Obesity Medicine 15 (2019) 100104

Contents lists available at ScienceDirect

Obesity Medicine

journal homepage: www.elsevier.com/locate/obmed

Original research

Playing in form of outdoor aerobic exercise is more effective than indoor treadmill exercise on serum Orexin-A and weight loss in obese adolescent boys

Ebrahim Moslehi[a,*], Zahra Moslehi[a], Bahman khalvati[b]

[a] Physical Education and Sports Science College, Payam Noor University, Tehran, Iran
[b] Medicinal Plants Research Center, Yasuj University of Medical Sciences, Yasuj, Iran

ARTICLE INFO

Keywords:
Outdoor aerobic exercise
Indoor treadmill exercise
Orexin-A
Obesity
Weight loss

ABSTRACT:

Purpose: Due to the major public health concern of obesity in children and adolescent and possible biochemical effects of orexin-A (OXA), and environment of exercise in metabolic energy hemostasis and obesity the effectiveness of playing in form of outdoor aerobic exercise and indoor treadmill exercise on serum OXA and weight loss in obese adolescent boys were investigated.

Methods: Thirty male adolescent boys aged 10–12 years with an average BMI of 29–31 kg/m^2 were randomly divided into three groups: playing in form of outdoor aerobic exercise (POAE), indoor aerobic treadmill exercise (ITAE) and control group (C).

Body mass index (BMI), body fat percentage (skinfold-based on Jackson Pollock's seven-point method), VO_2MAX (Modified Balke treadmill protocol test) and fasting level of serum OXA (human OXA ELISA Kit) measured before and after eight weeks (three session per week) of two different aerobic exercises method.

Results: Exercise cause to significantly increase in the serum OXA in both groups ($P = 0.001$). This increase in the POAE group was higher than relative to the ITAE group ($P = 0.004$). Also, Improvements in the BMI and body fat percentage in the POAE group significantly greater than ITAE group ($P = 0.001$).

Conclusion: playing in form of outdoor aerobic exercise is more effective than indoor aerobic treadmill exercise on serum OXA and weight loss.

1. Introduction

The high prevalence of overweight and obesity in children and adolescents constitutes a huge public health burden (Ahmad and Imam, 2015). It is estimated that over 340 million children and adolescents aged 5 to 19 are obese or overweight (Ahmad and Imam, 2015). The early onset of obesity leads to an increased likelihood of obesity into adulthood and links to increased prevalence of obesity-related disorders such as coronary diseases, insulin resistance, diabetes mellitus, hypertension, sleep apnea, arthritis, cancer, stroke and heart failure in later life (Hughes-Austin et al., 2013; Wensveen et al., 2015; Gorostegi-Anduaga et al., 2018). It has been shown that excess adipose tissue released many inflammatory cytokines which play an important role in obesity-induced metabolic disorders (Wensveen et al., 2015). Studies indicate that hormonal production and regulation in response to physical activity and exercise can have powerful effects on metabolic processes. In this regard, Orexin-A and B or Hypocertine 1 and 2 are two neuropeptides with a wide range of functions in the central nervous system and peripheral tissue that produced by neurons located in the brain perifornical and lateral hypothalamic area (LHA) (Sakurai et al., 2015). Due to the widespread distribution of Orexin neurons in the central nervous system, and rapid release of Orexin from the blood-brain barrier (Kastin and Akerstrom, 1999) and also the presence of large protein G receptors in various tissues, this neuropeptide is involved in many physiological actions and metabolic processes (Sakurai et al., 2015; Chieffi et al., 2017a, 2017b). Studies have shown that Orexin neuropeptides are involved in energy expenditure and Non-shivering thermogenesis (Blais et al., 2017). For example, animal models lacking a functional orexin system develop obesity despite consuming fewer calories than their wildtype counterparts (Hara et al., 2001). In this regard, central nervous system stimuli through the orexin neurons in the hypothalamus, as well as adrenergic agonists released from the sympathetic neurons, cause an increase in mitochondrial biogenesis and enhanced peripheral tissue thermogenesis (Zink et al.,

* Corresponding author. Tel.: +987433234428; fax: +987433232470.
E-mail address: Ebrahim.Moslehi@pnu.ac.ir (E. Moslehi).

https://doi.org/10.1016/j.obmed.2019.100104
Received 11 February 2019; Received in revised form 20 May 2019; Accepted 22 May 2019

Abbreviations:

OXA	orexin-A	C	control group
BMI	body mass index	LHA	lateral hypothalamus area
POAE	playing in form of outdoor aerobic exercise group	CSF	cerebrospinal fluid
ITAE	indoor aerobic treadmill exercise group	VO_2Max	maximum oxygen consumption
		TDEE	total daily energy expenditure
		SPA	spontaneous physical activity

2018). It has been reported that the single activation of orexin neurons is enough to increase total 24-h energy expenditure (Zink et al., 2018).

