Eight weeks of physical activity significantly increases BDNF levels in high school students in Indonesia: a randomized controlled trial

Ocho semanas de actividad física aumentan significativamente los niveles de BDNF en estudiantes de secundaria en Indonesia: un ensayo controlado aleatorizado

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Abstract

Background: Many factors influence cognitive function. One such factor is regular exercise. Previous studies have shown that acute physical activity increases BDNF, a biomarker of cognitive function. However, chronic exercise has not been widely discussed.
Objective: This study aims to determine the effect of eight weeks of physical activity on increasing BDNF levels in high school students in Indonesia.
Methods: This study involved 50 healthy women divided into 2 groups. The experimental group (CE) (n=25) and the control group (CO) (n=25) before and after being used in this experimental study. The study participants were between 17 and 20 years old. People were selected through random sampling, not forgetting they agreed to the informed consent given by the researcher to them as research respondents and after they were selected, two groups were formed, from which the treatment group (CE) did physical activity three times a week for eight weeks, and the control group (CO) did not receive any physical activity intervention. The study was conducted for eight weeks, starting with the collection of information about the characteristics of the subjects. The subjects were then instructed to do physical activities guided by professional physical education teachers. The training consisted of sports games including volleyball, basketball, and soccer. Before the training on the first day, blood was taken as pretest data, and after undergoing treatment for eight weeks, blood was taken again as posttest data.
Results: The results of the study showed that eight weeks of physical activity were proven to significantly increase BDNF levels in healthy women $p < 0.05$ *.
Conclusion: Therefore, it can be concluded that chronic physical activity can have a significant impact on cognitive function through BDNF levels. Therefore, regular physical exercise can be recommended to prevent cognitive decline.

Keywords

Physical activity; health; physical exercise; BDNF.

Resumen

Antecedentes: Muchos factores influyen en la función cognitiva. Uno de ellos es el ejercicio regular. Estudios previos han demostrado que la actividad física aguda aumenta el BDNF, un biomarcador de la función cognitiva. Sin embargo, el ejercicio crónico no se ha estudiado ampliamente.
Objetivo: Este estudio tiene como objetivo determinar el efecto de ocho semanas de actividad física en el aumento de los niveles de BDNF en estudiantes de secundaria en Indonesia.
Métodos: En este estudio participaron 50 mujeres sanas, divididas en dos grupos: un grupo experimental (GE) (n=25) y un grupo control (GC) (n=25). Las participantes tenían entre 17 y 20 años y fueron seleccionadas mediante muestreo aleatorio. Todas ellas firmaron el consentimiento informado proporcionado por la investigadora. Tras la selección, se formaron los dos grupos: el grupo experimental (GE) realizó actividad física tres veces por semana durante ocho semanas, mientras que el grupo control (GC) no recibió ninguna intervención de actividad física. El estudio se llevó a cabo durante ocho semanas, comenzando con la recopilación de información sobre las características de las participantes. Posteriormente, se instruyó a los participantes para que realizaran actividades físicas guiadas por profesores de educación física. El entrenamiento consistió en juegos deportivos como voleibol, baloncesto y fútbol. Antes del primer día de entrenamiento, se extrajo sangre como dato pretest, y tras ocho semanas de tratamiento, se extrajo sangre nuevamente como dato postest.
Resultados: Los resultados del estudio mostraron que ocho semanas de actividad física aumentaron significativamente los niveles de BDNF en mujeres sanas ($p < 0,05$*).
Conclusión: Por lo tanto, se puede concluir que la actividad física crónica puede tener un impacto significativo en la función cognitiva a través de los niveles de BDNF. En consecuencia, se recomienda el ejercicio físico regular para prevenir el deterioro cognitivo.

Palabras clave

Actividad física; salud; ejercicio físico; BDNF.

Introduction

One of the main causes of impairment and disability in the world is dementia (Nichols et al., 2019). One new case of dementia is predicted to be identified every three years, with the global number of dementia cases predicted to rise from 57.4 million in 2019 to 152.8 million in 2050 (Nichols et al., 2022). The progressive neurodegenerative disorders known as Alzheimer's disease and related dementias are mostly brought on by Alzheimer's disease, which mostly affects behavior, memory, and cognitive function (Zhao et al., 2025). Alzheimer's disease and other diseases are becoming more common as the world's population grows, which leads to serious public health problems that impact people individually, in families, and in healthcare systems (Pickett & Brayne, 2019). An important public health concern, dementia is an illness associated with a loss in cognitive abilities (Gale et al., 2018). Preventive actions are necessary if the dementia treatment has not yet been completed (Long et al., 2023). Physical activity is a learning approach that is commonly used to enhance cognitive performance and general wellness (Won et al., 2021). Additionally, physical activity can lower the risk of dementia, including Alzheimer's disease (Iso-Markku et al., 2022). Even though a lot of research shows that playing sports and engaging in physical activity improves brain health and memory (Gogniat et al., 2022), Sedentary behavior still has a relatively low level of study interest, however.

