes/session, frequency 5x/week for 2 weeks. During aerobic exercise, heart rate was controlled using the Polar Heart Rate Monitor H10. The intervention was implemented between 07.00-10.00 a.m. at Atlas Sport Club Malang (Indonesia). All procedures applied in this research have been approved by the Institute for Research and Community Service (LPPM), Research Ethics Committee (KEP) State University of Malang No. 07.12.4/UN32.20.2.9/LT/2023.

Blood samples were taken to measure BDNF expression before and after the aerobic exercise intervention, which was taken from the cubital vein in the amount of four ml. BDNF expression analysis using the (ELISA) Kits method (Catalog No. E-EL-H0010; Elabscience, Inc., USA). Data analysis used the Statistical Package for the Social Science (SPSS) application version 21.0. The normality test uses the Shapiro-Wilk test, while the homogeneity test uses Levene's test. Normally distributed data with homogeneous variance was tested using paired sample t-test and independent sample t-test. If the data was not normally distributed, then the non-parametric Wilcoxon signed-rank and Mann-Whitney tests were carried out. All data are presented as mean ± standard deviation (SD). All statistical analyses use a significant level of 5%.

3. Result

Based on the research results, Table 1 presents data on the characteristics of the subjects in this study that did not show any significant differences.

Table 1. Characteristics of study subjects

Variable	CN (*n* = 8)	AE (*n* = 8)	*p*-value
Age, yrs	22.75 ± 1.28	23.12 ± 1.64	0.619
SBP, mmHg	112.50 ± 6.40	116.37 ± 2.88	0.151
DBP, mmHg	70.37 ± 6.34	75.43 ± 2.56	0.065
HR, bpm	75.37 ± 8.14	76.87 ± 3.27	0.640
SpO_2, %	97.50 ± 1.19	97.50 ± 1.60	0.999
BT, °C	35.71 ± 0.76	35.21 ± 1.10	0.312
Height, m	1.55 ± 0.03	1.57 ± 0.05	0.319
Weight, kg	71.87 ± 4.70	72.97 ± 9.06	0.767
BMI, kg/m^2	30.01 ± 2.07	29.34 ± 1.84	0.507

Description: BMI: Body mass index; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; CN: control group; AE: Aerobic exercise (AE) group.

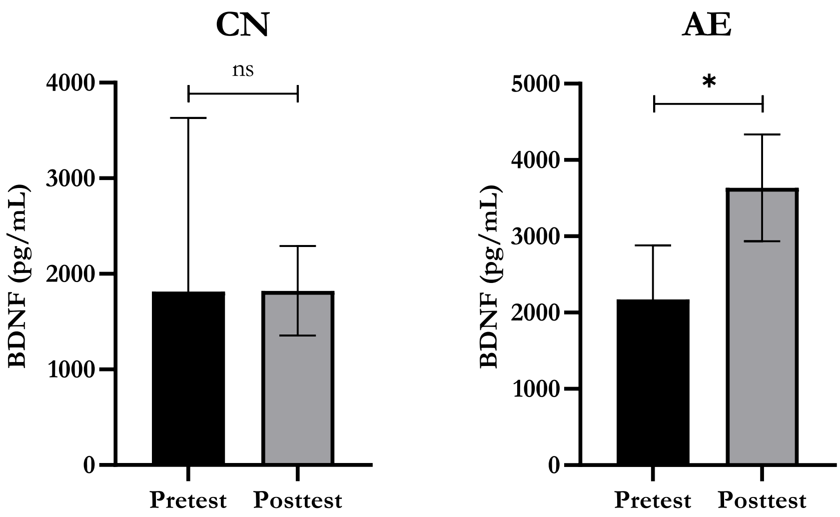

Figure 1. Results of BDNF Expression Analysis in Both Groups
Description: (ns) Not significant (p ≥ 0.05). (*) Significant with pretest (p ≤ 0.05).

The results of the paired sample t-test mean pretest and posttest BDNF expression in the control group (CN) showed 1816.66 ± 689.48 vs. 1822.86 ± 467.87 pg/mL; p = 0.974 and the aerobic exercise group (AE) showed 2173.81 ± 705.89 vs. 3635.01 ± 699.71 pg/mL; p = 0.013. Meanwhile, the results of the analysis of differences in BDNF expression between the two groups are shown in Figure 2. Figure 2 shows a difference in the increase in BDNF expression between the control group (CN) and the aerobic exercise group (AE).

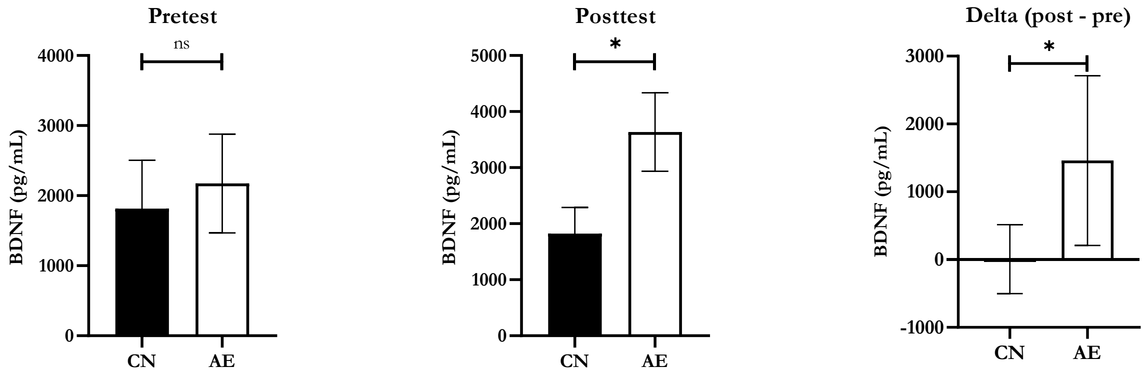

Figure 2. Pretest, Posttest, and Delta BDNF Expression in Both Groups (CN vs AE)
Description: (ns) Not significant (p ≥ 0.05). (*) Significant with a control group (CN) (p ≤ 0.05).

