Research Article

The effects of the task balance training program on the glial cell line derived neurotrophic factor levels, cognitive function, and postural balance in the old people

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Abstract
Exercise in the form of physical activity can provide neuroprotective benefits. The purpose of this study is to determine the effect of the Task Balance Training Program (TBT program) on the glial cell-derived neurotrophic factor levels, cognitive function, and postural balance in the old people. The population of this study was the old people members of the Batara Hati Mulia Gowa Foundation who were willing to participate in the study (n=66). The sample of this study was obtained through a random sampling technique to determine the treatment (n=32) and control (n=34) group. Before and after implementing the TBT Program, glial cell-derived neurotrophic factor (GDNF) levels measurement and cognitive function, and postural balance assessment were performed. Cognitive function was measured by using Montreal Cognitive Assessment (MoCA). Postural balance was measured in two ways by using the Timed Up and Go (TUG) test and Tinetti Performance – Oriented Mobility Assessment (POMA). The treatment group showed significantly greater changes than the control group in GDNF levels (1.57 (±0.84) vs. 1.24 (±0.43), *P*=0.001), cognitive function (21.34 (±4.671) vs. 19.13 (±2.670), *P*=0.001), and postural balance (TUG [17.98 (±5.67) vs. 19 (±3.96)]; POMA [24.22 (±3.25) vs. 23.03 (±3.08)], *P*=0.001) after training. The treatment group also showed a significant relationship between GDNF levels and cognitive function (*r*=0.840, *P*=0.001) and postural balance (TUG [*r*=0.814, *P*=0.001]; POMA [*r*=0.630, *P*=0.001). The TBT program affects the levels of GDNF in the old people. The TBT program involves cognitive function improvement and affects postural balance changes in the old people.

Keywords: Postural balance, Glial cell line-derived neurotrophic factor, Cognition, Physical therapy modalities

INTRODUCTION

Aging is a gradual process of the declining ability of tissues to repair or regrow themselves and maintain their normal functions. As the world's population rises, the population of older people is expected to continue to rise as well. The aging process causes continuous changes in the old people's bodies including a gradual loss of function, weakness, illness, and even mortality. In the old people, there is a decrease in muscle mass by 0.5%-1% per year, resulting in reduced strength and declining

physical condition. Inactivity and the lack of exercise may exacerbate the physical condition of the old people [1].

There are several types of degenerative diseases affecting the old people population, such as brain nerve damage or cognitive decline. A person is categorized as having a declining cognitive function, commonly known as dementia or senility, if s/he shows 3 or more of the following symptoms without disruption of consciousness: having attention and memory disturbances, place and time disorientation, and construction and execution inabilities (such as making decisions, solving problems). The cognitive function typically deteriorates as we age. As a result, this decline will impact the daily life of the old people [2, 3].

Impairments in mobility and cognition are common in many neurological conditions, making each movement requires more attention. Physiologically, attention is divided into two types; selective attention (focusing on one stimulus; for example, hearing the other person's voice when communicating in a noisy place) and divided attention (focusing on several stimuli; for example, calling while cooking). Divided attention is more often affected by neurological conditions. However, divided attention is necessary to perform two tasks simultaneously, such as walking and speaking [4, 5].

In everyday life, the ability to do work at the same time is necessary and expected. This represents the superiority of human evolution. However, when processing several stimuli and producing different responses, often there is a lower performance in one of the tasks being performed. Exercises are designed to improve walking and daily function in the old people (e.g., people with Parkinson's). More and more rehabilitation strategies employ motor training, which facilitates patients by integrating functional activities to improve daily abilities. The Task Balance Training (TBT) program is an advanced development of the strength and balance techniques and exercises with systematic procedures of repetitive muscle contractions. Muscle adaptation in the loading process causes muscle hypertrophy as the result of the training. Exercise can also improve joint flexibility and range of motion and stimulate proprioception by increasing motor unit recruitment, which activates the Golgi tendon organs and muscle spindles. The more the number of muscle fibers innervated by a motor nerve, the greater the strength of the muscle. Throughout the training, the intrafusal and extrafusal

threads receive sensory information, which will be relayed and processed by the brain to determine the necessary amount of force of the muscle co-contraction. Some of the responses will return to the extrafusal fibers and activate the Golgi tendon, resulting in better coordination between intrafusal and extrafusal fibers and afferent neurons in the muscle spindles and thus better proprioception. Sensory input, proprioception, nervous system, and muscular strength contribute to the old people's balance [6-8].