Also, when the orexinergic tone is amplified, either through intracranial peptide infusions or stimulation of orexin neuron activity, increases in spontaneous physical activity (SPA) and calories burned occurs (Kotz et al., 2012). Therefore, the potential role of the OXA in impulsive motor activity and energy expenditure related to the obesity disorders treatment can be attractive and interesting.

On the other hand, it seems that exercise, especially aerobic exercise with an effect on the orexin system and increases the neuronal excitation of these neurons in the LHA can alter the thermogenic properties and energy expenditure in the peripheral tissue (Messina et al., 2016). Messina et al. (Messina et al., 2014a, 2014b) reported that exercise at 75 W for 15 min on the cycle ergometer cause a significant increase in the OXA. They believed that possible increased plasmatic OXA during exercise can induce cerebral stimulation of areas that, in turn, control the sympathetic reactions. Also, it seems that exercise by the effect on many metabolic and physiological parameter which influence on orexin system can alter orexin neurons activity. Stimulants such as glucose hemostasis, insulin resistance, leptin, amino acids, myokines, and metabolite secretion during and after exercise are involved in this interaction (Chieffi et al., 2017a, 2017b).

On the other hand, orexin neurons receive different signals associated with environmental, physiological and emotional stimuli (Scammell and Winrow, 2011). So, in the brain, input coming from regions that implicated in emotions are important in the regulation of orexin neuron activity (Ohno and Sakurai, 2008). It has been shown that individuals who enjoy exercise may exhibit more positive affective responses compared to those who enjoy exercise less (Raedeke, 2007). Wu and his colleagues in comparison of the effectiveness of treadmill exercise and yard play on cerebrospinal fluid (CSF) of OXA believe that the emotional aspects of yard play account for the observed OXA enhancement (Wu et al., 2011).

In this regard participant in outdoor exercise reported greater enjoyment and satisfaction compared with indoor exercise (Yeh et al., 2017). So, it seems that greater enjoyment of children to do outdoor exercise will be associated with higher secretion of OXA. Therefore, from this aspect, the comparison of outdoor exercise and indoor treadmill exercise on the orexin system can be interesting. Notably, most studies related to the orexin system have focused on drug treatment, and few studies have been conducted on the interaction between exercise, orexin and its effect on weight loss. In addition, the study that compares the effects of playing in form of outdoor aerobic exercise and indoor treadmill exercise on the orexin system of adolescent boys has not been done so far. Therefore in this study, we investigated the effectiveness of playing in form of outdoor aerobic exercise and indoor treadmill exercise on serum OXA and weight loss in obese adolescent boys.

2. Methodology

2.1. Subjects

In order to calculate the number of participants G power software was used ($\alpha = 0.05$, power $(1\text{-}\beta) = 0.95$ and group number = 3). According to G power software, 30 boys aged 10 to 12 from Yasouj city schools with the characteristics listed in Table 1 participated. The selection of subjects was carried out in coordination with the Yasuj City Education Office in November 2017. After describing the goals and the research process in the seasonal gatherings of physical education teachers, they were asked to introduce the researchers from among 10–12 years old male students who had BMI over 25 and overweight. Then, in the list, 30 obese boys were randomly selected and divided into three equal groups: playing in form of outdoor aerobic exercise (POAE), indoor aerobic treadmill exercise (ITAE) and control group (C). After explaining the goals of the study and research process for subjects and their parents, the informed consent form of participation in research, was signed. In the form, the absence of any disease, including cardiovascular, kidney, liver, diabetes and inability, was emphasized. Also, during the research process, no systematic physical activity was performed, except as prescribed by the investigator. Although subjects were free to eat it was emphasized that no supplements or drugs would be used during the research process. Indicators in the pre-test and post-test were measured in similar conditions from 8 to 11 a.m.

