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The effect of eight weeks of walking on plasma levels of dopamine and the level of depression in elderly women with Alzheimer's disease

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Abstract

Purpose: Physical activity is effective on the serum level of the monoamine neurotransmitter dopamine and also reduces psychological disorders such as depression. The aim of this study was to investigate the effect of eight weeks of walking on plasma levels of dopamine and the level of depression in elderly women with Alzheimer's disease. **Method:** In this semi-experimental study, 20 women with Alzheimer's disease with an average age of 73.5 ± 7.72 years who were suffering from moderate to severe depression according to the Beck questionnaire with the opinion of a psychiatrist in a targeted manner and the sample available for were selected to participate in the research. The subjects were randomly divided into two equal groups of 10 people, including the experimental group (walking) and the control group (without regular physical activity). The subjects in the walking group exercised on the treadmill for eight weeks three sessions per week and each session lasted 30-45 minutes with an intensity of 60-75% of the maximum heart rate. Before and after the exercise intervention, blood samples were taken from the cubital vein of all participants in a 12-hour fasting state. Serotonin and dopamine levels were evaluated by ELISA method. The results were extracted using the paired t test and covariance at a significance level of 0.5. **Results:** 8 weeks of walking led to a significant increase in dopamine levels (p=0.005) and a significant decrease in depression (p=0.001) in the experimental group compared to the control group. **Conclusion:** It seems that walking can have positive effects on some neurotransmitters and reduce the level of depression in elderly women with Alzheimer's disease.

Keywords: Walking, Dopamine, Depression, Alzheimer's.

Introduction

One of the important areas of the health of the elderly is its psychological aspect, which requires special attention and prevention of disorders such as depression and anxiety in them (Veronese et al, 2019). Depression is one of the most common disorders of old age, which is the result of various factors related to this stage of life, along with the creation of negative emotions such as sadness, anxiety, low self-esteem, social isolation, and despair in the elderly, and it is the biggest psychological problem and serious consequence. It is dangerous, which is directly related to the reduction of the quality of life of the elderly. For several reasons, the elderly are very vulnerable in terms of mental health, and about 15 to 25% of the elderly have important mental problems, so that with each decade, depression disorders increase (Paillard et al, 2015). Studies of depressed adults show that people with depressive symptoms or those with a depressive disorder have poorer, equal, or worse functioning than people with chronic medical conditions (such as cardiopulmonary disease, arthritis, high blood pressure, and diabetes) (Brown et al, 2013). In addition, depression impairs health perception and increases utilization of medical services and health care costs. The causes of depression in older people, like younger people, can be biological and social. Illnesses and physical disorders and the use of certain drugs are considered to be effective factors in the occurrence of depression. Generally, depression is one of the main causes of death worldwide, which is related to the reduction of social, occupational, and interpersonal roles (Matura et al, 2016). Worse, with age, this terrible mental condition often becomes more severe due to environmental and physical factors.

According to the reports of the World Health Organization, Alzheimer's disease is a new challenge, so that 10 million people in the world suffer from this disease and it is expected that this number will increase four times by 2050 (Kim et al. 2019). These alarming numbers are explained by the fact that the main cause of this disease is age, and by 2050, it is estimated that the population over 65 years old will be three times more than the population in 2010 and will reach one and a half billion people (Pahlavani, 2023a). Alzheimer's disease is a chronic neurodegenerative disorder that is related to learning and memory disorders and reduces the quality of life through increased levels of depression (Pahlavani, 2023b). This disease is associated with

neuropsychiatric symptoms, cognitive and functional disabilities, and in more than 80% of patients, disturbed behaviors are also observed, which, in addition to this behavior, are caused by physical, mental and environmental factors that cause feelings of insecurity, anger and depression (Chen, C., & Nakagawa, 2023). The basic mechanisms of this disease are not well understood, however, chronic neuroinflammation, increase in reactive oxygen species in the brain and hypoxia and mitochondrial dysfunction are pathological factors that lead to the formation of tau plaques and amyloid Aβ as pathological markers of Alzheimer's disease (Hassanlouei et al, 2020).