Exercise is a physical activity that can provide neuroprotective benefits of increased neurogenesis, synaptogenesis, angiogenesis, and modulation of neurochemical levels in the brain. This process is mediated by a neurotrophic factor, glial cell-derived neurotrophic factor (GDNF), which is involved in neural plasticity, particularly in brain trauma and cognitive and memory impairment. Elevated GDNF levels can increase nerve cell survival in the nigrostriatal and other areas of the cerebral cortex. Activation of dopaminergic neurons produces neurotransmitters on the pathway to the basal ganglia to control body movements. Neurotransmitters are distributed in the prefrontal cortex which functions as memory storage and in the frontal lobe to maintain cognitive functions such as problem-solving, higher-order thinking, and learning [9-11].

GDNF is currently recognized as a critical component of nigrostriatal neuron development, maintenance, and protection and as a possible factor in the maintenance and repair of dopaminergic neurons damaged by Parkinson's disease. GDNF is a member of the neurotrophic factor family, a subfamily of the transforming growth factor-β (TGFb) superfamily, along with three other structurally similar factors – neurturin, artemin, and persephin. GDNF is also involved in the hippocampal synaptogenesis, playing a role as an instructional factor by activating presynaptic locations. The GDNF family receptor-1 (GFRa1) complex is needed for proper hippocampal circuit formation [11, 12].

MATERIALS AND METHODS

Participants

The population in this study were the old people members of the Batara Hati Mulia Gowa Foundation who were willing to participate in the study. This study was conducted on the old people using the Senior Welfare Center located in Changwon. Inclusion criteria are: (a) those who have not

had difficulty walking or fall within the last 3 months, (b) those who have no serious pain, musculoskeletal damage, or neurological damage, (c) those who understand the instructions of the examiner and can perform them. Exclusion criteria are (a) a person with acute inflammation, (b) a person with visual and hearing problems. All participants understood the content of the study and participated voluntarily. The random sampling approach was utilized to determine the participants of the treatment and control groups. The treatment group was assigned to the TBT program, while the control group was provided with therapeutic communication. Blood sampling collection, Montreal Cognitive Assessment (MoCA), Timed Up and Go (TUG) test and Tinetti Performance – Oriented Mobility Assessment (POMA) were applied in both groups before and after intervention, respectively. This study received approval from the Health Research Ethics Commission, Faculty of Medicine, Hasanuddin University (828/UN4.6.5.31/PP36/2020). The research ethics recommendations included a requirement to provide an informed consent form and agreement sheet to participants who met the inclusion criteria. If the subject were willing to become a participant, they must sign the consent form. The sample who refused to participate would not be forced and their rights would be respected. The second recommendation was anonymity, which required the author to give a specific code to each participant instead of listing participants' real names. Thirdly, the author must ensure confidentiality of the participants' information and only reported relevant information in the research results.

Intervention

The exercise program performed 3 times a week for 4 weeks. The exercise program comprised cognitive exercises and motoric exercises. The details of the exercise program are shown in Table 1.

Table 1. Task balance training program

Exercise stage	Program	Time	Week
Warm-up	Stretching	5 min	
Main exercise	• Walking straight simultaneously by answering questions about day, date, month, year, person and certain places.	30-sec exercise; 30 sec rest/set 3 sets 20 min	1-4

	• Walking sideways by mentioning names of objects and words starting with certain letters. • Walking straight (tandem gait) heel position touch the toes of the other while counting numbers. • Walking pass the obstacle by repeating words and sentences.	
Cool-down	Stretching	5 min

The time of a single round of exercise was set at 30 min, which included the warm-up (5 min), main exercise (20 min), and cool-down (5 min). Each exercise was performed for 30 sec followed by 30 sec of rest, and three sets were performed with 1 min break between the sets.

