Nat. Volatiles & Essent. Oils, 2022; 9(2): 114-122

NVEO
Natural Volatiles & Essential Oils

Effects Of Complex Exercise For 12 Weeks On The Bone Mass Content, Diabetes Risk Factors, Bdnfs, And Inflammation-Related Factors Of Type 2 Diabetic Patients

Jang-Jun Park[1] , Hyun-Jun Kim[*2] , Yeun-Suk Cho[3] , In-Joo Kim[4] , Sang-Soo Kim[5] , Won-Sik Bae[6]

[1]Ph.D.student, Dept. of Physical Education, Kyungnam University, 7, Kyungnamdaehak-ro, Masanhappo-gu, Changwon, Kyungsangnam-do, Korea.

[*2]Professor, Dept. of Physical Education, Kyungnam University, 7, Kyungnamdaehak-ro, Masanhappo-gu, Changwon, Kyungsangnam-do, Korea.

[3] Professor, Dept. of Marine Sports, Pukyong National University, 45, Yongso-ro, Nam-gu, Busan, Korea.

[4]Professor, Dept. of internal Medicine, Pusan National University Hospital, Pusan National University School of Medicine, 179, Gudeok-ro, Seo-gu, Busan, Korea.

[5]Professor, Dept. of internal Medicine, Pusan National University Hospital, Pusan National University School of Medicine, 179, Gudeok-ro, Seo-gu, Busan, Korea.

[6] Professor, Dept. of Physical Therapy, Kyungnam College of Information & Technology, 45, Jurye-Ro, Sasang-gu, Busan, Korea.

Abstract The purpose of this study was to examine the effects of complex exercise for 12 weeks on the bone mass content, diabetes risk factors(HDL-C, LDL-C, HbA1c, TC, TG), BDNFs, which are brain derived neurotrophic factors, inflammation-related factors(IL-6, TNF-α) of type 2 diabetic patients. The subjects of this study were 50-70 years old female type 2 diabetic patients residing in Busan selected through simple random sampling and assigned to an exercise group of 10 subjects and a control group of 10 subjects. A complex exercise program was administered to 20 type 2 diabetic patients (10 in an exercise group, 10 in a control group) for 60 minutes per time, three times per week for 12 weeks and differences in the amounts of changes were analyzed. As for changes in bone mass content (BMC), whereas the exercise group did not show any significant change, the control group showed significant decreases and the difference in mean values between the two groups was significant($p<.01$). Among diabetes risk factors, HbA1c was shown to be statistically different between the two groups after the execution of the complex exercise program($p<.05$). HDL-C was shown to be statistically different between the two groups after the execution of the complex exercise program ($p<.01$), and changed significantly in the complex exercise group but not in the control group($p<.01$). Changes in BDNF were analyzed and the results indicated significant intergroup differences ($p<.01$). The results of analysis of changes in IL-6 also showed significant intergroup differences ($p<.01$). Through this study, it could be seen that the 12-week complex exercise program is effective for the prevention and treatment of diabetes and diabetic complications because the program improved the factors such as the bone mass content, HDL-C, HbA1c, BDNF, IL-6 of type 2 diabetic patients.

Keywords: Brain-derived neurotrophic factor, Complex-exercise, Diabetic factor, IL-6, Type Ⅱ diabetes mellitus

1. Introduction

Diabetes and diabetic complications such as macrovascular, microvascular complications and diabetic neuropathy not only increase economic burdens but also degrade the quality of life and greatly affect even the family members of patients[1].

Exercise is a very important therapy for adult diseases due to such metabolic diseases and for brain nerve formation and activity, and can be more effective when complex with drug therapy and diet therapy. The hormones associated with exercise-induced brain cell formation and activity not only control our body as a whole but also regulate energy metabolism and are closely related to diabetes, one of metabolic diseases[2].