Other studies have also shown that the amount of neurotransmitters glutamate, acetylcholine, serotonin, gamma-aminobutyric acid, noradrenaline and dopamine changes during exercise (Lopez-Nieves, I., & Jakobsche, 2022). Depression is related to low levels of serotonin and norepinephrine neurotransmitters, and exercise increases the concentration of these neurotransmitters by stimulating the sympathetic autonomic nervous system (Domaszewska et al, 2020). Dopamine is mainly related to depression among psychological injuries. This connection is proposed in the hypothesis of mood disorders due to biological amines. This hypothesis simply states that depression is related to an excessive lack of serotonin and mania is related to an excess of serotonin. The reasons for the effect of aerobic exercise on reducing depression should be sought in connection with the level of some neurotransmitters such as serotonin, epinephrine and dopamine in the brain (Okahara et al, 2023). Due to the movement of the sympathetic nervous system, these exercises increase the density of these neurotransmitters. Aerobic exercises stimulate the secretion and increase of endorphins, which makes it easier to bear the pressure of the exercise and create a state of happiness. Also, aerobic exercises draw a person's attention from negative things to positive and relaxing things 18 (Zhang et al, 2023). In a 2012 study, Odell and colleagues investigated the effect of exercise on the improvement of dopaminergic and serotonergic terminal damage in methamphetamine-addicted rats and stated in their report that performing 7 days of exercise training in rats resulted in significant changes in the amount Serotonin and dopamine and their receptors in areas of the brain (Oliveira, J. T., & Pieniz, 2024). In his research, Odell suggests that voluntary exercise can be used as a non-pharmacological adjunctive treatment in improving the damage caused by Alzheimer's due to the increase in

dopamine and serotonin. Exercise can affect the brain's neurotransmitters and also the lifespan of neurons. increase by stimulating neurotrophic factors. This mechanism shows that the action of an antidepressant is valid. In this regard, among the types of sports activities and exercises, walking is more welcome due to its simplicity and ease of implementation and significant effects in many dimensions of health. However, how effective it can be in certain patients, especially those suffering from Alzheimer's and depression, remains in the aura of uncertainty due to the small number of researches and the difficulty of accessing them. Therefore, the aim of this study was to investigate the effect of eight weeks of walking on dopamine plasma levels and the level of depression in women with Alzheimer's disease.

Methods

The current research is a semi-experimental type of research. A number of 20 women with Alzheimer's disease who were suffering from moderate to severe depression based on the Beck questionnaire were selected with the opinion of a psychiatrist in a purposeful and available sample. After providing the necessary explanations, the subjects completed the written consent form to participate in the research and were randomly divided into two experimental groups (10 people walking) and control (10 people without regular physical activity). It should be mentioned that all the people participating in the research had the necessary criteria to participate in this research. These criteria were: having Alzheimer's disease, being depressed, not suffering from infectious and contagious diseases, cardiovascular, joint and mental diseases, not using drugs and cigarettes, not having any sports activity at least in the last one month. Four days before the pre-test, the subjects followed the same food program (in order to control the nutrition of the two groups) and it was decided to avoid intense physical activities and to attend the laboratory in fasting state for blood sampling. The temperature, humidity and time of the test were recorded in order to maintain these conditions in the post-test phase. The control group followed their normal life, did not do any sports activities during the 8 weeks of the research. The experimental group also continued to exercise according to the prepared exercise program.

Walking program

A walking program with an intensity of 60-70% of the reserve heart rate, which was calculated from the equation HRR=HRmax-HRrest,

was selected in each session. Here, HRrest is the person's heart rate at rest, and HRmax or the maximum heart rate was calculated from the age-220 HRmax formula (Oliveira, J. T., & Pieniz, 2024).

