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Effect of Physical Exercise on Catecholamine Levels in Individuals over 65 Years of Age

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Abstract **Introduction:** The physical and hormonal changes associated with aging can be facilitated by exercise via its effects on hormone release and adaptive responses in the body. The present study aims to investigate the impact of a six-week exercise program on catecholamine (epinephrine, norepinephrine, and dopamine) levels in elderly individuals. **Materials and method:** This study included 20 sedentary elderly male volunteers aged 65–74 from a care center. The participants were divided into the experimental group (n = 10) and control group (n = 10) by randomized blind selection. A six-week physical exercise program was implemented in the experimental group, while the control group continued with their daily routine. Venous blood samples were taken from the forearm before the start of the exercise program (week 0) and 12 hours after the end of the exercise program to determine the levels of catecholamines (epinephrine, norepinephrine, and dopamine). **Results:** After the six-week exercise program, dopamine levels in the experimental group participants increased significantly compared to baseline levels ($p < 0.05$). In contrast, epinephrine and norepinephrine levels decreased after the program, but the change was insignificant ($p>0.05$). **Conclusions:** The findings indicate that the six-week exercise program implemented in this study significantly increased dopamine levels in older adults. In the future, the effects of exercise programs of varying duration and intensity should be examined to maintain metabolic and hormonal changes in elderly individuals at an optimum level.

Keywords Aging, Exercise, Training Epinephrine, Norepinephrine, Dopamine

1. Introduction

Aging in humans is an irreversible process that progresses with reducing and remodeling various body functions [1]. As aging progresses, physiological changes and functional losses occur in all biological systems, including the endocrine [2]. The endocrine system is an essential mediator of the body's physiological adaptive responses to various physical, environmental, and behavioral stressors. Catecholamines secreted from the adrenal medulla are crucial to these adaptive processes, both in the resting state and in response to acute stress [3].

Catecholamines are a group of monoaminergic neurotransmitters, including dopamine, norepinephrine, and epinephrine, that are secreted as a result of an increase in sympathetic activities [4]. The sympathetic nervous system stimulates catecholamine release via sympathetic nerve impulses that reach the adrenal medulla and mediate adaptive responses to acute stressors. Some symptoms, such as increased heart rate, increased breathing rate and depth, and high blood pressure, are caused by stimulation of the sympathetic nervous system (SNS) in the body and are accompanied by the release of catecholamines into the blood [3]. Catecholamine release increases during exercise, cold, hypoglycemia, oxygen deficiency, and hypotension [1]. Moreover, catecholamines are linked to long-term memory of events that evoke strong emotions, such as fear, anger, and stress, as catecholamine release increases in such situations [5].

Changes in the metabolism of biogenic amines, such as catecholamines, with advancing age, have been demonstrated in various tissues, especially the brain, in both experimental and human studies [6]. While a study on aging has shown that basal norepinephrine [2] and epinephrine [7] concentrations increase with age, some studies have not found such an effect of aging [8]. Nonetheless, animal studies and postmortem studies of the human brain in the literature generally show a decrease in brain dopamine activity with aging [9], and studies have also demonstrated an age-related decline in dopamine release [10].

Because of their effects on the SNS, catecholamines secreted from the adrenal medulla are crucial for hormonal, metabolic, and circulatory adjustments during exercise [3]. Exercise can be considered as a stressor that can stimulate the sympathoadrenal system. Exercise activates the hypothalamic-pituitary-adrenal (HPA) axis and the SNS, increasing catecholamine release [11]. However, the sympathoadrenal response to exercise varies according to the specific characteristics of physical exercise, and the type, duration, and intensity of exercise, as well as the subject's posture during exercise, are factors that have the most substantial effect on catecholamine responses [3]. In addition, studies have also revealed that there are age-related differences in the catecholamine response to exercise [7,8,9].