Numerous pharmacological treatments have been developed over the past forty years as a consequence of intensive and persistent efforts to reduce symptoms and delay the disease's progression (Ribeiro et al., 2021). There is mounting evidence that the sedentary lifestyle of contemporary society, coupled with insufficient physical activity, is a significant risk factor for impaired growth factor production, release, and regulation, which affects the development of structural and functional alterations in the brain (Ribeiro et al., 2021). Proteins known as growth factors regulate several facets of cellular activity, including migration, differentiation, proliferation, and survival (Sleiman & Chao, 2015). Each of these neurotrophic factors exerts its physiological activity by binding to one or more cellular receptors (Lippi et al., 2020). Therefore, a lack of physical exercise and mobility is closely linked to a decline in cognitive function.

A member of the neurotrophin family, brain-derived neurotrophic factor (BDNF) is crucial for fostering the survival, differentiation, and development of neurons. It is generally known that neurodegenerative diseases like Alzheimer's disease are characterized by physiological events involving decreasing levels of neurotrophic factors, including brain-derived neurotrophic factor (BDNF) and its receptor (Lima Giacobbo et al., 2019). BDNF is essential for both neuroplasticity and cognitive function (Ventriglia et al., 2013). The neurological system contains the majority of the polypeptides that comprise neurotrophins. Neurotrophins have an impact on brain nerve cell survival, differentiation, and activation (Wang et al., 2012). This factor controls the BDNF/TrkB/PI3K/Akt signaling cascade, which in turn controls neuronal lifespan and synaptic function (Jiang et al., 2023). It is essential for maintaining the health of neurons and promoting neuroplasticity.

BDNF is essential for several brain processes, including learning, memory, and emotional control. Additionally, in the context of neurodegenerative illnesses or following injury, BDNF has been connected to the protection and recuperation of the nervous system (Tsai, 2018). Additionally, it has been demonstrated that BDNF enhances cognitive performance by facilitating the generation of neurotransmitters by repairing mitochondrial function in neurons during physical exercise (Dany et al., 2025). It has been demonstrated that exercise therapies affect cognitive performance, especially executive function (Gogniat et al., 2022). Furthermore, a prior systematic study demonstrated that exercise also contributes to elevated BDNF levels (Dany et al., 2025). Research on the effects of chronic physical exercise on enhancing BDNF function is few, despite the fact that physical activity has been demonstrated to have a favorable impact on BDNF function. Thus, by measuring BDNF levels, this study will show how eight weeks of exercise can improve cognitive performance.

Research Methods

Study Design

After being randomly selected, fifty high school students were divided into two groups (n=25) for chronic physical activity intervention (CE) and (n=25) for control (CO). The control group did nothing, while the physical activity intervention group did physical activity 3 times a week for 8 weeks following a health physical education learning program that included volleyball, soccer, and basketball. The following exercise intervention will discuss the physical activity program in more detail.

Subjects

The ethics committee of the State Polytechnic of Health of Malang approved this experimental study, which was conducted in accordance with the Declaration of Helsinki. The study involved sixty healthy women (Table 1 displays subject characteristics). The researchers established inclusion and exclusion criteria to assess whether volunteers met the study requirements. Subjects were required to be between 16 and 20 years old, have a normal body mass index (BMI), be non-smokers, have no history of cancer, cardiovascular disease, or musculoskeletal disorders, not use dietary supplements or ergogenics, and be willing to participate in the study. Furthermore, respondents were not required to engage in regular exercise. Participants under the age of sixteen were not permitted to participate in the study. Our study also excluded respondents with hypertension, those with very high blood pressure (systolic ≥130 mmHg and/or diastolic ≥85 mmHg) before the activity. Furthermore, subjects were disqualified if they were taking nonsteroidal anti-inflammatory drugs (NSAIDs).