In order to implement the pedestrian program, a treadmill model WETL26806-0 made in China was used. The duration of each training session was 30 to 40 minutes (Ferreira et al, 2020). The heart rate of the subjects while working on the treadmill was continuously adjusted using the heart rate monitor of the control device and to maintain the intensity of the exercise within the determined limit (Ikenouchi et al, 2022). At the beginning of the activity, due to the lack of physical preparation of the subjects, the duration and intensity of the activity was gradually increased so that at the beginning of the activity, the duration of the training session was considered to be 20 minutes, after two weeks of the activity, the subjects practiced for 30 minutes. In this time interval, the activity intensity also increased gradually from 60 to 75%. This training program was implemented 3 sessions a week for 8 weeksd (Kulesskaya et al, 2023) .

Measuring tool

Initial information about depression was obtained using Beck's self-assessment questionnaire. Beck depression questionnaire BDI-II form is also one of the most common depression measurement scales. This questionnaire has a scale of 21 items and each item contains 4 options (Kulesskaya et al, 2023). Option 1 has zero points, option 2 has one point, option 3 has two points, and option 4 has three points. The sum of scores is 5-10 normal, 11-16 slightly depressed, 17-20 in need of counseling, and 21-30 towards depressed, 31-40 severe depression. The reliability and validity of the Beck Depression Test have been reported in several cases. This questionnaire has good validity in the Iranian population and the scores obtained from it can be trusted for statistical and psychometric analysis (Jimenez-Ferrer et al, 2021). In order to determine the blood levels of plasma dopamine in 2 stages, before and after the walking program, after 12 hours of overnight fasting and at rest in the morning, in the presence of an expert, 5 cc of blood was taken from the arm vein of the subjects in a sitting position. And after the aforementioned walking period, this blood sampling was repeated. The

collected blood was poured into dry sterile tubes and sent to the laboratory and centrifuged at 3000 rpm for 15 minutes (EDTA was used as an anticoagulant). After that, to measure variables, serum was separated from plasma and frozen at -70°C. In order to determine plasma dopamine, the Glory Science-Human kit, made in the USA, was used using the ELISA method (Song et al, 2024). Also, the level of depression of the subjects was determined at the same time as blood sampling (after the test) through the Beck Depression Questionnaire .

Statistical method

In this study, in order to check the normality of the data distribution, Kalmograph-Smirnov and Lone test was used. In order to describe the data, central parameters including mean and standard deviation were used. In the inferential statistics section, paired t-test was used for intra-group comparison and covariance test was used for inter-group comparison. All statistical calculations of this research were done using SPSS software. The significance level was considered $p<0.05$ in all steps .

Results

The mean and standard deviation of the anthropometric characteristics and physiological variables measured in the pre-test and post-test phases are presented in Table 1.

Table 1: Average variables measured in the control and experimental groups in the pre-test and post-test phases

Variables	Groups	Pre-test	Post-test
Weight (kg)	control	51.11±10.3	52.56±11.12
	walking	52.53 ± 9.13	51.57±8.26
Age (Year)	control	24.95	-
	walking	25.24	-
Height (cm)	control	154.01 ± 5.15	-
	walking	153.47±4.47	-
BMD (kg/m2)	Control	25.08± 4.24	25.68±4.18
	walking	24.13 ± 5.26	24.61±5.12

Table 2: The results of analysis of covariance and dependent t test regarding in-group and out-group comparison

variable	Group	levels	Standard deviation ± mean	Intragroup significance level	between groups significance level	
					Pre-test	post-test
Dopamine (ng /L)	walking	Pre-test	201.20±45.40	0.005	0.654	0.003
		post-test	264.50±42.04			
	Control	Pre-test	203.50±31.14	0.424		
		post-test	202.80±22.40			
Depression	walking	Pre-test	35±15.	0.001	0.709	0.004
		post-test	19±13			
	Control	Pre-test	34±10	0.651		
		post-test	33±8			

The results of the analysis of covariance, taking into account the pre-test values of each of the variables in the studied groups, showed that there was a significant difference between the two groups in dopamine levels after the walking intervention (Table 2). The investigated variables in each of the control and experimental groups showed that after 8 weeks of walking, dopamine levels increased significantly in the experimental group and insignificantly in the control group (Table 2). Examining the mean of pre-test and post-test depression of the training group shows that the level of depression has decreased significantly compared to the pre-test. In the case of the control group, there was a decrease in the level of depression of the subjects, but the decrease was not significant. Therefore, it can be said that activeness and regular walking had a significant effect on increasing dopamine and reducing depression in the subjects of the experimental group .

