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The Effect of Eight Weeks of Aerobic, Anaerobic and Resistance Training on some factor of Endocannabinoid System, Serotonin, Beta-Endorphin and BDNF in Young Men

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The aim of this study was investigated the effect of eight weeks of aerobic, anaerobic and resistance training on some endocannabinoid, serotonin, beta-endorphin and BDNF agents of young men. Thirty-two young men (19 to 25 years old) who did not have regular physical activity were randomly divided into four groups, and each of them were participated in various sports exercises for eight weeks. A group for aerobic exercises (two exercises with 65-70 maximum heart rate 3 sessions per week), an anaerobic exercise group (two exercises with a maximum intensity of 3 sessions per week), a group for circular resistance exercises (6-8 Station Which is repeated 8-12 times, and for three times a week) and finally a group was selected as a control. ELISA method was used to measure endocannabinoid system, serotonin, beta-endorphin and BDNF factors. The results showed that eight weeks aerobic training significantly increased serotonin levels and eight weeks aerobic and anaerobic exercise significantly increased BDNF. Aerobic, anaerobic, and resistive exercises have no significant effect on arachidonoyl glycerol (2-AG), anandamide(AEA) and beta-endorphin. There was a significant increase in happiness in all three training groups compared to the control group.The results of this study indicated an increase in mediation associated with pleasure and happiness in humans. Concerning the particular effect of long-term exercise on the endocannabinoid system, it is difficult to conclude.

Keywords: Training, Anandamide (AEA), Arachidonoyl glycerol (2-AG), Beta-endorphin, serotonin, BDNF.

One of the most common conditions for challenging human physiological systems is exercise. Although several studies have been done on the role of exercise and its effects on various systems, such as the catecholamine system[1] or the hypothalamic-pituitary axis (HPA) [2], few studies have examined the role of endocannabinoid system under stressful conditions[3]. Recent researches on human and animal models confirm the strong role of exercise in endocannabinoid system and physiological mechanisms that may eventually lead to "runners high"[4-5]. The system that was discovered in the late 1980s includes the following elements: 1- cannabinoid receptors, 2- endogenous ligands (neurotransmitters), 3- Specific proteins involved in endocannabinoid biosynthesis, and 4- degradable enzymes such as FAAH (Fatty Acid Amide Hydrolase). The endocannabinoid system has intrinsic nervous carriers and its ligands are cannabinoid receptors CB1 and CB2, which were originally identified as active receptors of THC, the main psychoactive substance in marijuana[4-6]. The two intrinsic substances of the endocannabinoid system are

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anandamide (N-arachidonylethanolamide, AEA) and 2- arachidonoylglycerol (2-AG), they are an important intermediary in the interaction of psychological/emotional stressors, as well as the physical response to physical activity[7-8]. Sports exercises and the intrinsic communication system of endocanninoids in the hypothalamus depend heavily on each other. The endocannabinoid system function in the hypothalamus is heavily influenced by physiological changes, and appropriate sports exercises can lead to activation of the system[9] .The performance of the endocannabinoid system improves with regular exercise, although the role of these exercises is still not fully understood[10] .It seems that endocannabinoid activity induced by exercise in humans, changes with the intensity of exercise[10], although the results of researches on the impact of different exercise methods on endocannabinoid system factors are contradictory and insignificant[11-13]. During the past researches, it has been shown that BDNF plays an important role in the sports exercise as an effective factor in the treatment of depression[14]. AEA and 2-AG have the capacity to affect the CB1 receptor through their agonist to change the cognitive and emotional behavior, neurogenesis and neurotrophin levels[15]. About the effects of endurance and resistance sports on BDNF values, the existing information are contradictory and unconvincing. While it is reported that chronic endurance exercise has led to an increase in BDNF levels[16-17], some studies have shown a lack of change or even a decrease in BDNF levels following an endurance exercise[18-19]. In studies about resistance exercise, such as endurance exercise, also increased[20-21] and decreased or lack of change[22-24] of BDNF levels have been reported following exercise and at baseline levels. Azuma et al. (2015) also, after 16 weeks of periodic exercises, over 90% of the maximum oxygen intake in 12 healthy men did not find a significant increase in BDNF levels compared to the control group[25]. Prior to the discovery of the positive role of exercise on the endocannabinoid system (ECB), analgesic effects are often described as direct results related to changes in endogenous opioids such as endorphins on the pain system[26]. The activation of CB2 surface receptors lead to the release of opioid endogenous peptides, such as â-endorphin, from human and wolf skin cultured linear cells in genetic labs[27]. Researches on exercise and its effect on concentration of endorphins have contradictory results[28-34]. During researches, the researchers concluded that throughout the continuous and prolonged exercise with moderate level, the level of beta-endorphin in the plasma increases, although the beta-endorphin response varies with intensity of exercise[28-30]. However, the results of some studies showed that long-term resistance and rapid activity reduced or did not change beta-endorphin levels[31-33], while others indicated an increase in â-endorphin levels[34]. Research results have shown that the endocannabinoid system affects serotonin release[35]. Some researchers have shown that long-term aerobic exercise increases the concentration of free tryptophan in the plasma, which results in increased serotonin synthesis and its' release into the bloodstream[36-38]. This is while in the case of resistance and anaerobic exercises, the results are contradictory[39-40]. Given that so far, few studies have been conducted on the endocannabinoid system and its relation to happiness associated hormones such as serotonin, beta-endorphin and BDNF, so to examine the characteristics of the response of cannabinoids to sports exercise and its relation with hormones associated with happiness, doing this research seems necessary. For this purpose, important factors related to them such as duration and intensity of physical activity, type of activity, gender, and weight of volunteers were considered in this research. Therefore, the present study attempts to investigate the effect of eight weeks of various exercises, such as anaerobic, aerobic, and resistance on endocannabinoid system and hormones related to happiness such as serotonin, beta-endorphin and BDNF in young men.