Pregnancy, starting a special diet, taking medications, and not wanting to continue the recommended exercise intervention (not attending all sessions) were reasons for exclusion. A formal consent form was read and signed by each selected participant. Two groups of 50 volunteer high school female students participated in this study: 25 were assigned to the chronic physical activity (CE) group, and 25 to the control (CO) group. The study was conducted at the Indonesian National Sports Committee (KNPI) field in Trenggalek City, East Java Province. In addition, all participants were guided by a team of certified professional physical education teachers during the exercise intervention.

Research Instruments

Blood pressure, height and weight measurements, data collection sheets, stationery, blood collection equipment, exercise equipment including game balls are some of the materials used in this research.

Physical Activity Procedures and Interventions

There were several steps in the data collection process for this study. Before the study began, subjects underwent a screening procedure. This method was based on inclusion criteria established by the researchers and allowed for data to be added or removed from the study. Next, after being educated about the study protocol, including a detailed explanation of the planned physical activity, respondents provided informed consent to participate in the study without coercion. From the trial participants, two groups were randomly selected and divided into an intervention group that received physical activity three times a week for eight weeks and a control group that received no intervention. Respondents who did not meet the inclusion criteria were excluded from the study. Furthermore, respondents who did not follow and implement the intervention as prescribed by the researchers were also excluded and not included in our analysis.

The treatment in this study was to implement game-based Physical Education, Sports, and Health learning adapted from the Physical Education, Sports, and Health curriculum at the high school level in Indonesia. However, the learning intervention focused on several sports games including soccer, volleyball, and basketball. The treatment was carried out on high school students in Trenggalek Regency. The treatment was carried out during physical education lessons, which were held once a week for eight weeks. The physical activity treatment was carried out for eight meetings, with each meeting lasting 3 x 45 minutes, with physical activity in the form of games. The treatment was supplemented with structured tasks outside of learning, namely physical activities such as running and walking with intervals of 3 minutes of running and 3 minutes of walking for a duration of 30 minutes. These activities were carried

out twice a week for eight weeks. Thus, the total activity was three times a week during the eight-week intervention.

Blood Sampling and Laboratory Examination Procedures

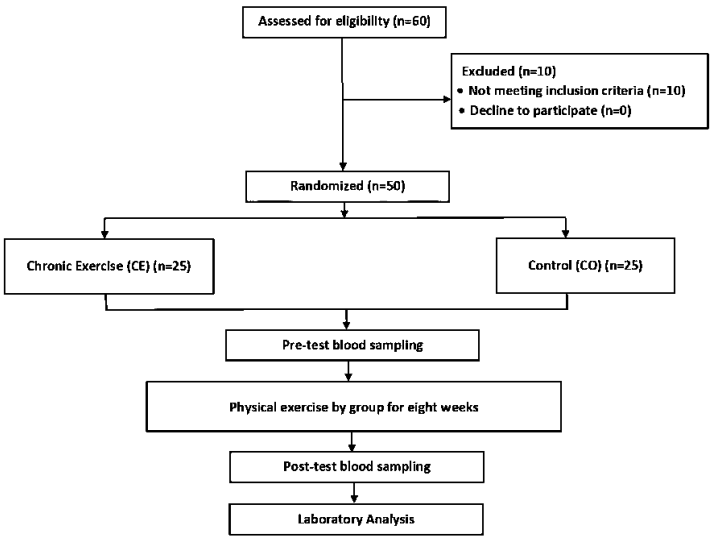
Before the exercise program began, blood samples were drawn as the initial step in collecting physiological data. A 3cc blood sample was drawn from each participant by a qualified medical professional. This blood sample was taken in the morning after a minimum of 8 hours of fasting to ensure stable biochemical levels and minimize inter-individual variability. The blood sample obtained at this stage served as pre-test data, reflecting baseline Brain-Derived Neurotrophic Factor (BDNF) levels before the subjects received the exercise intervention. The participants then underwent an eight-week physical exercise program according to a protocol determined by the researchers. This exercise program was performed regularly at a specified intensity, frequency, and duration to achieve the desired physiological state. After the exercise period ended, another 3cc of blood was drawn using the same procedures as the pre-test. This post-test blood sample was used to obtain comparative data that could be used to analyze changes in BDNF levels following the physical activity treatment.