Brain-derived neurotrophic factors (BDNFs) include insulin-like growth factor-1 and fibroblast growth factor-2, which are neurotropic protein factors that have diverse effects on the central nervous system. BDNFs are expressed in diverse brain regions and are known to play important roles for the growth and development of neurons while enhancing neuronal survival by increasing resistance to nerve damage[3]. Increases in BDNFs through exercise have been reported to reduce blood sugar and free fatty acid (FFA), and TC by glucose oxidation while increasing food intake and reducing body weight by increasing oxygen consumption and body temperature[4]. This indicates that the increase in BDNFs through exercise promotes insulin secretion through the activity of pancreatic β-cells thereby helping the improvement of diabetic patients' insulin resistance.

BDNFs and IL-6 released from skeletal muscles when stimulated by exercise have been reported to play a major role in improving insulin sensitivity. However, studies that attempted to identify the association between IL-6 and TNF-α responses to exercise and insulin resistance and the regulation of BDNF secretion are very insufficient.

In particular, since the levels of changes in BDNFs, IL-6, and TNF-α are considered to appear differently according to the individual characteristics of type 2 diabetic patients, studies are necessary on how complex exercise affects changes in BDNFs, IL-6, and TNF-α in type 2 diabetic patients to improve diabetes risk factors.

2. Materials and Methods

For this study, the researcher completed the IRB training and this study passed the IRB deliberation (H-1306-004-019) by the Pusan University Hospital Clinical Examination Committee. The subjects of this study were 50-70 years old female type 2 diabetic patients residing in Busan selected through simple random sampling and assigned to an exercise group of 10 subjects and a control group of 10 subjects. The physical characteristics of the study subjects are as shown in table 1.

Table 1: The physical characteristics of the study subjects

Variables / Group	Ages (yrs)	Height (cm)	Weight (kg)	BMI (kg/m²)
EG(n=10)	61.00±7.30	154.87±4.77	57.71±8.92	23.99±2.99
CG(n=10)	57.80±4.24	155.79±5.02	61.47±7.27	25.28±2.31
t	1.199	-.420	-1.033	-1.079

Values are Means±SD, EG: exercise group, CG: control group

2.1. Measurements

Height, weight, body fat mass, body fat percentage and muscle mass were measured using dual energy x-ray bone densitometer(DPX-NT & MD, GE LUNAR Co., USA). A 2 ml blood sample were obtained from the antecubital vein of each participant before and after the program. Blood samples were drawn into chilled tubes containing Na2EDTA (1 mg/ml) and aprotinin (500 U/ml) and were used for determination of BDNF, IL-6 and TNF-α. Serum was immediately separated by centrifugation (2,000×g) at 4ºC and stored at -70ºC until assayed. Blood TC, TG, HDL-C, LDL-C, HbA1c were analyzed using high performance liquid chromatography (Neuroblastoma Analyzer, Bio-Rad, U.S.A). Serum BDNF(Ab frontier human BDNF ELISA kit Catalog # LF-EK5005), IL-6 (Ab frontier human IL-6 ELISA kit Catalog # LF-EK0260), TNF-α (Ab frontier human TNF-α ELISA kit Catalog # LF- ED0193) Concentration analysis was performed according to the Enzyme-Linked Immunosorbent Assay (ELISA) Kit (Promega, USA) using Multiskan Go (Thermo. Co. USA).

2.2. Intervention

The exercise program was a complex exercise program composed of step box(aerobic exercise) and gymstick(resistance exercise) and was implemented three times per week for 12 weeks, The exercise time, frequency, and intensity were set as shown in table 2.

Table 2: The exercise program

Other	Contents	Period (weeks)	Intensity	Time (min)
Warm-up	Stretching & Walking			5
Main Exercise (Aerobics)	① stepbox basic movement(up & down) ② stepbox basic movement(up & down and side step) ③ stepbox basic movement(up & down and knee up)	1-4 (① - ②)	RPE 11-12 Bpm 130-135	25
		5-12 (① - ③)	RPE 13-14 Bpm 130-135	
Main Exercise (Anaerobics)	Gymstick ① Squat ② standing body rotation ③ biceps curl ④ triceps curl ⑤ upright row ⑥ backward leg extension ⑦ body extension while lying on your back ⑧ crunch with upright row ⑨ lunge with press ⑩ lunge with body rotation	1-4 (green tube)	RPE 11-12 (8-12times×1-2set) Bpm 122-132	25
		5-12 (blue tube)	RPE 13-14 (8-15times×2set) Bpm 122-132	
Cool down	stretching & meditation			5
Total				60