METHODOLOGY

Research Subjects

40 young men from 19 to 25 years old from Babol were selected who did not have regular physical activity. At the end of the exercise, 8 subjects were excluded from the study. Subjects were divided into four groups of ten; where one group performed eight weeks of aerobic exercise, another group performed eight weeks of anaerobic exercise, one group performed eight weeks of circular resistance exercise, and finally a control group were selected that did not perform any

specific sports activities during these eight weeks. The present study received an ethics code number of (IR.MEDSAB.REC.1395.127) from Sabzevar University of Medical Sciences.

Research Methodology and Data Collection Method

The present research is semi-experimental. Inclusion criteria included non-use of supplements and joying materials and non-smoking. In the first session, height, weight, and fat percentage and aerobic exercise information of subjects were measured using a 2400-meter test, and information about the anaerobic power of the subjects was were collected using rest test. One hour after having the same breakfast, blood samples were collected from all subjects, and at the end of 8 weeks of exercise, and after the last exercise session, the second blood samples were collected while resting from all subjects after breakfast according to the first step[41]. The number of exercise sessions was 3 days a week. To measure the happiness level, this general question was used that whether are you generally feeling happy? Which subjects rated it from zero to 10 based on the visual analogue [42].

Workout Protocol

Aerobic exercise was performed periodically, with a maximum heart rate of 65-70%; running time was 3 minutes in each set and rest between sets was one minute; the first week was started with 4 sets, and ended with 11 sets in the eighth week. The anaerobic exercise was considered in each set of running at 30, 60, and 90 meters with the maximum intensity and power with 30, 45, and 60 seconds of rest between the marked distances. The first week started with 8 sets and ended with 16 sets in the eighth week. The resistance exercise was circularly designed, and began with 6 stations in the first week, and ended with 8 stations in the last week. The number of repetitions in each set were 8 to 12 repetitions maximum, and a one-minute rest was considered between stations. Weight exercises consisted of 4 stations for the lower trunk and 4 stations for the upper trunk.

Measuring the Changes in Hormonal Concentration

5 cc blood was collected in two steps, before and after the end of the course of long-term exercises while resting from the right ventricle, and then immediately poured in the test tubes containing EDTA (anticoagulant), and then it was centrifuged for 10 minutes at 3000 rpm, and the isolated plasma was kept at -20° C so as to measure the variables. Plasma concentrations analysis of 2-arsidonyl glycerol (2-AG) and anandamide (AEA) and serotonin, â-endorphin and BDNF hormones were measured by ELISA method. 2-AG was measured from the German ZellBio kit with a sensitivity of 0.02 ng/L and also AEA was measured with German ZellBio kit. To measure plasma concentrations of beta-endorphin, serotonin, and BDNF, the ELISA kit of Eastbiopharm Corp. of China was used with a sensitivity of 2.59 ng/l, 0.22 ng/ml, and 0.01 ng/ml, respectively.

Statistical Methods

Shapiro-Wilk test was used to check the normality of the data. Finally, for analyzing the normalized data, SPSS software version 20 was used and ANCOVA and dependent T-test were used and in case the initial change was significant, then Bonferroni's post hoc test was used for pairwise comparison of the means. Data confidence limits were considered at a level of 0.05.