4. Discussion

Based on the research results, there was a delta difference in the increase in BDNF expression between the aerobic exercise group (AE) of 1461.19 ± 1251.98 pg/mL (67.24%) and the control group (CN) of 6.19 ± 509.50 pg/mL (0.34%). The effects of aerobic exercise cause an increase in BDNF expression. Aerobic exercise carried out for 2 weeks can increase the expression of BDNF circulating in the blood. These results align with previous research that reported that moderate-intensity aerobic exercise significantly increased BDNF expression (Azevedo et al., 2020). The results of prior research by Jeon & Ha (2017) reported that moderate-intensity aerobic exercise carried out for a long duration can increase serum BDNF expression.

The increase in BDNF expression is thought to be caused by the effects of aerobic exercise. Muscles will experience contractions caused by aerobic exercise, which causes an increase in energy requirements using body fat by simulating lipolysis in adipose tissue, resulting in the release of free fatty acid (FFA) into the circulation and oxidation in the muscles, which can reduce the amount of body fat mass through the brain (Mika et al., 2019). The brain is the primary source of BDNF secretion after exercise (Rasmussen et al., 2009). Some studies report that aerobic exercise can improve depressive-like behavior by increasing hippocampal BDNF expression, increasing plasticity and synaptogenesis, and reducing neurodegeneration (Lu et al., 2013). Given that histone acetylation in the hippocampus and cortex is associated with effects on learning and memory, the ketone body DBHB serves as a metabolic signal to link environmental changes with epigenetic effects on the transcription of neurotrophic factors, such as BDNF. After intensive aerobic exercise, ketone bodies are widely distributed from the liver to the heart, muscles, and brain. When glucose levels fall, ketone bodies are produced in the liver from fatty acids in the form of DBHB, and acetoacetate serves as an energy source. The effect of exercise on increasing BDNF expression may involve multiple mechanisms. For example, exercise has been reported to induce BDNF expression through induction of Fndc5 expression in the hippocampus (Wrann et al., 2013), a myokine dependent on PGC-1α and ERRα. When BDNF protein expression increases, TrkB signaling inhibits FNDC5 expression in a negative feedback mechanism. It was reported that prolonged exercise decreased the expression level of FNDC5, which was consistent with the increase in BDNF protein in the hippocampus (Wrann et al., 2013).

BDNF plays a neurological and metabotropic role, namely as a regulator of homeostasis throughout the body and fat oxidation in skeletal muscles (Jamali et al., 2020). Recent research reports that BDNF modulates cognition, angiogenesis, and neuroplasticity and strengthens neural connections because this activity is significant for learning and memory abilities and plays a vital role in better brain health performance, which plays an essential role in aspects of brain plasticity and regulates the role of metabolism (absorption glucose and fat oxidation), contributing to cardiovascular improvement and preventing neurodegenerative risks (Tapia-Arancibia et al., 2004). BDNF belongs to a family of related nerve growth factors expressed in the central and peripheral nervous systems (Mazur-Bialy et al., 2021). It has been proven that adipose tissue is a storage place for fat reserves and an active endocrine organ (Prickett et al., 2015). Research conducted by Karczewska-Kupczewska et al. (2012) reported that BDNF participates in central metabolism and disrupts the energy metabolism of peripheral organs. Many studies show that BDNF has specific effects on central pathways involved in energy expenditure. BDNF can also regulate glucose metabolism. Serum BDNF directly correlates with metabolic syndrome risk factors such as body mass index, total cholesterol, and triglycerides. Plasma BDNF is also inversely associated with the risk of insulin resistance (Karczewska-Kupczewska et al., 2012).

The aerobic exercise carried out in this study also paid attention to the intensity used because the subjects of this study were women who were obese. Aerobic exercise using high intensity can cause inflammation-related tissue damage (Cavalcante et al., 2017). Then, aerobic exercise carried out using moderate intensity will reduce tissue damage (Chen et al., 2014). Moderate-intensity aerobic exercise can reduce fat mass and prevent tissue damage (Geliebter et al., 2015). Recent research reports that exercise using moderate intensity increases the expression of BDNF in the circulation (Garcia-Suarez et al., 2021). In theory, aerobic exercise stimulates the release of neurotransmitters and neurotrophins in a way that depends on the level of activity, which acutely functions to improve nerve function and induce increased structural plasticity and brain function (Lommatzsch et al., 2005). However, other studies report that exercise duration drives this response (Dinoff et al., 2017).

The results of this study provide information related to increased BDNF expression in obese women. However, this research is not free from shortcomings because the research had a small sample size, only one parameter was measured, and the research was only conducted on obese women. This study only used a small sample size with 16 obese female subjects. Therefore, future research should include more subjects in obese women. Furthermore, this study only used one parameter to measure BDNF expression. In contrast, other parameters like irisin will provide more detailed information about BDNF expression. Thus, it is hoped that thorough research will be carried out on different parameters so that the mechanism of change in each parameter can be explicitly known.

5. Conclusion and Recommendation

Based on the research results, it can be concluded that aerobic exercise with moderate intensity 60-70% HRmax, for 40 minutes/training session, 5x/week during 2 weeks increases BDNF expression in obese women. Therefore, it is suggested that aerobic exercise can be used as a promising strategy to combat, manage, and overcome obesity in preventing an increase in risk factors and improving metabolic health.

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