Data collection

The instruments used to measure the variables studied consisted of a Riester mercury sphygmomanometer, One Med stethoscope, questionnaire, informed consent, and stopwatch. The instruments for blood sampling collection consisted of a 3-cc syringe, 25 G wing needle, tourniquet, 3-cc EDTA tube, plaster, and alcohol cotton ball. The instruments for storing blood samples consisted of a centrifuge, Eppendorf tube, filter tip, micropipette, and -20^{0}C refrigerators. To measure GDNF levels, the Enzyme-Linked Immunosorbent Assay (ELISA) test was performed using a Kit GDNF. Blood tests were performed on all subjects after 12 hr of fasting. The blood was drawn at the same time under the same conditions before and after the intervention. A disposable needle was used to draw 3 mL from the anterior cubital vein. The blood was stored in serum separating tubes for serum and centrifuged for 10 min at 3,000 rpm; 200 µL of the serum was stored in a sample tube. The GDNF levels were assessed using the enzyme linked immunosorbent assay (ELISA) method with the GDNF ELISA kit (Mybiosource, Inc., San Diego, USA, MBS3800791), respectively. Cognitive function was measured by using Montreal Cognitive Assessment (MoCA). Postural balance was measured in two ways by using the Timed Up and Go (TUG) test and Tinetti Performance – Oriented

Mobility Assessment (POMA). The Timed Up and Go (TUG) test was conducted to evaluate changes in dynamic balance following the intervention. The subject began in a seated position. At a start signal, they stood up, walked 3 m away, turned around, walked back, and returned to a seated position. The time was measured from the start signal to when the subject was seated in the chair again.

Statistical analysis

The data were analyzed using univariate analysis (frequency distribution) to produce the distribution and percentage of each variable. Paired t-test was also conducted to determine the effect of the TBT program on GDNF levels, cognitive function, and postural balance. Paired sample t-test measured the difference experienced by the subjects from the same group after being subjected to treatment. Furthermore, to find the mean difference of each variable, an independent sample t-test was performed. The independent sample t-test was carried out to examine if there was a statistically significant mean difference between the two independent groups. To examine the correlation between GDNF levels with cognitive function and postural balance, Spearman's correlation test was performed using the SPSS program. The Spearman's correlation test was selected in this study because the type of data to be processed from both independent and dependent variables was ordinal data. Spearman's correlation test was also able to provide the correlation coefficient value and show the direction of the relationship, whether it was negative or positive.

RESULTS

Sample characteristics

The participant' characteristics are presented in Table 2. In the treatment group, the proportion of participants in the younger group (62.5%) is higher than the older group (37.5%). Similarly, in the control group, the proportion of participants in the younger group (76.5%) is also higher than the older group (23.5%) with the mean age for the treatment and control group was 68.09 (±3.00) and 67.32 (±2.28), respectively. The proportion of female participants in the treatment group (59.4%) is higher than male participants (40.6%). Likewise, the number of female participants in the control group (67.6%) is also higher compared to the male participants (32.2%). The mean GDNF levels for

the treatment and control groups are 1.57 (±0.84) and 1.24 (±0.43), respectively. The mean cognitive function for the treatment and control groups is 21.34 (±4.671) and 19.13 (±2.670), respectively. In this study, both TUG and POMA tests are employed to examine the risk of falling in old people participants. The mean TUG test scores in the treatment and control groups are 17.98 (±5.67), and 19 (±3.96), respectively. The mean POMA scores in the treatment and control group are 24.22 (±3.25) and 23.03 (±3.08), respectively.

Table 2. Participants' characteristics

Baseline Characteristics	Value	
	Treatment (n=32)	Control (n=34)
Age (years old)	68.09 (±3.00)	67.32 (±2.28)
Younger old people (60-69)	20 (62.5)	26 (76.5)
Older old people (≥ 70)	12 (37.5)	8 (23.5)
Sex		
Male	13 (40.6)	11 (32.4)
Female	19 (59.4)	23 (67.6)
GDNF level (ng/mL)	1.57 (±0.84)	1.24 (±0.43)
Cognitive function (MoCA)	21.34 (±4.67)	19.13 (±2.67)
Postural balance (TUG)	17.98 (±5.67)	19 (±3.96)
Postural balance (POMA)	24.22 (±3.25)	23.03 (±3.08)

Values are presented as number (%) or mean ± standard deviation.

GDNF, glial cell line-derived neurotrophic factor; MoCA, montreal cognitive assessment; TUG, timed up and go; POMA, performance – oriented mobility assessment.