Several studies have examined the acute effects of catecholamine levels immediately after exercise [3,7,12,13,14]. However, very few studies have examined the effect of catecholamine levels under daily living conditions on older adults following a regular exercise program, that is, one that allows for rest after exercise [15,16]. Accordingly, the study aimed to investigate the effect of a short-term six-week exercise program on the levels of catecholamines (epinephrine, norepinephrine, and dopamine) in elderly individuals.

2. Materials and Methods

A total of 20 sedentary elderly male volunteers aged between 65 and 74 years who lived in a care center randomly participated in the study. After obtaining the necessary permission to conduct the study, the participants were informed about the research and the experimental procedures, and their written informed consent was obtained. It was checked whether the individual had an orthopedic or mental disability that would prevent or restrict him from exercising, and then everyone was asked whether he had any health-related problems. People with health problems such as cardiovascular disease, respiratory failure, high blood pressure, or physical and mental disabilities were not included in the study (according to the statements of the medical staff at the center). Participants were divided into two groups by a randomized blind selection method: the experimental group (n = 10) and the control group (n = 10). The experimental group participants underwent a physical exercise program for six weeks, while the control group continued their daily routine for the same period. The lowest training level required for improvement in VO_2 max corresponds to an effort level of 60% of the maximum heart rate reserve (or 50% of VO_2 max) [17]. The experimental group performed 30 min of walking and moderate-intensity jogging exercises five days a week in the care center facility. During the activities, the exercise intensity was determined based on the heart rate and speech test: speaking generally during the exercise indicated that a moderate pace was appropriate [1]. In addition to aerobic exercises, the program also included strength exercises for the lower and upper extremities, consisting of two sets of 8–12 repetitions performed two days a week. In the exercise group, necessary adjustments were made in the program by considering the initiation, development, and maintenance periods. The upper extremity strength exercises included dumbbell chest press, dumbbell upright row, dumbbell front, shoulder raise, biceps curl, triceps extension, and dumbbell lateral raise, and the lower extremity strength exercises included seated leg extension, standing hamstrings curl, standing calf raises, chair squats, supine hip lifts, abdominal crunch, and back extension.

The levels of catecholamines (epinephrine, norepinephrine, and dopamine) were measured in both groups by collecting venous blood samples from the forearm at two time points, that is, before the start of the exercise program (week 0) and after a 12-h fasting period on completion of the exercise program (week 6) [18]. Blood samples were collected in vacutainers containing EDTA, and plasma was separated by centrifugation at 3500 rpm for 10 min at room temperature. The tops of the pieces in the tubes were transferred to Eppendorf tubes and stored at -80 ℃ until analysis. Biochemistry experts at Gazi University Medical Biochemistry Laboratory analyzed the collected blood samples. Serum epinephrine, norepinephrine, and dopamine levels were measured using the sandwich enzyme immunoassay method with the Sunred brand (Shanghai, China) ELISA kit. In the sandwich enzyme immunoassay method, the substance to be measured in the samples is bound to the reaction plate coated with monoclonal antibodies. A second monoclonal antibody labeled with an enzyme (horseradish peroxidase) binds to this substance. The intensity of the color formed due to the enzyme interaction with the added chromogenic solution is directly proportional to the concentration of the substance to be measured. Study data were obtained by calculating the results according to the standard curve drawn for each parameter. This study was approved by the Atatürk University Research Ethics Committee (2022/11) and the Administrative Board of Care Facility (2022/397]).

The data obtained from the research were transferred electronically with the SPSS v.20 software for statistical analyses. The normality of the data was analyzed with the Kolmogorov-Smirnov test, and parametric statistical analyses were performed according to the normality results. The participants' age, height, weight, and body mass index (BMI) values were analyzed with descriptive statistical methods. At the same time, chi-square analysis was applied for the homogeneity test between the experimental and control groups. The related sample *t*-test was used to determine the differences between the pre-test and post-test data of the experimental and control groups. The statistical analysis determined the significance level as $p < 0.05$.