2.2. Body composition

BMI calculated by using height and weight that measured with the Sahand Digital Scale Model BSR 85. Furthermore, according to the Jackson Pollock's seven-point formula (Eqs. (1) and (2)) fat percentage by using of England's Harpenden Caliper at the chest, midaxillary, triceps, abdomen, thigh, subscapular and super iliac region measured and calculated (Jackson et al., 1985). As shown below, in this formula, SUM7 is the sum of seven points in millimeter.

$$\text{Body Density} = 1.112 - (0.00043499 \times \text{SUM7}) + (0.00000055 \times \text{square of the SUM7}) - (0.00028826 \times \text{age}) \quad (1)$$

$$\text{Body Fat Percentage (\%)} = (495/\text{Body Density}) - 450 \quad (2)$$

2.3. Maximum oxygen consumption (VO2Max)

In the pre and post-test VO2Max estimated in similar conditions from 8 to 11 a.m. based on Modified Balke treadmill protocol test

Table 1
Mean and standard devotion of demographic characteristics of subjects involved in the research process.

group	N	variable					
		Age (Year)	Height (cm)	Weight (kg)	BMI (kg/m2)	VO2 MAX (lit/min)	fat percentage (%)
control	10	10.93 ± 0.53	156.6 ± 3.02	71.91 ± 4.32	29.66 ± 1.89	29.23 ± 1.82	31.65 ± 2.81
ITAE	10	10.87 ± 0.54	155.9 ± 3.57	72.72 ± 3.89	30.27 ± 2.06	30.71 ± 2.01	32.57 ± 3.02
POAE	10	11.12 ± 0.51	154.6 ± 2.41	71.00 ± 4.1	29.94 ± 2.06	30.94 ± 1.62	31.90 ± 3.2

(calculated by Eq. (3)) on the treadmill device Model T9300 turbo manufactured in Taiwan after a brief breakfast meal. Each subject following a 5 min warm-up (3.5 km/h and 0% grade) started the test at 5.6 km/h and 0% grade. Then the slope was set to 6% after 1 min and then every minute thereafter the slope is increased by 2% until the subject does not continue the test. In this point exercise heart rate (calculated by Eq. (4)) equal or greater than 95% maximum heart rate calculated by Karvonen method or ratings of perceived exertion (RPE) greater than 8 using the Borg Category Ratio scale-CR-10 (Marinov et al., 2003).

$$VO2max = 1.444\,(T) + 14.99 \quad (3)$$

$$\text{Maximum heart rate} = [207 - (\text{age} \times 0.7)] \quad (4)$$

2.4. Exercise protocol

As shown in Table 2 the ITAE and POAE groups exercised three sessions per week for eight weeks after a brief breakfast meal. The ITAE group exercised alone in the closed area with 12 m in length, 8 m in width and 5 m in height dimensions, 1870 m above the sea level at 8–11 a.m. in 21–24 °C and 50% humidity on the treadmill device Model T9300 turbo manufactured in Taiwan. The POAE group also performed the outdoor aerobic exercise in form of a football game in the 20 × 40 m artificial turf football field. The outside environment has a temperate temperature of 21–24 °C, a height of 1870 m above sea level, a moderate forest cover, gentle wind blowing and the training was done in the morning under the sun shine with 50–60% humidity.

The Subjects of each group trained at 65% of the reserve heart rate (estimated by using a polar pulsating belt (T31) made in Finland) in the first two weeks, 65–75% reserve heart rate in third to fifth weeks and at 75–85% reserve heart rate in six to eight weeks after 5 min warm up in each session. The duration of each session in groups was 25, 35 and 40 min respectively. In order to equalize the training intensity in POAE group with the ITAE group, subjects were trained in a specific reserve heart rate (according to the training protocol) that monitored by polar pulsating belt and Garmin GPSMAP 78s device made by Taiwan which placed in the small bags mounted on their wrists and maintained this intensity until the end of the training session. The distance traveled by the subjects and their average of speed measured and, analyzed each session to use for next session managing.

2.5. Blood analysis

Blood samples were collected 24 h before and after the exercise period following 12 h of overnight fasting. For serum isolation samples were centrifuged for 10 min at 1200 x g in room temperature in the tubes with clot activator and immediately transferred to the laboratory. Means of triplicate serum OXA measured according to the protocol of the human OXA ELISA Kit (Cat# EK-003-30) Phoenix company. The detectable range was 0–100 ng/ml and as a result, both inter-assay and intra-assay coefficient of variation was below 10%.

2.6. Statistical analysis

Normality of data and equality of variances tested by Kolmogorov–Smirnov and Levene's test. In order to eliminate the covariate factors, the mean differences between the pre and post-test in each variable were calculated. changes between groups investigated by one-way ANOVA and Tukey post hoc test. Inter-group comparisons also, examined by paired sample t-test. The correlations between serum OXA variations and the other parameters such as weight, BMI and fat percentage estimated by person's bivariate correlation. All statistical analysis was performed using Excel version 2016 and SPSS version 24 at a significant level $\alpha < 0.05$.