Discussion

The aim of this research was to determine the effect of eight weeks of walking on dopamine plasma levels and the level of depression in

women with Alzheimer's disease. Research findings show that eight weeks of walking can cause a significant increase in dopamine serum levels and a significant decrease in depression in the walking group compared to the control group .

Based on the obtained results, the level of depression in the training group significantly decreased compared to the control group. The results of the researches of McCann and Holmes (1984) and Dunn and colleagues (2002) found intermittent running activity to be effective in the treatment of depression, which is consistent with the results of the present study. Usually, the level of depression of athletic students is significantly lower than that of non-athletic students. And exercise reduces nervous pressure and depression in the work environment 35. Some other researchers came to the conclusion that physical exercises have a significant effect in increasing the levels of serotonin secretion as an effective hormone in improving mood. Therefore, it seems that exercise helps to reach more endorphins and serotonin in the body and maintain them for a long time during exercise. To be the results of this research are in line with the findings of Day (1994). They showed that long exercises improve serotonin and its receptors and also reduce the level of depression. Dunn et al. 2002) stated that exercise improves monoamines, including dopamine. The increase of these chemical transporters causes better transmission of nerve messages and improves mood. The effect of physical activity on serotonin levels happens quickly. Serotonin is an important brain signaling molecule for depression that not only improves mood, but also increases neuronal health by increasing nerve survival and viability, improving synaptic plasticity and stimulating nerve repair. However, physical activity acts even more integrally on nerve transmission. Movement, in addition to affecting serotonin, increases the transmission of GABA, acetylcholine and dopamine. The integrated effect of this neural transmission is the key to the antidepressant effect of physical activity. The neurotrophic hypothesis of depression has gained wide support in a short period of time. Researches have shown that the reduction of neurogenesis increases the possibility of depression. Also now, it seems that antidepressants act through integrated neurocognitive mechanisms that go beyond the action of neurotransmitters. This issue has led to the

recognition of this fact that perhaps the neurotrophic factor from the brain has a key role in depression and the common mechanism of the effect of exercise and antidepressant drugs. Brain neurotrophic factor is a member of the neurotrophin family that secretes proteins that signal neurons for growth and survival. It has been observed that physical activity stimulates the neurotrophic factor from the brain, which is caused by increasing the nerve transmission caused by movement. However, physical activity has a more general effect on the brain, modulating dopamine. This effect can be the reason for faster therapeutic response and lack of side effects of physical activity. Explain the comparison with drug treatment

In fact, psychological stimuli not only inhibit dopamine transmitters and increase the amount of dopamine release; rather, they inhibit reabsorption of serotonin and increase it in the extracellular space. Dopaminergic and glutamatergic and gamma-aminobutyric acid system receptors, which regulate the release of neurotransmitters, receptors in 5-HTIB of the mesocorticolimbic system act very strongly, which seem to cause psychological stimulation. Odell and colleagues (2012) reported that exercise specifically affects certain levels of dopamine transmitters. Aerobic exercise induces an increase in endothelial growth factor, and it is possible that it helps the damage caused by stimulating angiogenesis and has a direct effect on the neurotrophic growth factor, which restores and restores the damaged monoaminoenergic dopamine. On the other hand, long-term sports increase the activity of enzymes or endogenous antioxidants. In long-term aerobic exercise, free tryptophan increases in the plasma, enters the brain cells and causes the synthesis of serotonin and its distribution in the blood circulation .

Conclusion

In general, the findings of this research showed that walking along with drug treatments can have positive effects on increasing dopamine plasma levels and reducing depression in women with Alzheimer's disease and improving their health. Therefore, the prescription of sports activity, especially of the aerobic type, due to its effect on depression and its effect on the internal organs of the human body, can be used as a constructive solution to improve mental health and prevent depression in people with Alzheimer's in society.

Conflict of Interests

The authors declare that they have no conflict of interests to disclose.

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