3. Results

The results presented in Table 1 demonstrate statistically significant differences between the pretest and posttest results for the weight and BMI of participants in the experimental group ($p < 0.05$).

The results in Table 2 reveal a statistically significant difference between the pretest and posttest dopamine values of the participants in the experimental group ($p < 0.05$).

There was no statistically significant difference between the groups for the pre-test and post-test values of weight and BMI as shown in Table 3 ($p > 0.05$).

There was no statistically significant difference between the groups about the pre-test and post-test levels of dopamine, epinephrine, and norepinephrine as shown in Table 4 ($p > 0.05$).

Table 1. Comparison of the pretest and posttest results for mean weight and BMI within both groups

	Experimental Group				**Control Group**			
Test	**Pre-Test ($\bar{X}$ ±SD)**	**Post-Test ($\bar{X}$ ±SD)**	**t**	**p**	**Pre-Test ($\bar{X}$ ±SD)**	**Post-Test ($\bar{X}$ ±SD)**	**t**	**p**
Age (years)	67.1 ±10.365	-	-	-	65.7 ±9.117	-	-	-
Height (cm)	169.1 ±8.116	-	-	-	168.1 ±7.852	-	-	-
Weight (kg)	72.5 ±6.485	70.9 ±5.216	3.361	**.008**	70.74 ±6.680	71.3 ±6.412	-1.319	.220
BMI (kg/m²)	25.42 ±2.373	24.88 ±2.306	3.530	**.006**	25.13 ±2.856	25.34 ±2.920	-1.426	.188

Table 2. Comparison of the pretest and posttest results for mean dopamine, epinephrine, and norepinephrine values within both groups

	Experimental Group				**Control Group**			
Test	**Pre-Test ($\bar{X}$ ±SD)**	**Post-Test ($\bar{X}$ ±SD)**	**t**	**p**	**Pre-Test ($\bar{X}$ ±SD)**	**Post-Test ($\bar{X}$ ±SD)**	**t**	**p**
Epinephrine (ng/mL)	8.51 ±5.057	6.69 ±3.076	-1.708	.122	8.77 ±5.856	8.81 ±4.118	-.032	.975
Norepinephrine (ng/L)	312 ±114.414	257.26 ± 111.857	-1.872	.094	292.94 ± 116.296	289.07 ±93.402	.171	.868
Dopamine (nMol/L)	265.06 ±113.364	402.38 ± 203.334	-3.286	.009	352.88 ± 227.894	359.08 ±214.227	-.314	.761

Table 3. Comparison of the pre-test and post-test values of age, height, weight, and BMI between groups

Variables		**Experimental Group ($\bar{X}$ ±SD)**	**Control Group ($\bar{X}$ ±SD)**	**t**	**p**
Age (years)	**Pre-Test**	67.1 ±10.365	65.7 ±9.11	-.321	.848
	Post-Test	-	-	-	-
Height (cm)	**Pre-Test**	169.1 ±8.116	168.1 ±7.852	-.280	.783
	Post-Test	-	-	-	-
Weight (kg)	**Pre-Test**	72.5 ±6.485	70.74 ±6.680	-.598	.973
	Post-Test	70.9 ±5.216	71.3 ±6.412	.153	.670
BMI (kg/m²)	**Pre-Test**	25.42 ±2.373	25.13 ±2.856	-.247	.740
	Post-Test	24.88 ±2.306	25.34 ±2.920	.389	.574

Table 4. Comparison of the pretest and posttest values of dopamine, epinephrine, and norepinephrine between groups

		Experimental Group	Control Group	t	p
Variables		**(X̄ ± SD)**	**(X̄ ± SD)**		
Epinephrine, (ng/mL)	**Pre-Test**	8.51 ± 5.057	8.77 ± 5.856	.994	.054
	Post-Test	6.69 ± 3.076	8.81 ± 4.118	.143	.262
Norepinephrine, (ng/L)	**Pre-Test**	312 ± 114.414	292.94 ± 116.296	.699	.936
	Post-Test	257.26 ± 111.857	289.07 ± 93.402	-.491	.583
Dopamine, (nMol/L)	**Pre-Test**	265.06 ± 113.364	352.88 ± 22.894	1.091	.082
	Post-Test	402.38 ± 203.334	359.08 ± 214.227	-.464	.923