The effect of the TBT program on GDNF levels, cognitive function, and postural balance.

The mean GDNF level before treatment is 0.90 (±0.31). The GDNF level rises to 2.24 (±0.63) after treatment, suggesting a statistically significant difference in the mean GDNF levels before and after treatment (Table 2). The mean values of cognitive function pre-and post-treatment are 18.03 (±3.16) and 24.66(±3.42), respectively; hence,

there is a statistically significant difference between the mean value of cognitive function before and after treatment. The mean TUG test scores before and after treatment are 21.97 (±4.00) and 14.00 (±4.04), respectively. As a result, there is a statistically significant difference in the mean TUG test scores before and after treatment. The mean POMA scores pre-and post-treatment are 22.59 (±3.06) and 23.47 (±3.06), respectively. Thus, there is a statistically significant difference in the mean value of the POMA scores before and after treatment. The GDNF levels in the treatment group increased with a *P*-value < 0.001, indicating that the TBT program influenced the GDNF levels. Cognitive function was significantly improved in the treatment group with a *P*-value < 0.001, indicating that the TBT program affected cognitive performance. With a p-value a *P*-value < 0.001 for both the TUG and POMA scores, it can be concluded that there is a significant improvement in postural balance in the treatment group, suggesting that the TBT affected postural balance (Table 3).

Table 3. Comparison of GDNF levels, cognitive function, postural balance (TUG), and postural balance (POMA) between before and after intervention

Variable	Group	Pre	Post	*P*-value
GDNF Levels	Treatment	0.90±0.32	2.24±0.63	0.001
(ng/mL)	Control	1.24±0.42	1.24±0.43	0.815
Cognitive Function	Treatment	18.03±3.16	24.66±3.42	0.001
(MoCA)	Control	19.09±2.71	19.18±2.67	0.697
Postural Balance	Treatment	21.97±4.03	14.00±4.04	0.001
(TUG)	Control	19.32±3.98	18.68±3.98	0.034
Postural Balance	Treatment	21.91±2.73	26.53±1.74	0.001
(POMA)	Control	22.59±3.09	23.47±3.06	0.001

Values are presented as mean±standard deviation.

GDNF, glial cell line-derived neurotrophic factor; MoCA, montreal cognitive assessment; TUG, timed up and go; POMA, performance – oriented mobility assessment.

Table 4. Comparison of GDNF levels, cognitive function, postural balance (TUG), and postural balance (POMA) between treatment and control group

Variable	Treatment	Control	*P*-value
GDNF (ng/mL)	2.24±0.63	1.24±0.43	0.001
Cognitive Function (MoCA)	24.66±3.42	19.18±2.67	0.001
Postural Balance (TUG)	14.00±4.04	18.68±3.98	0.001
Postural Balance (POMA)	26.53±1.74	23.47±3.06	0.001

Values are presented as mean±standard deviation.

GDNF, glial cell line-derived neurotrophic factor; MoCA, montreal cognitive assessment; TUG, timed up and go; POMA, performance – oriented mobility assessment.

The mean values of GDNF levels for the treatment and control groups are 2.24 (± 0.63) and 1.24 (± 0.43), respectively. The mean values of cognitive function for the treatment and control group are 24.66 (± 3,42) and 19.18 (± 2,67), respectively. The mean TUG scores for the treatment and control groups are 14.00 (± 4.04), and 18.68 (± 3.98), respectively. The mean POMA scores for the treatment and control groups are 26.53 (± 1.74) and 23.47 (± 3,06), respectively. Therefore, it can be concluded that there is a statistically significant difference in the mean POMA score between the treatment and control groups. All variables measured in this study showed a statistically significant difference between the treatment and control groups ($P < 0.001$) (Table 4).

Table 5. Relationship between GDNF levels, cognitive function, and postural balance

Variable	Correlation Coefficient	*P*-value
GDNF Levels - Cognitive Function (MoCA)	0.840	0.001
GDNF Levels - Postural Balance (TUG)	0.818	0.001
GDNF Levels - Postural Balance (POMA)	0.630	0.001

GDNF, glial cell line-derived neurotrophic factor; MoCA, montreal cognitive assessment; TUG, timed up and go; POMA, performance – oriented mobility assessment.