RESULT AND DISCUSSION

Table 1 shows the demographic characteristics of the subjects. Aerobic exercises resulted in a significant increase in Vo2max compared to the control group and the resistance exercise group. Anaerobic exercise also significantly increased Vo2max. However, resistance exercises did not significantly change Vo2max. Aerobic exercises and anaerobic exercises significantly increased the maximum anaerobic power in comparison with the control group. Resistance exercises did not significantly change the maximum anaerobic power (table2.)

Eight weeks of aerobic exercise significantly increased the plasma serotonin compared to the control group and anaerobic exercise group. Anaerobic and resistance exercise did not have a significant effect on this index. Eight weeks of anaerobic, aerobic and resistance exercises had no significant effect on plasma anandamide. Only the plasma anandamide in the control group was significantly higher in comparison to the resistance exercise group (Table 3). There was no significant effect on arachidoneyl

glycerol and plasma beta-endorphin in the eight weeks of anaerobic, aerobic and resistance exercises. Eight weeks of aerobic and anaerobic exercises increased plasma BDNF significantly compared to resistance exercise group. However, resistance exercise did not have a significant effect on this index (Table 3).

Anaerobic, aerobic, and resistance exercises significantly increased happiness compared to the control group. There was no significant difference between the exercise groups in terms of this variable (Table 2).

The purpose of this study was to investigate the effect of eight weeks of anaerobic, aerobic and resistance exercise on some endocannabinoid system factors and some hormones related to happiness in young men. Eight weeks of aerobic, anaerobic, and resistance exercises did not have a significant effect on plasma beta-endorphin levels in the participants. Tagashira et al. (2004) stated anaerobic exercise, and Sharifi et al. (2013) expressed aerobic exercise as ineffective on the plasma levels of beta-endorphins[43-44]. While the results of Sadat Jamali et al. (2013), Koseoglu et al. (2003), Doiron et al. (1999) do not coincide with the results of this research[29-30-34]. The main reasons for these differences are the gender of the subjects, as well as the difference in practice protocol and lack of control group. Another important factor that may cause variation in the measurement of endorphin levels is the method used to measure the level of blood hormones that can easily affect the outcome of the research[45]. Individual differences may also result in different research results [46-47].

In this study, eight weeks of aerobic exercises significantly increased the plasma serotonin compared to the control group and the anaerobic and resistance exercise did not have a significant effect on this index. Researches on addicted women and men showed that the eight weeks of aerobic exercise would result in a significant increase in their serum serotonin, which is consistent with the results of this study[48-50], Hakkak Dukht et al. (2015) in a research titled as the comparison of the effect of eight weeks of resistance exercise and aerobic exercise on

Table 1. Anthropometrics characteristics of subjects

Group/Parameter	Height (cm)	Age (year)	Fat Body percentage	Weight(Kg)
Control group	181.12±2.79	21±1.19	20.51±6.81	78.87±11.88
Anaerobic group	182.12±7.92	21.12±1.72	17.62±7.14	72.88±20.27
Aerobic group	179±7.17	20.27±1.4	15.64±6.04	68.25±12.89
Resistance group	180±11.2	20.12±1.55	22.67±6.15	85.11±22.29
P	0.88	0.48	0.1	0.2

Table 2. Statistics related to physiological variables and happiness

	Parameter	Before Exercises	After Exercises	P of Intergroup	P of Out of group
Aerobic Power	Control group	38.42±8.25	38.84±7.8	0.56	
(ml/kg.min)	Anaerobic group	42.79±6.27	46.61±4.41	0.004	
	Aerobic group	44.9±4.13	51.15±5.25	0.0001	
	Resistance group	39.2±9.2	40.11±6.76	0.51	0.001
Anaerobic Power	Control group	432.86±116.39	415.73±92.16	0.43	
WAT	Anaerobic group	415.84±177.57	605.45±209.7	0.0001	
	Aerobic group	469.13±68.58	604.26±85.18	0.002	
	Resistance group	472.75±100.97	463.08±88.33	0.74	0.02
The amount of joy	Control group	8±0.92	7.88±1.45	0.78	
10-unit scale	Anaerobic group	8.25±0.88	9.37±0.74	0.03	
	Aerobic group	7.75±1.03	9.25±1.116	0.003	
	Resistance group	7.37±1.59	8.75±0.88	0.02	0.04