3. Result

As shown in Fig. 1 and Table 3 in the pre-test the differences between the groups in all variables were not significant. However, after aerobic exercise intervention in the POAE and ITAE groups mean comparison between the pre and posttest indices related to the body composition including BMI (13.92% and θ = 1.14 vs 7.63% and θ = 0.671), weight (13.35% and θ = 1.32 vs 7.7% and θ = 0.79), and skinfold body fat percentage (10.62% and θ = 1.26 vs 1.42% and θ = 0.34) significantly decreased. serum OXA (23.53% and θ = 2.42 vs 10.7% and θ = 1.4) and VO2MAX (5.97% and θ = 1.1 vs 7.88% and θ = 1.15) also increased significantly. However, this improvement in the POAE group relative to the ITAE group was higher. Furthermore, in the pre and posttest mean differences comparison between groups One-Way ANOVA and Tukey post hoc test shown that playing in form of aerobic exercise was more effective than indoor aerobic exercise. As shown in Fig. 1 this difference with the control group in POAE group was greater than to the ITAE group (BMI: θ = 0.45 vs θ = 0.17, weight: θ = 0.71 V θ = 0.23, skinfold body fat percentage: θ = 0.51 vs θ = 0.03 and serum OXA: θ = 1.03 vs θ = 0.65). Also, the differences between POAE group and ITAE group in BMI (θ = 0.27), weight (θ = 0.48), skinfold body fat percentage (θ = 0.47) and serum OXA (θ = 0.37) indices was significant (P = 0.001). Also, as shown in Fig. 1, after aerobic exercise intervention the RPE scale significantly reduced in booth group (P = 0.001 and θ = 0.98 V p = 0.01 and θ = 0.96). The differences between POAE group and ITAE group in this scale after aerobic exercise intervention also significant (P = 0.01 and θ = 1.15). Also, as shown in Table 4 the person's correlation estimated between serum OXA and weight, BMI and fat percentage were significant (P = 0.005, P = 0.026 and P = 0.006 respectively).

4. Discussion

In this study, we investigated the effects of playing in form of outdoor aerobic exercise and indoor treadmill exercise on serum OXA and weight loss in obese adolescent boys. As shown in Fig. 1 results indicated that eight-weeks of aerobic exercise results in a significant increase in the serum OXA both in POAE group (23.5%) and in the ITAE group (10.7%). Whereas this increase in the POAE group relative to the

Table 2
Training protocol of each group during research process.

Group	Stage (week)	Warm-Up				Training Protocol			
		Slope (degree)	Reserve Heart Rate (%)	Speed (km/h)	Time (min)	Reserve Heart Rate (%)	Speed (km/h)	Time (min)	Sessions per week
ITAE	1–2	0	20	3	5	65	Flexible	25	3
	3–5	0	20	3	5	65–75	Flexible	35	3
	5–8	0	20	3	5	75–85	Flexible	40	3
POAE	1–2	0	20	3	5	65	Flexible	25	3
	3–5	0	20	3	5	65–75	Flexible	35	3
	5–8	0	20	3	5	75–85	Flexible	40	3