The relationship between GDNF levels and cognitive function, with a correlation coefficient value of 0.840. According to the degree of closeness between the two variables, there is a strong relationship and positive linear pattern, indicating that the higher one's GDNF level, the higher his/her cognitive function will be. The value of *P*-value < 0.001 signifies a relationship between GDNF levels and cognitive function. The correlation coefficient values of 0.818 (TUG) and 0.630 (POMA) indicate a correlation between GDNF levels and postural balance. According to the degree of closeness between the two variables, a strong relationship and positive linear pattern indicate that the higher one's GDNF levels, the better one's postural balance will be. The value of *P*-value < 0.001 signifies a relationship between GDNF levels and postural balance, either measured using the TUG test or POMA (Table 5).

DISCUSSION

In the old people, motor tasks require a higher level of control in executive information and memory processing, making it difficult for the old people to perform activities simultaneously (e.g., walking while conversing). This indicates that one or both abilities have weakened due to declining metabolism in the frontal area. It is necessary to combine physical activity with cognitive stimulation; hence, a TBT Program was designed to enhance cognitive capacities and slow brain aging by engaging cognitive and motor stimulations. Physical activity can provide neuroprotective benefits mediated by GDNF. GDNF is an essential protein that is required to develop, maintain, and protect nigrostriatal neurons, particularly in protecting and restoring dopamine neurons affected by Parkinson's. Therefore, it is necessary to determine whether the TBT Program affects GDNF levels, cognitive function, and postural balance in the old people. The effect of the TBT program on the GDNF levels, cognitive function, and postural balance in the old people will be discussed according to the research objectives, as follows:

The Effect of the TBT program on GDNF levels in the old people

Glial cell line-derived neurotrophic factor (GDNF) supports neuroplasticity in the neuromuscular system from childhood to maturity. To maintain a healthy neuromuscular system, a steady supply of neurotrophic factors (NF) is required to support motor neuron growth and maturation. NFs contribute

to the survival of motor neurons throughout their lives by encouraging their growth during embryonic development, maintaining them till adulthood, and regenerating them after injury [13].

In adults and the old people, NF has been shown to act independently and synergistically in promoting healthy neuronal development and plasticity. Among the several known NFs, GDNF is the strongest neurotrophic factor in promoting motor neuron survival in vitro and in vivo [14].

GDNF has neurotrophic characteristics by being expressed in target skeletal muscle tissue, being transported retrogradely to the axonal cell body, and sustaining motor neurons throughout their lifespan. GDNF is up to 2,500 times more potent than other neurotrophins, preserving approximately 100% of axotomized motor neurons and the only factor capable of reversing axotomy-induced motor neuron atrophy [13].

The results of this study are in line with the study conducted by Gyorkos et al. [13] on rats being randomly assigned to running training (running group), swimming training (swimming group), or sedentary control group. The results indicated an increase in GDNF protein content ($P < 0.05$). GDNF is activity-dependent, and by changing the type and intensity of exercise, it is possible to increase the protein content of GDNF in slow and fast-twitch muscle fibers. This also strengthens the notion that GDNF affects the NMJ structure in slow and fast-twitch muscle fibers. Exercise may enhance the protein content of GDNF in skeletal muscle, resulting in improved NMJ plasticity and neuromuscular health [13]. Likewise, the results of the study conducted by McCullough [15], long-term exercise of voluntary running for 6 months showed a similar result ($P < 0.05$). These findings suggest that a rise in the GDNF protein content in the muscles of the treated mice. It can be inferred that intensified physical activity increases structural neuroplasticity in the neuromuscular junction (NMJ) elements, resulting in improved neuromuscular function [15].

The training protocol was adequate to produce an increase in GDNF level, providing additional evidence for activity-dependent neurotrophic support mechanisms. The CSA of SOL muscle fibers reduced in response to this exercise plan shows that these muscles are engaged during this activity. The reduction in fiber diameter caused by training is an indication of recruitment. It can be viewed as an excellent adaptation to a faster oxygen, carbon dioxide, and waste product exchange, which prolongs fatigue time [13, 14].

The Effect of the TBT program on Cognitive Function in the old people

A high level of cognitive function is critical for integrating and interpreting sensory-motor information necessary for maintaining equilibrium in the everyday environment. Individuals frequently complain about their memory as they age. However, compared to memory, other cognitive domains such as processing speed, executive function, and attention are more affected, which can have an impact on sensorimotor functions. Executive function and attention deficits have been linked to deteriorating physical function, such as slower gait and poor balance [5] (Taylor et al., 2019).