The pre- and post-test blood samples were immediately processed in the laboratory to maintain the stability of their biochemical components. Centrifugation was performed to separate blood serum from cellular elements such as erythrocytes, leukocytes, and platelets. After centrifugation, the clear serum layer at the top of the tube was carefully separated using a sterile micropipette and stored in a clean, labeled microtube. The separated serum was then analyzed to determine BDNF (Brain-Derived Neurotrophic Factor) levels. The analysis was conducted in the Physiology Laboratory, Faculty of Medicine, Brawijaya University, Malang. The method used was the Enzyme-Linked Immunosorbent Assay (ELISA), a highly sensitive immunological technique for detecting the concentration of specific proteins in serum. The assay was performed using the Human BDNF ELISA Kit reagent, according to the manufacturer's instructions. The pretest and posttest results for each subject were then recorded, processed, and statistically analyzed to determine differences and changes in BDNF levels resulting from the physical activity program.

The final stage of this entire process was the preparation of the research report. All laboratory analysis data was systematically compiled and interpreted. This report included a description of the results, a comparative analysis of the pretest and posttest data, and a discussion based on theory and previous research findings. This final document serves as a form of scientific accountability for the implementation and results of the research, as well as a contribution to the development of exercise physiology and neuroscience related to the role of physical exercise on BDNF expression.

CONSORT flowchart

Figure 1. The CONSORT flowchart



Statistical analysis

SPSS software was used to do statistical analysis after the data was collected. To determine the mean and standard error, a descriptive analysis was performed on the data. The Shapiro-Wilk test was also used in this investigation as a normality test. Using the paired t-test approach, a difference test was created to ascertain whether the data were normally distributed. The Wilcoxon signed-rank test was used to examine the data, however if the findings indicated otherwise.

Ethics

Prior to data collection, we obtained ethical approval from the Ethics Committee of Malang Health Polytechnic with registration number DP.04.03/F.XXI.30/01055/2025.

Results

Statistics and details regarding the general description of the participants in Table 1 are presented in this section. These statistics provide information about the characteristics of each group. Mean ± standard deviation is used to display the data. There was no significant difference between the chronic exercise and control groups, based on the t-test results (p>0.05).

Table 1. Characteristics of research subjects

Data	Group	N	Mean ± SD	p-value
Age (y)	CE	25	16.52±5.10	1.000
	CO	25	16.52±5.10	
Height (cm)	CE	25	153.92±4.66	0.067
	CO	25	156.36±6.57	
Weight (kg)	CE	25	49.00±7.48	0.296
	CO	25	51.96±7.90	
BMI (kg/m^2)	CE	25	21.00±2.94	0.765
	CO	25	21.23±2.67	
Systolic (mmHg)	CE	25	111.12±11.30	0.708
	CO	25	109.96±12.13	
Diastolic (mmHg)	CE	25	73.68±6.36	0.144
	CO	25	76.92±8.33	

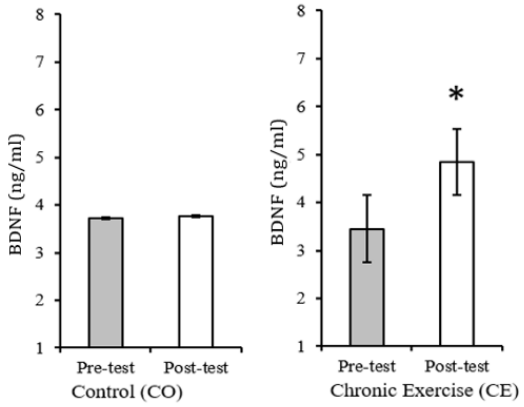
Table 2. Normality test results

Data	Group	Shapiro-Wilk	
		N	P-value
BDNF	Chronic Exercise (Pre-test)	25	0.970
	Chronic Exercise (Post-test)		0.892
	Control (Pre-test)	25	0.894
	Control (Post-test)		0.858

The BDNF data of all groups were normally distributed (p>0.05), based on the normality test in Table 2. Therefore, the paired sample t-test was the next test.

Figure 2 displays the findings of the BDNF analysis for each group between the pre-test and post-test.

Figure 2. Shows that the chronic exercise group given chronic physical activity intervention significantly increased BDNF levels in high school female students (*p<0.05).



The paired-samples t-test results are displayed in Table 3. The mean ± standard deviation is used to display the data.

Table 3. Results of BDNF (ng/ml)

Data	Group	Paired-Samples T Test	
		Mean ± SD	P-value
BDNF	Chronic Exercise (Pre-test)	3.45 ± 0.81	*0.027
	Chronic Exercise (Post-test)	4.84 ± 2.73	
	Control (Pre-test)	3.72 ± 0.87	0.950
	Control (Post-test)	3.77 ± 3.33	

Information: in the chronic exercise (CE) group with an eight-week physical activity intervention, there was a significant difference between pre-test and post-test results (*p<0.05). Meanwhile, there was no significant difference in the control (CO) group (p>0.05).