the serum serotonin concentration of depressed female students, showed that aerobic exercise had a greater effect on the increase in the serum concentrations than resistance exercise[51]. In another study on brain tissue of the mouse, the results showed that both aerobic and anaerobic exercise significantly increased the serotonin levels in the brain tissue, with serotonin synthesis increased in the brain, its serum levels also increase[40]. For the findings of this study, a number of possible mechanisms can be suggested; during exercise, brain blood flow increases, resulting in increased levels of tryptophan in the brain after exercise, leading to more serotonin synthesis. By increasing serotonin synthesis and metabolism, blood serum levels also improve; changes in platelets following an aerobic exercise result in improved serotonin levels, because the platelets are the main carrier of serotonin in the blood[52]. Another possible mechanism that increases serotonin is the neurotrophic growth factor. Aerobic exercises induces an increase in the vascular endothelial growth factor that may stimulate angiogenesis and has a direct effect on the neurotrophic growth factor, which leads to the reconstruction and repair of the serotonin monoaminergic terminals[53]. On the other hand, blood serotonin levels are affected by factors such as decreased carbohydrate of the blood, increased blood fatty acids, and increased oxidation of branched-chain amino acids, and these factors develop in endurance and long-term sports activities with moderate severity[54]. Therefore, it can be a factor affecting serotonin significantly in aerobic activity compared to other exercise methods. Also, the level of free fatty acids increase due to lipolysis and separated the binding of albumin to tryptophan and it binds to albumin due to a higher inclination, which is the reason why free tryptophan is increased in plasma[55].

In the present study, eight weeks of aerobic and anaerobic exercise significantly increased plasma BDNF compared to the control group, but resistance exercises did not have a significant effect on this index. Long-term aerobic exercise results in a significant increase in serum BDNF levels[56]. Regarding the mechanisms of blood circle BDNF increase, in response to the exercise program, it has been concluded that exercise increases BDNF expression in the brain, and in particular increases the hippocampal region, by stimulating the receptor tyrosine kinase B[57]. Raffaelli et al. (2009) stated that BDNF could be released from major source

Table 3. Statistics related to variables related to happiness

	Parameter	Before Exercises	After Exercises	P of Intergroup	P of Out of group
AEA	Control group	3.59±0.61	4.58±2.07	0.26	
(ng/L)	Anaerobic group	4.17±1.17	4.29±1.07	0.85	
	Aerobic group	3±0.94	3.09±1.06	0.88	
	Resistance group	2.77±1.03	2.78±1	0.98	0.02
2-AG	Control group	3.49±0.6	5.11±1.57	0.058	
(ng/L)	Anaerobic group	4.72±1.8	5.37±2.8	0.36	
	Aerobic group	4.94±1.74	5.53±1.33	0.01	
	Resistance group	4.89±1.53	4.37±1.99	0.37	0.19
Serotonin	Control group	82.48±7.21	80.79±9.75	0.63	
(ng/L)	Anaerobic group	82.14±21.67	91.40±	0.32	
	Aerobic group	64.46±14.24	99.4±13.47	0.0001	
	Resistance group	61.06±22.29	74.31±20.87	0.09	0.006
Beta-Endorphin	Control group	141.08±67.86	208.84±92.07	0.09	
(ng/L)	Anaerobic group	157.69±81.86	176.91±82.70	0.19	
	Aerobic group	195.66±10.45	225.67±104.25	0.04	
	Resistance group	245.26±99.31	289.77±119.81	0.04	0.45
BDNF	Control group	1.25±0.39	1.20±0.25	0.71	
(ng/L)	Anaerobic group	1.08±0.31	1.64±0.80	0.03	
	Aerobic group	1.23±0.15	1.74±0.28	0.002	
	Resistance group	0.97±0.52	0.81±0.44	0.53	0.005

of it storage such as platelet [58].Studies show that the intensity and duration of the exercise program affects levels of BDNF, and moderate exercise results in elevated levels of BDNF[59]. Also, Yarrow et al. (2010) considered the cause of not changing and decreasing BDNF after 5 weeks of resistance exercise, as increasing BDNF uptake, increasing BDNF purification from the circulation, or reducing BDNF secretion during recovery[20].