4. Discussion

Aging is associated with a decline in physical activity levels, metabolic dysfunction, and a decrease in hormonal balance. Exercise programs are recommended to ameliorate aging-related changes by improving physical function and hormonal balance, as these programs are easy to implement and entail low costs [18]. The body is exposed to external stress during exercise, which induces specific adaptive responses to changes in environmental conditions to maintain homeostasis [3]. To restore homeostasis, the organism must respond quickly, requiring the release of catecholamines (epinephrine, norepinephrine, and dopamine) from the adrenal medulla that act as rapid first-responder biomolecules [19].

Increased stress due to exercise causes increased activation of the HPA axis and SNS. As a result, catecholamines are released from the adrenal medulla in appropriate concentrations and enter circulation to induce a wide range of effects in the body. However, it has been reported that many factors, such as type of exercise (dynamic or static/aerobic or anaerobic), intensity and duration [which are the main factors], age, gender, and BMI, affect the relationship between exercise and catecholamine release [19].

With age, catecholamine levels increase significantly due to increased sympathetic activity [2,7,20]. Studies have shown that catecholamine concentrations can increase 20 times compared to resting levels after acute exercise [3]. However, the effect of exercise on the catecholamine levels of elderly individuals is a controversial topic in the literature [21]. Some studies reported that regular exercise did not affect or cause an increase in catecholamine levels in older people [8], while others reported an increase in catecholamines [3,7,12,14]. In contrast, some studies have reported that a statistically significant decrease in blood catecholamine concentrations was observed according to the type, intensity, and duration of physical exercise [15,20,21],

In our study, the effects of a six-week exercise program designed for older adults on catecholamine (epinephrine, norepinephrine, and dopamine) levels were examined, and the results showed that after six weeks of exercise, the dopamine levels increased significantly, and the epinephrine and norepinephrine levels decreased, although not considerably. There are studies in the literature with a similar design. For example, Pal et al. [20] examined the effect of a three-month yoga training program on catecholamine levels in individuals over 40. They observed a decrease in epinephrine and a significant decrease in norepinephrine levels. They speculated that this decrease may be related to reduced stress, which results in a reduction of adrenocorticotropic hormone and cortisol levels following yoga practice (Figure 1).