2.3. Statistical analyses

Using the SPSS Ver. 18.0 program, the mean values (M) and the standard deviations (SD) of the measurement items were calculated and statistically processed. The differences between before and after the exercise differences in each group were analyzed with paired t-tests. The interaction effects according to groups and times and intergroup differences were analyzed with two-way ANOVA repeated measures. Pearson's correlation coefficients were used to analyze the correlations between BDNFs changed by the exercise program and health-related physical fitness, diabetes risk factors, and inflammation-related factors. All statistical significance levels were set to .05.

3. Results and Discussion

Changes in the body composition and bone mass content, diabetes risk factors and BDNFs and inflammation-related factors of the subjects are as shown in table 3. The bone mass content of the exercise group (EG) decreased by 14.4 g while that of the control group (CG) significantly decreased by 65.1 g ($p < .001$). The bone mass content was shown to be statistically significantly different between the two groups ($p < .01$). TC decreased by 13.5 mg/dl in the EG and by 6.4 mg/dl in the CG. There was no statistically significant difference between the groups. TG significantly decreased by 59.5 mg/dl in the EG ($p < .05$) and decreased by 41.2 mg/dl in the CG. There was no statistically significant difference between the groups. HDL-C group significantly increased by 10.6 mg/dl in the EG ($p < .01$), and increased by 0.8 mg/dl in the CG. Changes in HDL-C were significantly different between the groups($p<.01$). LDL-C decreased by 11.2 mg/dl in the EG and by 2.8 mg/dl in the CG. There was no statistically significant difference between the groups. HbA1c decreased by 0.36% in the EG and increased by 0.36% in the CG. The amounts of changes were statistically significant different between the groups ($p < .05$). BDNFs significantly increased by 2.6 ng/ml in the EG ($p < .01$), but did not change in the CG resulting in a significant intergroup difference ($p < .01$). IL-6 decreased by 0.78 pg/ml in the EG and the decreased was not significant but significantly increased by 1.48 pg/ml in the CG ($p < .001$). There was a statistically significant difference between the groups ($p < .01$). TNF-α decreased by 1.09 pg/ml in the EG but increased by 0.23 pg/ml in the CG. There was no statistically significant difference between the groups.

Table 3: Changes in the body composition and bone mass content diabetes risk factors and BDNFs and inflammation-related factors of the subjects

Variables	Group	Pre	Post	Diff	t	t
Height (cm)	EG	154.87±4.77	155.35±4.68	-.66±.57	-3.649**	2.285##
	CG	155.79±5.03	155.83±4.82	-.04±.64	-.198	
Weight (kg)	EG	57.71±8.93	57.73±8.99	-.02±.87	-.72	.343
	CG	61.47±7.27	61.31±7.06	.16±1.30	.390	
BMI (kg/m^2)	EG	23.99±2.99	23.79±2.87	.20±.45	1.406	-.601
	CG	25.28±2.31	25.20±2.25	.08±.50	.503	
FM (g)	EG	20664.50±5797.03	20031.40±5485.93	633.10±821.66	2.437*	1.023
	CG	22828.90±4525.19	21788.00±4174.25	1040.90±956.75	3.440**	