Discussion

This study set out to ascertain how eight weeks of exercise affected BDNF levels. According to earlier studies, high school students who engaged in physical activity three times a week for eight weeks saw a considerable increase in BDNF levels. The pre-test and post-test results in the control group did not differ significantly. Our findings that 16 weeks of taekwondo instruction significantly raised serum BDNF levels in healthy youngsters, demonstrating the activation of neuroplastic mechanisms akin to those of aerobic exercise, are supported by previous studies (S. Y. Cho et al., 2017). It was demonstrated that there was a substantial increase in BDNF levels following the intervention as compared to the pre-test based on a combined exercise intervention consisting of walking, balance, and resistance training performed five times per week for 12 weeks (Lukkahatai et al., 2025). This supports our findings that long-term, consistent exercise intervention does, in fact, improve cognitive performance by raising BDNF levels.

Additionally, 40 male junior high school students who had no prior medical history took part in an experimental investigation. Participants were randomized to either the stretching (control) group or one of three treadmill exercise groups: low, moderate, or high intensity. For 12 weeks, the workouts were done four times a week. Following the intervention, the students' BDNF levels increased, according to the data (Lukkahatai et al., 2025). This study demonstrates that a long-term physical exercise intervention raises BDNF levels significantly, which affects cognitive performance. In particular Griffin et al., 2011 examined the effects on young adults of both short-term and long-term cycling activity. They discovered that acute exercise enhanced both BDNF and cognitive performance, and that the group engaged in extended aerobic activity experienced a brief rise in motor-responsive BDNF expression levels. Acute physical exercise is also known to raise BDNF levels in the brain, which offers a promising paradigm for enhancing cognitive function in both healthy and sick people (Roig et al., 2013).

This earlier study looked at how a short session of high-intensity aerobic exercise affected BDNF levels and cognitive function in people with mild cognitive impairment. The findings demonstrated that in a population with mild cognitive impairment, a short session of high-intensity aerobic exercise raised peripheral BDNF (Devenney et al., 2019). Learning and memory depend on brain-derived neurotrophic factor (BDNF), which is involved in the development, maintenance, and repair of neurons (Miranda et al., 2019). Exercise intensity may have an impact on post-exercise BDNF alterations (Weaver et al., 2021), The results, however, differ according to the fraction of blood that was analyzed. For example, post-exercise increases in serum BDNF have been observed in both high-intensity interval training (HIIT) and prolonged moderate-intensity exercise (Weaver et al., 2021). Conversely, compared to steady-state exercise at lower intensities, higher intensity sprint intervals were linked to larger increases in plasma BDNF (Reycraft et al., 2020). Although little is known about BDNF levels, it has been connected to higher BDNF levels in serum and plasma after exercise at V̇O2 max (H. C. Cho et al., 2012). Although the BDNF response to low-intensity exercise in whole blood fractions has not been thoroughly studied, there is evidence that low-intensity exercise has no effect on serum BDNF levels (Hötting et al., 2016; Jeon & Ha, 2017; Piepmeier et al., 2020). Therefore, raising BDNF levels is also influenced by the intensity of physical activity.

The Mechanism of Physical Activity in Increasing BDNF Levels

Exercise has a significant impact on enhancing the quality of life for those with chronic illnesses and lowering morbidity and mortality. It has demonstrated efficacy in halting cognitive deterioration. However, the majority of people do not exercise enough, and there are few supervised programs available in global healthcare systems, which restrict the adoption of long-term plans to encourage active lives (Pollán et al., 2020). The American College of Sports Medicine (ACSM) has acknowledged that exercise has a major positive impact on disease prevention and treatment, mainly through its effects on the neurological system and brain (Romero Garavito et al., 2024). Activities like moderate-intensity treadmill walking three times a week have been demonstrated to strengthen brain networks, enhance spatial memory, and increase hippocampus capacity by 2% in older adults (55–80 years old) (Erickson et al., 2011). Furthermore, this kind of exercise improves memory by strengthening brain network connections (Vivar et al., 2016). Furthermore, the hippocampus and cerebral cortex have been shown to exhibit angiogenesis and endothelial cell growth (Lammers et al., 2020). Consistent physical activity has a demonstrable favorable impact on neuroplasticity and cognitive function, mainly by stimulating the creation of BDNF. Better neuron formation, enhanced learning and memory, and a reduction in cognitive decline are all facilitated by this rise in BDNF. Exercise so greatly enhances cognitive function and neural plasticity in addition to promoting overall well-being (Sáenz Jiménez, 2021).