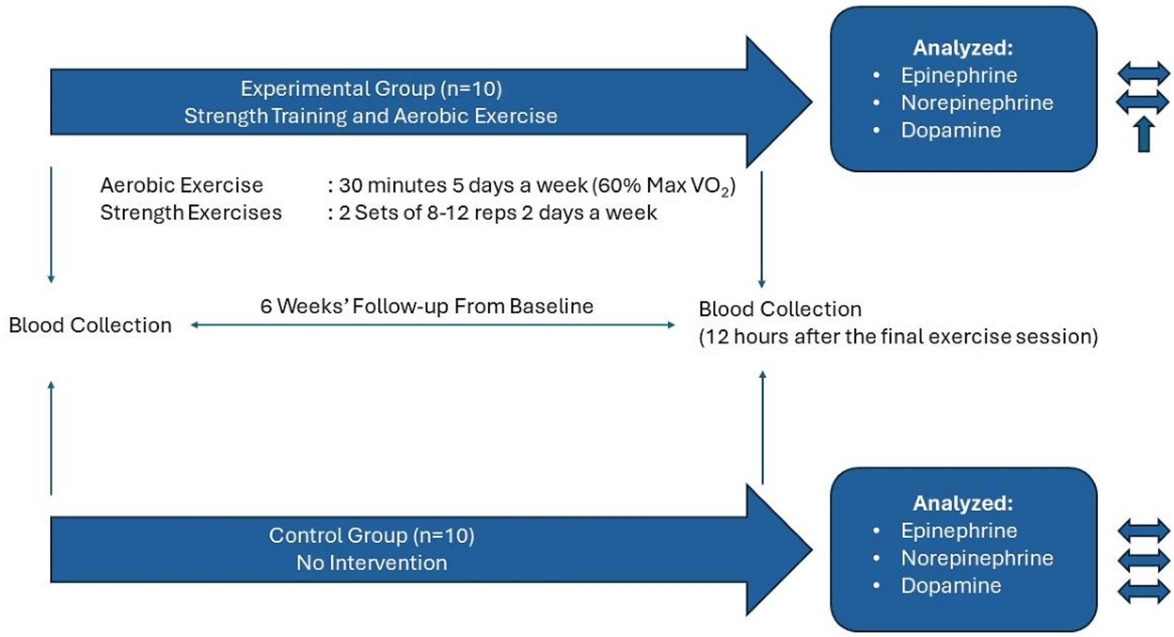

Figure 1. Flow chart depicting the study procedure

Similarly, Selvamurthy et al. [15] also observed that the epinephrine and norepinephrine levels of male subjects (age 50±3,3 years) decreased after a three-week yoga program. In their study, the 24-hour catecholamine concentrations of the participants were examined, and it was found that the catecholamine level decreased after three weeks of yoga training. Further, Turner et al. [12] observed that long-term (10 weeks) treadmill exercise in young rats induced adaptive changes that led to a decrease in the expression of tyrosine hydroxylase and the activity of catecholamine, which is a precursor amino acid in the production of catecholamines in the adrenal medulla. However, Sullivan et al. [22] observed an insignificant decrease in epinephrine and norepinephrine levels after a six-week strenuous exercise program in the 34-54-year-old group. In addition, Korth et al. [8] also studied the effect of a 9-month exercise program on 48 elderly subjects. They found that the initial increase in epinephrine and norepinephrine levels immediately after exercise decreased after 5 min of rest. Along the same line, Sothmann et al. [23] revealed that a 3- to 4-week exercise program did not induce statistically significant changes in plasma epinephrine and norepinephrine levels. In another similar study, Kim et al. [16] observed that epinephrine and norepinephrine levels measured in older people after 24 weeks of strength exercises (48 h later) decreased significantly in the strength exercise group but did not decrease in the control group. Our study's results revealed that the decrease in epinephrine and norepinephrine levels after exercise aligns with the literature's findings mentioned above. The change was insignificant because the six-week duration of the exercise program was too short to induce any chronic changes in epinephrine and norepinephrine. Accordingly, in the literature, it has been shown that variations in the intensity and duration of exercise programs may result in differences in their effects on sympathetic activity that subsequently result in hormonal changes [22]. As a result of aging, the sympathoadrenal response is weakened due to a decrease in aerobic capacity caused by the deterioration of SNS activity. Although these effects can be ameliorated with training, short-term exercise programs may not be sufficient to regulate and change the catecholamine levels of individuals [23]. This may explain the lack of significance in our epinephrine and norepinephrine data.

Studies examining the effect of exercise on catecholamine levels [3,13] generally focus on acute changes in blood samples that occur immediately after exercise. Thus, the results of these studies focus on indicators of critical response. However, our study took blood samples 12 hours after completing the exercise program. Therefore, our focus was on whether aerobic and strength exercises in older adults significantly affected catecholamine levels over a more extended period rather than an acute effect. Contrary to our findings, it has been reported in the literature that there is an increase in the activation of SNS, similar to the critical stress response, immediately after exercise [12] and significant increases in catecholamine levels, too [3,7,12,14]. Studies have suggested that a temporary rise in catecholamine levels is necessary to respond to exercise-induced stress during moderate and vigorous exercise [12]. Researchers have emphasized that lactate, which begins to accumulate in the body above the point at which effort reaches 50–80% of VO_2 max, depending on the intensity of exercise, causes an increase in catecholamine release [19]. However, there is also evidence that epinephrine and norepinephrine concentrations increase even with low-intensity exercise [3]. In this regard, researchers have reported that exercise causes an increase in epinephrine and norepinephrine levels by effectively activating the HPA axis [13]. However, the data in our study do not support the above studies.