%fat (%)	EG	35.04±4.52	34.17±4.48	.86±1.04	2.618*	.365
	CG	36.12±4.54	35.08±4.04	1.05±1.23	2.694*	
LBM (g)	EG	35566.50±5013.77	35932.70±5473.68	-366.20±1054.02	-1.099	.744
	CG	37673.50±3155.41	37744.80±3089.86	-71.30±678.24	-.332	
BMC (g)	EG	2054.70±310.89	2039.10±316.33	15.60±36.22	1.362	3.769##
	CG	2275.10±263.58	2210.00±262.71	65.10±20.33	10.127***	
TC (mg/dℓ)	EG	171.7±27.50	158.20±25.06	13.50±28.37	1.505	-.451
	CG	184.80±37.11	178.40±44.34	6.40±40.96	.494	
TG (mg/dℓ)	EG	171.30±102.42	111.80±64.04	59.50±69.94	2.690*	-.618
	CG	181.20±82.38	140.00±56.89	41.20±62.30	2.091	
HDL-C (mg/dℓ)	EG	56.00±14.16	66.60±15.72	-10.60±6.92	-4.847**	3.519##
	CG	46.50±9.14	47.30±7.57	-.80±5.45	-.464	
LDL-C (mg/dℓ)	EG	95.90±28.95	84.70±22.32	11.20±28.75	1.232	-.544
	CG	117.30±31.25	114.50±41.49	2.80±39.46	.224	
HbA1c (%)	EG	7.14±1.03	6.78±.73	.36±.65	1.760	-2.370#
	CG	7.21±.85	7.57±1.21	-.36±.71	-1.602	
BDNF (pg/ml)	EG	1.96±1.13	4.56±2.40	2.6±2.24	-3.664**	3.479**
	CG	1.90±.86	1.83±1.06	-.07±.92	.246	
IL-6 (pg/ml)	EG	3.06±1.75	2.28±.20	-.77±4.64	1.489	-.3.973**
	CG	2.36±.20	3.84±2.31	1.48±.73	-6.428***	
TNF-α (pg/ml)	EG	10.82±2.21	9.73±.70	-1.09±1.73	1.988	-1.659
	CG	10.11±.91	10.34±2.31	.23±1.83	-.402	

Values are Means±SD, EG: exercise group, CG: control group

BMI: body mass index, FM: fat mass, LBM: lean body mass, BMC: bone mineral content, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TG: triglyceride, TC: total cholesterol, HbA1c: hemoglobin A1c, BDNF: Brain-derived neurotrophic factors , IL-6: interleukin-6, TNF-α: Tumor Necrosis Factor- α

*:significantly different within group by paired t-test, *: p<.05, **: p<.01, ***: p<.001

#:significantly different between group by independent t-test , #: p<.05, ##: p<.01, ###: p<.001

Diabetes can lead to complications such as heart diseases, renal diseases, ophthalmologic diseases, neurological disorders, stroke and foot disease, leading to death[5].

Diabetes can cause osteoporosis by reducing bone mass content and it has been reported that calcium

and vitamin D intake and exercise should be complex in order to increase bone mass content in patients with diabetes whose bone mass content decreases. With regard to changes in bone mass content (BMC) in this study, whereas the exercise group did not show any significant change, the control group showed but significant decreases and the difference between the two groups was significant. [6] reported that when intervention with a combination of drug and exercise was administered to 104 diabetic patients for two years, the bone density of the group that performed exercise increased compared to the control group. [7] also reported that complex exercise for 12 weeks significantly improved bone density. The results of previous studies as such seem to be similar to the results of this study and based on such results, complex exercise is considered to affect the bone mass content to maintain the bone density and suppress bone loss thereby reducing the risk of osteoporosis.

According to a study conducted by [8], body weight is associated with HbA1c, which has linear relationships with diabetic vascular complications. HbA1c is useful to reflect the mean blood glucose concentration over the last 2-3 months rather than the short-term blood glucose control effect, and it is recommended that the target value of elderly diabetic patients should not exceed 6.5-7%[9]. Recently, as an exercise program for type 2 diabetes management, complex exercise consisting of aerobic exercise and resistance exercise has been recommended as a way to increase glucose uptake by skeletal muscles. In this research, although there was no statistical difference in HbA1c within the complex exercise group or the control group after undergoing the complex exercise program, a statistical difference was shown between the two groups. Previous studies have also reported that complex exercise performed by type 2 diabetic patients significantly reduced HbA1c[10]. That is, complex exercise can be regarded to be effective in reducing HbA1c, which is an essential goal of blood glucose control in the management of elderly diabetes. Meanwhile, among blood lipids, HDL-C was shown to be have been changed significantly in the complex exercise group and the intergroup difference was also shown to be significant. [11] reported that HDL-C increased in diabetic patients after performing regular exercise and attributed the results to the fact that regular exercise reduced blood glucose levels and increased muscles' insulin sensitivity thereby improving lipid metabolism. The increase in HDL-C through regular exercise training has been reported to have a positive effect on blood lipids and [12] conducted a study with obese middle-aged men and women and reported significant increases in HDL-C as the result of the study. This suggests that exercise improved blood lipids not only in general persons and obesity patients but also in diabetic patients leading to increases in the HDL-C level thereby positively affecting blood lipids.