Exercise is a feasible strategy for improving cognition and delaying the onset of cognitive decline. This is a practical, non-pharmacological, and low-cost technique that has been thoroughly investigated: aerobic training, strength training, or a combination of both, have been shown to improve brain structure and function, behavior, and cognition. Multimodal training is suggested in the recommendations. These recommendations are based on the studies that have investigated how exercise contributes to physical and cognitive function. It is advised for the old people to perform a moderate exercise and monitor their heart rate while performing it [16].

The findings of this study are supported by the survey conducted by Jardim et al. [16], showing that there is an effect of Dual-Task Exercise (DTEx) on cognitive function in the old people. The effects of GDNF on neuronal atrophy, a condition associated with cognitive decline in old age, were investigated in another study. GDNF has exceptional regenerative and therapeutic capabilities on nigrostriatal dopaminergic neurons. GDNF was found to be a stable neurotrophic factor that operates on a wide variety of nerves and displays neuroprotective effects in various experimental paradigms of nerve damage. For instance, GDNF protects nerves against harms produced by axotomized neurons, experimental brain trauma, and ischemia, as well as some excitotoxic and neurotoxic injury. Therapeutic administration of GDNF has raised hopes that it might be used to prevent or treat Parkinson's disease, amyotrophic lateral sclerosis, and Huntington's disease. Thus, it has been established that astrocyte-mediated GDNF protects motor neurons and dopaminergic neurons in

vivo. Endogenous GDNF is necessary for cognitive abilities, as shown in a study of heterozygous mice with targeted GDNF gene deletion which resulted in a reduced spatial learning capacity. Spatial memory and learning are associated with proper hippocampal function. Memory declines linked with age have long been acknowledged to be equivalent to those induced by bilateral hippocampal lesions. Numerous drugs, including neurotrophins, antioxidants, and cholinergic agents, have been investigated in older animals in the hope of identifying a successful and safe memory reversal therapy. Normal aging processes and memory loss are impaired, particularly in Alzheimer's disease-induced pathological aging. The impact of GDNF on age-related cognitive decline has not been fully explored [17].

There is mounting evidence that GDNF levels may play a role in the etiology and progression of illness, as they do in Alzheimer's disease. According to the study by Sharif et al. [18], the mean GDNF levels in individuals with Alzheimer's disease were 2.45 (±0.93) ng/mL and 4.61 (±3.39) ng/mL in age-matched controls. GDNF levels were significantly lower in individuals with Alzheimer's disease than in age-matched controls ($P < 0.001$). Furthermore, GDNF levels were shown to be strongly associated with disease severity ($P < 0.001$) and cognitive impairment ($P < 0.001$). The study discovered that GDNF levels fell considerably in people with Alzheimer's disease, implying that GDNF may have a role as a disease biomarker. This finding is consistent with Wang et al. [19], who attempted to determine whether GDNF levels in plasma were abnormal in late-onset depression (LOD) and whether they were linked with cognitive impairment in LOD [19].

The Effect of the TBT program on Postural Balance in the Old people

Walking and falling disorders are problems that often occur in old people patients. In the old people, there is a physiological decline in the musculoskeletal system, which manifests in a reduction of the number and size of muscle fibers, resulting in a weaker lower extremity muscle, endurance, coordination, and limited range of motion (ROM). Balance is a complex positional defense against outside interference. Impaired balance and gait and weakness of lower extremity muscles can cause falls in the old people [20, 21].

Falls are the main cause of morbidity in old people patients. The TUG test is a sensitive and objective method of assessing balance and walking disorders. TUG test evaluated the time taken to complete the entire series of tests. Tinetti POMA, on the other hand, can provide additional benefit as the assessment minimize falls and at the same time train physical balance in the old people. Physical balance exercise is an exercise to control movement and position in the center of the body. This exercise is also an essential component in maximizing other physical activities [21].

Physical activity appears to help prevent premature death of dopamine cells. In the basal ganglia, exercise-induced improvement in the synthesis of GDNF has been observed. In parkinsonism mice (or) monkeys motor deterioration can be delayed and dopamine levels in the brain can be preserved by running on a treadmill [22-23].