In the present study, eight weeks of anaerobic, aerobic, and resistance exercises had no significant effect on the plasma anandamide levels. But plasma anandamide significantly decreased in resistance exercise group than control group. Also, eight weeks of anaerobic, aerobic, and resistance exercises had no significant effect on the 2-AG. Studies on the endocannabinoid system and physical activity are very limited, however, most of these studies have been performed on mice and the number of studies conducted on humans is very limited. Oliveira et al. (2014) in a study on healthy individuals and people with migraine headaches, the effect of 12 weeks of aerobic exercise with a protocol of 3 sessions per week for 30 minutes with a standard intensity on a treadmill showed that plasma AEA levels in healthy subjects significantly decreased[11], which is not consistent with the results of the present study, but the result of this study did not show a significant increase. The causes of this difference seem to be related to the aerobic exercise protocol, as well as the difference in subjects' status. The results of the studies indicate that the endocannabinoid signaling system affects the release of serotonin. Indeed, under live conditions, the activation of endocannabinoid receptors will inhibit the release of serotonin from the front of the brain and the hippocampus[35]. In contrast, the drug siege of the receptor CB1, or its reduction, leads to an increase in serotonin release from the outer surface in the middle cerebral cortex[60-61]. Concomitant with the above results, a significant increase in serotonin levels was observed after aerobic activity, while anandamide did not show a significant change. On the other hand, it has been shown that endocannabinoid signaling is stimulated by stress and glucocorticoid hormones, especially cortisol[9], it has been observed that there is a positive correlation between serum cortisol levels and serum AEA in healthy individuals[12] and the assumption of Heyman et al. (2012) was that part of the change in AEA levels during exercise and during recovery was related to changes in cortisol levels resulting from exercise in individuals[12]. On the other hand, many of the studies carried out over a long period of time in a variety of aerobic, anaerobic, and power methods, show that no significant changes occur in cortisol levels, and even in many of them, it has been shown to significantly decrease cortisol levels[62-64]. Therefore, it seems that due to the stated relationship, one of the reasons for not changing the AEA in aerobic, anaerobic, and resistance exercise is to reduce or not to change cortisol. Research findings emphasize that long-term exercise alone cannot change the levels of endocanninoid bases[12]. You et al. (2011), while studying the effect of 20 weeks of aerobic exercise with a caloric restriction in a study, stated in the end that about the specific long-term effect on the endocannabinoid system, a definitive conclusion is difficult[65]. In summary, further researches is necessary on the long-term effects of endurance sports on endocannabinoids and their interactions with the activation of Peroxisome proliferator-activated receptors (PPAR) and its metabolic consequences in different tissues on humans and animals[12], and this research literature clearly implies the limitation of information in this field.

In this study, eight weeks of anaerobic, aerobic, and resistance exercises significantly increased happiness compared to the control group. There was no significant difference between the exercise groups in terms of this variable. Beta-endorphin is produced during exercise in the brain and its secretion becomes more active after exercise[39], when exercise ends, the effects of this secretion in the body create a sense of mental relaxation, and this feeling is due to an evolutionary process[65]. Further analysis of statistical results shows that there is a strong relationship between sport and sense of happiness, but this relationship is not clear, therefore it is called the underlying factor[66]. In the present study, after 8 weeks of aerobic and anaerobic exercise, BDNF level and 8 weeks of aerobic exercise, serotonin levels had a significant difference with the control group, but other endogenous factors expressed in this study were not increased. However, Mir Shahi et al. (2002) stated that in addition to leisure activities and exercise, there are other factors that affect

people's happiness, including: personality, self-esteem, religious beliefs, social capital, economic status, job satisfaction, health, marital status and gender[67]. Therefore, it seems that the only factors that affect happiness are not physiological factors, despite there are other physiological factors that affect the level of happiness and have not been addressed in this study. However, unlike the lack of significant increase in some endogenous factors that lead to happiness, participants in this study stated that all three types of exercise led to a significant increase in happiness after eight weeks. Antunes et al. (2016) showed that after two weeks of exercise deprivation, young men who were addicted to exercise, a 60-minute aerobic exercise on treadmill, led to an increase in the AEA, but level of happiness and positive mental states increased[68]. There is evidence that aerobic exercise two or three times a week with moderate intensity for a long time reduces depression and increases happiness[69-71]. Swan (2015) in a study on the effect of resistance exercise on the behavior of healthy individuals showed that 6 weeks of resistance exercise reduced depression and increased happiness among them[72], which is consistent with the results of the present study. Happiness is a complex concept and a combination of several factors. In general, these factors can be divided into endogenous and exogenous segments. Although exogenous factors are effective on feelings of happiness, the basis of this feeling is from endogenous factors.

CONCLUSION

The results of this study show that variables such as serotonin in aerobic exercise and BDNF in aerobic and anaerobic exercises indicate significant increase. On the other hand, endocannabinoid factors including AEA and 2-AG and also beta-endorphins are not affected by different exercises. Affected by sports exercises, happiness is improved, but there is no difference between the different types of exercises from the perspective of this study.

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