BDNFs are neurotropic factors that act in the cortex, hippocampus, and frontal lobe responsible for memory, learning, and thinking functions in the brain[3]. Exercise is also known to increase the expression of nerve growth factors such as BDNFs and other neurotransmitters such as serotonin thereby affecting nerve cell production, memory, and learning ability[3].

In this study, changes in BDNFs following the 12-week program were analyzed and the results indicated significant intergroup differences in BDNFs. BDNFs in the exercise group significantly increased by 2.60 pg/ml after the 12-week program. [13] reported that there were statistical differences in BDNF concentrations between before and after exercise in healthy adults. BDNFs increased after three months of endurance exercise in seven healthy men[14], and a study reported that BDNFs increased in 13 healthy men who underwent an endurance circuit exercise program for five weeks[15]. In addition, many other studies also reported findings of increases in BDNF levels after exercise programs[16].

Although the results of this research and previous researches suggest that regular complex exercise increases the expression of BDNFs in patients with type 2 diabetes, the necessity of studies on the relationship between the BDNFs secreted in the hippocampus and cerebral cortex of the brain and the expression of blood BDNF is raised.

IL-6 is known as a factor that controls BDNF secretion[17], and is known to be involved in the process of regeneration by directly affecting or stimulating neuronal survival regulation, peripheral nerve regeneration, and nerve growth factors[18]. As for studies on exercise and IL-6, although diverse reports have continued, among them, after the relationships between exercise and the process of the development and progression of vascular diseases and eating restrain in central nerves were reported, the importance of exercise as an inflammation and eating inhibitory factor has been magnified and it has been reported that physical activities and aerobic exercise for long periods of time reduce IL-6 concentrations in muscle tissues[19]. In this study, IL-6 was shown to be significantly different between the groups. [20] reported that when study subjects were divided into an aerobic exercise group and muscle strength exercise group and training was implemented 45 minutes per time, three times per week for 10 months, IL-6 levels decreased in both groups and [21] reported that when treadmill or ergometer exercise was implemented at 60% of the maximal oxygen uptake for 45 minutes per time, 3-4 times per week for six months, IL-6 levels significantly decreased thereby showing a tendency similar to the results of this study. It has been reported that IL-6 and exercise intensity are positively correlated[22], and that improvement in muscle strength, flexibility, and balance reduces IL-6[23]. In this study too, the improvement in muscle strength, flexibility, and balance through regular complex exercise is thought to have brought about the positive reduction in IL-6.

TNF-α is an adipocytokine associated with the inflammatory response and is known to be an indicator of senile diseases such as hypertension, atherosclerosis, and insulin resistance due to elevated body fat, including abdominal fat, and reduction in fat-free mass including muscle mass. Exercise increases cardiac output to increase tissue blood flow and increase shear stress in the vessel walls. This surface stress can improve inflammatory markers because it reduces platelet activity, prevents platelet clotting and adhesion, induces vasodilatation, as well as further activating blood vessel functions by preventing inflammatory reactions around the blood vessels and thrombus formation.