The results of this study are in line with the study conducted by Marques et al. [24], which showed that there is a relationship between balance training and the frequency of falls in the old people. Similarly, in the study by Alfieri et al. [25], it was found that balance training affected the functional mobility and harmony of senior participants in the treatment group. Neuroprotection and neuroplasticity have been related to GDNF. The results above indicate that neurotrophins are critical for neurodevelopment, nerve transmission, and dopaminergic nerve loss, resulting in better motor function in individuals with Parkinson's disease. As a result, neurotrophins may be beneficial in treating motor dysfunction and related comorbidities, such as those observed in Parkinson's disease. Interventions with GDNF should begin considerably earlier in the patient with Parkinson’s disease. Preclinical findings suggest that treating these individuals within 5 years after illness started may be the optimal usage of GDNF. Developing a less invasive and safer technique for cerebral administration of either the GDNF protein or the GDNF delivery vector will allow testing for such treatments in much younger individuals [26].

In conclusion, the Task Balance Training Program improved GDNF, cognitive function, and postural balance in the old people. Therefore, it could be suggested as an intervention program for improving the cognitive function, and postural balance in the old people. The limitations of this study were a relatively small sample size, the intervention period was short, and no laboratory examination of neurotrophic factor receptors which specifically bind to GDNF that might affect. Further study

should be conducted to analyze the role of GDNF receptors through exercise on cognitive function and postural balance in the old people.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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REFERENCES

[1] Cvecka J, Tirpakova V, Sedliak M, Kern H, Mayr W, Hamar D. Physical Activity in Old people. Eur J Transl Myol. 2015 Aug 25;25(4):249-52.

[2] Abellán-Martínez M, Castellanos López MÁ, Delgado-Losada ML, Yubero R, Paúl N, Unturbe FM. Executive Control on Memory Test Performance across Life: Test of Memory Strategies. Span J Psychol. 2019 Nov 26;22:E50.

[3] Klimova B, Valis M, Kuca K. Cognitive decline in normal aging and its prevention: a review on non-pharmacological lifestyle strategies. Clin Interv Aging. 2017 May 25;12:903-910.

[4] Viaje S, Crombez G, Lord SR, Close JCT, Sachdev P, Brodaty H, Delbaere K. The role of concern about falling on stepping performance during complex activities. BMC Geriatr. 2019 Nov 27;19(1):333.

[5] Taylor ME, Boripuntakul S, Toson B, Close JCT, Lord SR, Kochan NA, Sachdev PS, Brodaty H, Delbaere K. The role of cognitive function and physical activity in physical decline in older adults across the cognitive spectrum. Aging Ment Health. 2019 Jul;23(7):863-871.

[6] Wollesen B, Mattes K, Schulz S, Bischoff LL, Seydell L, Bell JW, von Duvillard SP. Effects of Dual-Task Management and Resistance Training on Gait Performance in Older Individuals: A Randomized Controlled Trial. Front Aging Neurosci. 2017 Dec 13;9:415.

[7] Suzuki Y, Iijima H, Tashiro Y, Kajiwara Y, Zeidan H, Shimoura K, Nishida Y, Bito T, Nakai K, Tatsumi M, Yoshimi S, Tsuboyama T, Aoyama T. Home exercise therapy to improve muscle

strength and joint flexibility effectively treats pre-radiographic knee OA in community-dwelling old people: a randomized controlled trial. Clin Rheumatol. 2019 Jan;38(1):133-141.

[8] Lievens E, Klass M, Bex T, Derave W. Muscle fiber typology substantially influences time to recover from high-intensity exercise. J Appl Physiol (1985). 2020 Mar 1;128(3):648-659.

[9] O'Leary JD, Hoban AE, Murphy A, O'Leary OF, Cryan JF, Nolan YM. Differential effects of adolescent and adult-initiated exercise on cognition and hippocampal neurogenesis. Hippocampus. 2019 Apr;29(4):352-365.

[10] Quintino L, Avallone M, Bränstrom E, Kavanagh P, Lockowandt M, Garcia Jareño P, Breger LS, Lundberg C. GDNF-mediated rescue of the nigrostriatal system depends on the degree of degeneration. Gene Ther. 2019 Feb;26(1-2):57-64.