Accordingly, BDNF has been identified as a key mediator of central synaptic plasticity, a process that is essential for learning and memory formation. By maintaining existing synapses and encouraging the development of new connections, BDNF has been shown to have an impact on both the facilitation and induction of synaptic alterations (Farmer et al., 2004). Exercise stimulates the production of the gene encoding BDNF, which sets off a cascade of molecular and cellular processes that support neural plasticity and neurogenesis (Romero Garavito et al., 2024). One type of physical activity that depends on the metabolic use of circulatory oxygen for muscle function is aerobic exercise. By interacting with a particular cell surface receptor called tropomyosin receptor kinase B (TrkB), BDNF can start either excitatory or inhibitory signaling pathways that help neurons survive, develop, and differentiate (Erickson et al., 2012). Depending on the target neuron, BDNF-induced TrkB activation can initiate a variety of excitatory and inhibitory signaling pathways (Wan et al., 2024). The combination of moderate exercise and enriched environments led to significant improvements in learning and memory in mice, as well as increased levels of BDNF and TrkB expression in their brains, according to a study assessing the cognitive abilities of mice exposed to different experimental conditions (enriched environments with stimulating toys and activities, while others underwent moderate exercise, such as running on a spinning wheel) (Xu et al., 2021).

Lactate, a molecule linked to enhanced learning and memory, is one way that physical activity increases BDNF expression in the hippocampus and TrkB signaling. Fibronectin type III domain-containing protein 5 (FNDC5) is a myokine involved in this process that is controlled by PGC1a and ERRa transcriptional activity. PGC-1α increases the protein with five fibronectin type III domains 5 (FNDC5) which is cleaved and released into the bloodstream as irisin (Putra et al., 2025). While the exact method by which

cleaved FNDC5 activates BDNF is unknown, prior research identifies a significant mechanism by which exercise helps the central nervous system and provides a possible treatment approach for neurological conditions (El Hayek et al., 2019). The relationship between BDNF, glutamate release, and calcium permeability is crucial for synaptic plasticity. The BDNF released from postsynaptic neurons can function in both postsynaptic and presynaptic neurons. In presynaptic neurons, BDNF increases the number of glutamate-containing vesicles, which increases synaptic transmission (Tyler & Pozzo-Miller, 2001).

AMPA and NMDA glutamate receptors become more active and more prevalent on the cell membrane in postsynaptic neurons when BDNF activates TrkB receptors. Long-term potentiation (LTP) depends on increased Ca2+ entrance into the cell, which is made possible by NMDA receptor activation. This enhanced calcium permeability, which is made possible by glutamate release and receptor activation, promotes neuronal survival, development, and synaptic function as well as neuroplasticity in important brain regions including the cerebral cortex and hippocampus (Ding et al., 2006). Additionally, it has been demonstrated that BDNF increases the density of TrkB receptors on cell membranes, which supports the growth, survival, and synaptic plasticity of neurons in regions such as the cerebral cortex and hippocampus (Haapasalo et al., 2002). Therefore, the synaptic plasticity mechanism during physical activity is centered on the interplay of BDNF, glutamate release, and calcium influx.

Strength and Limitations

This study's strength is its randomized controlled experiment, which removes the chance of unclear cause-and-effect linkages and is the most trustworthy scientific approach. We also go over our study's shortcomings, namely its small sample size. We admit that a bigger sample size would help us better understand the findings. This is undoubtedly a research limitation. Additionally, we only included physical activity-based activities like volleyball, basketball, and soccer in our intervention. Maybe in the future, we may investigate the ways in which particular activity types like high-intensity or moderate-intensity physical exercise, or a combination of both affect increases in BDNF levels. Determining the type of activity that effectively raises BDNF levels is crucial. Additionally, we limited our age rationale to people between the ages of 16 and 20. Future studies could look at increases in BDNF levels following exercise in those who are 30 years of age or older. Examining the impact of physical activity on people who are experiencing cognitive impairment is also crucial. This would make it possible to understand how exercise affects these patients' cognitive deterioration in a more tangible way.

Conclusions

Eight weeks of physical activity has been shown to significantly increase BDNF levels in young women. Therefore, regular physical activity can be recommended to increase BDNF levels.

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