Although no intragroup or intergroup difference in TNF-α appeared in this study. [24] reported that when patients accompanied by a acute heart failure or coronary artery disease performed nine items of endurance exercise for 20 minutes with two sets of 10 repeats at 90 % of the peak heart rate (HR) and at 50% of the 1repetitive maximum (1RM) three times per week for 16 weeks, there was no change in TNF-α and [25] reported that when the elderly aged 65-85 years performed aerobic exercise for 12 weeks (70-80% heart rate reserve, 20 minutes), there was no change in TNF-α. Therefore, the response of inflammatory cytokines to exercise is unclear. Based on the study results as such, it is thought that when study subjects were obese persons, the elderly, or diabetic patients, although the mean value of TNF-α decreased compared to the control group but the differences were not statistically significant because the study subjects' sensitivity to exercise was low. Therefore, changes in TNF-α may be expected through the application of diverse exercise periods to more diverse study subjects than those of this study.

4. Conclusion & recommendation

Through this study, the 12-week complex exercise program increases the amount of physical activity

in type 2 diabetic patients and improves factors such as upper limb endurance, lower limb endurance, balance, bone mass, HDL-C, HbA1c, and IL-6. It was found that there is an effect of improving cell production and activating factors.

However, in this study, although the production and activity of cranial nerves are determined by the influence of various hormones, only BDNF is considered as a cranial nerve production and activation factor. In addition, it was limited to type 2 diabetic patients, and although there were differences in some items of physical fitness and physical activity according to gender, gender could not be distinguished. Research should be continued by analyzing more hormones related to cranial nerve production and activity and increasing various research subjects.

5. References

1. Lin T, Chou P, Lai MS, Tsai ST, Tai TY. Direct costs-of-illness of patients with diabetes mellitus in Taiwan. Diabetes Res Clin Pract. 2001 Nov;54(Suppl 1):S43-6. DOI:10.1016/S0168-8227(01)00308-4.
2. Kim HJ. The relationship between brain-derived neurotrophic factor, serotonin, physical fitness, energy expenditure and exercise intensity in children. Korean J Obes. 2013 Jun;22(2):107-13.
3. Cotman CW, Berchtold NC. Exercise: A behavioral intervention to enhance brain health and plasticity. Trends in Neuroscience. 2002 Jun;25(6):295-301. DOI:10.1016/S0166-2236(02)02143-4.
4. Tsuchida A, Nonomura T, Nakagawa T, Itakura Y, Ono-Kishino M, Yamanaka M, et al. Brain-derived neurotrophic factor ameliorates lipid metabolism in diabetic mice. Diabetes Obes Metab. 2002 Jul;4(4):262-9. DOI:10.1046/j.1463-1326.2002.00206.x.
5. Lisle DK, Trojian TH. Managing the athlete with type 1 diabetes. Curr Sports Med Rep. 2006 Apr;5(2):93-8.
6. Al-Maatouq MA, El-Desouki MI, Othman SA, Mattar EH, Babay ZA, Addar M. Prevalence of osteoporosis among postmenopausal females with diabetes mellitus. Saudi Med J. 2004 Oct;25(10):1423-7.
7. Byeon JK, Kim HJ, Goong SS, Park SH, Seo JK, Byeon JM, et al. The effects of 12-week combined exercise program on BMD, PTH, and IGF-Ⅰ in elderly women. The Official Journal of the Korean Academy of Kinesiology. 2010 Jan;12(1):55-64.
8. Succurro E, Marini MA, Arturi F, Grembiale A, Fiorentino TV, Andreozzi F, et al. Usefulness of hemoglobin A1c as a criterion to define the metabolic syndrome in a cohort of Italian non diabetes white subjects. Am J Cardiol. 2011 Jun;107(11):1650-5. DOI:10.1016/j.amjcard.2011.01.055.
9. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010 Jan;33(Suppl 1):62-9. DOI:10.2337/dc10-S062.
10. Lambers S, Van Laethem C, Van Acker K, Calders P. Influence of Complex Exercise Training on Indices of Obesity, Diabetes and Cardiovascular Risk in Type 2 Diabetes Patients. Clin Rehabil. 2008 Jun;22(6):483-92. DOI:10.1177/0269215508084582.
11. Kirk A, Mutrie N, Mac-Intyre P, Fisher M. Increasing physical activity in people with type 2 diabetes. Diabetes Care. 2003 Apr;26(4):1186-92. DOI:10.2337/diacare.26.4.1186.
12. Greene NP, Martin SE, Crouse SF. Acute exercise and training alter blood lipid and lipoprotein profiles differently in overweight and obese men and women. Obesity(Silver Spring). 2012 Aug;20(8):1618-27. DOI:10.1038/oby.2012.65.
13. Currie J, Ramsbottoma R, Ludlowa H, Nevill A, Gilder M. Cardio respiratory fitness, habitual

physical activity and serum brain derived neurotrophic factor in men and women. Neurosci Lett. 2009 Feb;451(2):152-5. DOI:10.1016/j.neulet.2008.12.043.