[11] Virachit S, Mathews KJ, Cottam V, Werry E, Galli E, Rappou E, Lindholm P, Saarma M, Halliday GM, Shannon Weickert C, Double KL. Levels of glial cell line-derived neurotrophic factor are decreased, but fibroblast growth factor 2 and cerebral dopamine neurotrophic factor are increased in the hippocampus in Parkinson's disease. Brain Pathol. 2019 Nov;29(6):813-825.

[12] Cintrón-Colón AF, Almeida-Alves G, Boynton AM, Spitsbergen JM. GDNF synthesis, signaling, and retrograde transport in motor neurons. Cell Tissue Res. 2020 Oct;382(1):47-56.

[13] Gyorkos AM, McCullough MJ, Spitsbergen JM. Glial cell line-derived neurotrophic factor (GDNF) expression and NMJ plasticity in skeletal muscle following endurance exercise. Neuroscience. 2014 Jan 17;257:111-8.

[14] Cortés D, Carballo-Molina OA, Castellanos-Montiel MJ, Velasco I. The Non-Survival Effects of Glial Cell Line-Derived Neurotrophic Factor on Neural Cells. Front Mol Neurosci. 2017 Aug 22;10:258.

[15] McCullough MJ, Gyorkos AM, Spitsbergen JM. Short-term exercise increases GDNF protein levels in the spinal cord of young and old rats. Neuroscience. 2013 Jun 14;240:258-68.

[16] Jardim NYV, Bento-Torres NVO, Costa VO, Carvalho JPR, Pontes HTS, Tomás AM, Sosthenes MCK, Erickson KI, Bento-Torres J, Diniz CWP. Dual-Task Exercise to Improve Cognition and Functional Capacity of Healthy Older Adults. Front Aging Neurosci. 2021 Feb 16;13:589299.

[17] Pertusa M, García-Matas S, Mammeri H, Adell A, Rodrigo T, Mallet J, Cristòfol R, Sarkis C,

Sanfeliu C. Expression of GDNF transgene in astrocytes improves cognitive deficits in aged rats. Neurobiol Aging. 2008 Sep;29(9):1366-79.

[18] Sharif M, Noroozian M, Hashemian F. Do serum GDNF levels correlate with severity of Alzheimer's disease? Neurol Sci. 2020 Nov 19.

[19] Wang X, Hou Z, Yuan Y, Hou G, Liu Y, Li H, Zhang Z. Association study between plasma GDNF and cognitive function in late-onset depression. J Affect Disord. 2011 Aug;132(3):418-21.

[20] Crocker T, Forster A, Young J, Brown L, Ozer S, Smith J, Green J, Hardy J, Burns E, Glidewell E, Greenwood DC. Physical rehabilitation for older people in long-term care. Cochrane Database Syst Rev. 2013 Feb 28;(2).

[21] Hagen M, Seidel S, Sanchez Bergmann D, Muehlbauer T. Associations between Subtalar Muscle Strength and Balance Performance in Healthy Young and Old Adults. Gerontology. 2020;66(1):15-23.

[22] Cohen AD, Tillerson JL, Smith AD, Schallert T, Zigmond MJ. Neuroprotective effects of prior limb use in 6-hydroxydopamine-treated rats: possible role of GDNF. J Neurochem. 2003 Apr;85(2):299-305.

[23] Jankovic J. Parkinson's disease: clinical features and diagnosis. J Neurol Neurosurg Psychiatry. 2008 Apr;79(4):368-76.

[24] Marques EA, Figueiredo P, Harris TB, Wanderley FA, Carvalho J. Are resistance and aerobic exercise training equally effective at improving knee muscle strength and balance in older women? Arch Gerontol Geriatr. 2017 Jan-Feb;68:106-112.

[25] Alfieri FM, Riberto M, Gatz LS, Ribeiro CP, Lopes JA, Battistella LR. Functional mobility and balance in community-dwelling old people submitted to multisensory versus strength exercises. Clin Interv Aging. 2010 Aug 9;5:181-5.

[26] Manfredsson FP, Polinski NK, Subramanian T, Boulis N, Wakeman DR, Mandel RJ. The Future of GDNF in Parkinson's Disease. Front Aging Neurosci. 2020 Dec 7;12:593572.