Contrary to the increase in epinephrine and norepinephrine levels reported in the previous studies, our study observed a decrease in the ranks of these catecholamines, although this was not statistically significant. It should be noted that in the above studies, an acute increase in these catecholamines was observed immediately after exercise. In contrast, catecholamine levels were measured after a 12-hour rest period and not immediately after exercise in the present study. Because the stress response to activity decreases with time after exercise, we can deduce that the biosynthesis of catecholamines (and, therefore, the circulating levels of catecholamines) decreases as exercise-induced stress decreases [22]. Thus, the results of our study are similar to those of other studies in the literature that report catecholamine levels after exercise under normal daily life conditions [13,15,16].

Dopamine has a mood-enhancing effect and promotes long-term memory. It has been suggested that the dopaminergic system deteriorates with age and, thus, causes a decrease in cognitive ability, and higher dopamine levels are generally thought to be beneficial for working memory in older adults [24]. Juarez et al. [10] suggested that an increase in physical activity can cause an increase in dopamine receptor availability, which would increase cognition. Jonasson et al. [24] implemented a program comprising aerobics, resistance, and stretching exercises in 54 sedentary older adults and found that it resulted in cognitive improvements associated with changes in dopamine receptors. Similarly, Rosso et al. investigated whether structured physical activity for 2.5 years in sedentary older adults was associated with their dopamine-related genotype and whether participation in physical activity resulted in increased response in the form of increased dopamine signaling [25]. In a similar study, Tsai et al. [13] reported that high-intensity intermittent exercise and moderate-intensity continuous exercise protocols in middle-aged and older adults caused an increase in dopamine levels. Similar to the studies in the literature, in this study, dopamine levels increased significantly in older adults after the six-week exercise program. The findings imply that the application of the aerobic and strength exercises for six weeks was sufficient to affect the dopaminergic system for a period of 6 weeks.

5. Conclusions

Overall, the results of this study indicate that performing aerobic and strength exercises for six weeks affected catecholamine [epinephrine, norepinephrine, and dopamine] levels in older people, with dopamine levels increasing significantly and epinephrine and norepinephrine levels decreasing, although not considerably. The results largely agree with previously reported findings in the literature that exercise can cause significant improvements in catecholamine levels, especially in elderly individuals. In the future, the metabolic and hormonal effects of such exercise programs could be optimized by designing programs with different durations, intensities, and types of exercises.

6. Limitations

One of the limitations of this study is that data were not obtained immediately after exercise and daily activity, as the posttest data were determined from blood samples collected 12 h after the last exercise session when the participants were resting. Another limitation is that many variables, including genetic and environmental factors, are associated with catecholamine levels that were not measured. A third limitation is that blood lactate levels were not measured, and the exercise intensity was based on the speech test and heart rate. However, it is known that catecholamine levels are affected by the lactate threshold of blood, which varies according to the intensity of exercise [19]. The fourth limitation is that the number of samples in both groups needs to be increased. This led to an increase in standard deviation caused by individual differences. If the traditional deviation values had been lower, the changes in epinephrine and norepinephrine levels may have been significant.

Author Contributions

FE was responsible for the procurement of finding, conceptualization, and design of the study, development, and implementation of the study protocol and drafted the manuscript; FE, CY was responsible for the conceptualization and design of the study, development, and implementation of the study protocol, and drafted the manuscript. CS, MP, and ÖEK collected the data. FE and CS analyzed the results. FE, CS, MP, and ÖEK drafted the manuscript. CS, FE, and CY critically revised the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of Interest

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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