14. Seifert T, Brassard P, Wissenberg M, Rasmussen P, Nordby P, Stalknecht B, et al. Endurance training enhances BDNF release from the human brain. Am J Physiol Regul Integr Comp Physiol. 2010 Feb;298(2):372-7. DOI:10.1152/ajpregu.00525.2009.
15. Zoladz JA, Pilc A, Majerczak J, Grandys M, Zapart-Bukowska J, Duda K. (2008). Endurance training increases plasma brain-derived neurotrophic factor concentration in young healthy men. J Physiol Pharmacol. 2008 Dec;59(Suppl 7):119-32.
16. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci U S A. 2011 Feb;108(7):3017-22. DOI:10.1073/pnas.1015950108.
17. Schulte-Herbrüggen O, Nassenstein C, Lommatzsch M, Quarcoo D, Renz H, Braun A. Tumor necrosis factor-α and interleukin-6 regulate secretion of brain-derived neurotrophic factor in human monocytes. J Neuroimmunol. 2005 Mar;160(1-2):204-9. DOI:10.1016/j.jneuroim.2004.10.026.
18. Nybo L, Nielsen B, Klarlund Pedersen B, Møller K, Secher NH. Interleukin 6 release from the human brain during prolonged exercise. J Physiol. 2002 Aug;542(3):991-5. DOI:10.1113/jphysiol.2002.022285.
19. Ostrowski K, Rohde T, Asp S, Schjerling P, Pedersin BK. Pro-and anti inflammatory cytokine balance in strenuous exercise in humans. J Physiol. 1999 Feb;515(1):287-91. DOI:10.1111/j.1469-7793.1999.287ad.x.
20. Kohut ML, McCann DA, Russell DW, Konopka DN, Cunnick JE, Franke WD, et al. Aerobic exercise, but not flexibility/resistance exercise, reduces serum IL-18, CRP, and IL-6 independent of beta-blockers, BMI, and psychosocial factors in older adults. Brain Behav Immun. 2006 May;20(3):201-9. DOI:10.1016/j.bbi.2005.12.002.
21. Ryan AS, Nicklas BJ. Reductions in plasma cytokine levels with weight loss improve insulin sensitivity in overweight and obese postmenopausal women. Diabetes Care. 2004 Jul;27(7):1699-705. DOI:10.2337/diacare.27.7.1699.
22. Ostrowski K, Schjerling P, Pedersen BK. Physical activity and plasma interleukin-6 in humans effect of intensity of exercise. Eur J Appl Physiol. 2000 Dec;83(6):512-5. DOI:10.1007/s004210000312.
23. Park SK, Park JK, Kwon YC, Kim EH. The effects of complex training on self-reliance physical fitness, IL-6, TNF- and carotid artery in older women with sarcopenia. Journal of Sport and Leisure Studies. 2011 Aug;45(2):771-81.
24. Conraads VM, Beckers P, Bosmans J, De Clerck LS, Stevens WJ, Vrints CJ, et al. Complex endurance/resistance training reduces plasma TNF-α receptor levels in patients with chronic heart failure and coronary artery disease. Eur Heart J. 2002 Dec;23(23):1854-60. DOI:10.1053/euhj.2002.3239.
25. Stewart LK, Flynn MG, Campbell WW, Craig BA, Robinson JP, Timmerman KL, et al. The influence of exercise training on inflammatory cytokines and C-reactive protein. Med Sci Sports Exerc. 2007 Oct;39(10):1714-9. DOI:10.1249/mss.0b013e31811ece1c.