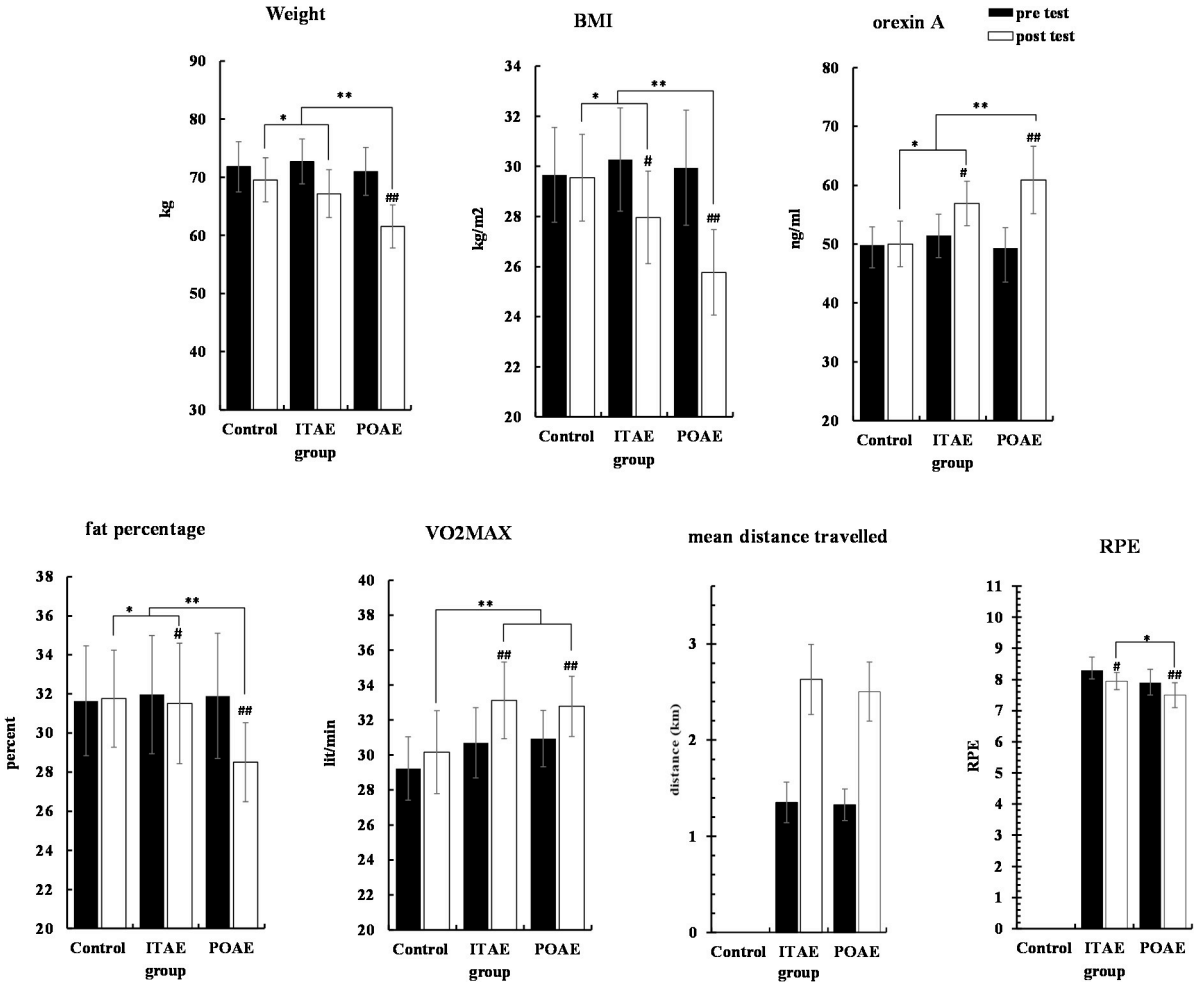

Fig. 1. Alteration of weight, BMI, orexin-A, mean distance traveled, VO2MAX and body fat percentage in different groups during the research process. (**POAE**): playing in form of outdoor aerobic exercise, (**ITAE**): indoor aerobic treadmill exercise and (**C**): control group. (#): Significant sign with pre-test, (*): Significant sign with another group.

Table 3
Mean, standard devotion and effect size (θ) of variable in different group during research process.

variable	group						effect size (θ)		
	control		ITEA		POAE		C vs ITEA	C vs POAE	ITEA vs POAE
	pre-test	post-test	pre-test	post-test	pre-test	post-test			
Weight (kg)	67.81 ± 4.32	67.53 ± 3.79	68.61 ± 3.89	65.45 ± 4.11*	66.68 ± 4.1	61.52 ± 3.7$^{**\#\#}$	0.23	0.71	0.48
BMI (kg/m2)	27.66 ± 1.89	27.54 ± 1.73	28.27 ± 2.04	26.96 ± 1.84$^{*\#}$	27.94 ± 2.06	25.77 ± 1.71$^{**\#\#}$	0.17	0.45	0.27
fat percentage (%)	31.65 ± 2.81	31.76 ± 2.49	32.57 ± 3.02	31.52 ± 3.08$^{*\#}$	31.9 ± 3.2	28.51 ± 2.03$^{**\#\#}$	0.03	0.51	0.47
VO2MAX (lit/min)	29.23 ± 1.82	30.16 ± 2.38	30.71 ± 2.01	33.13 ± 2.19$^{**\#\#}$	30.94 ± 1.62	32.79 ± 1.73$^{**\#\#}$	0.57	0.5	0.06
Orexin-A (ng/ml)	49.83 ± 3.07	50.01 ± 3.87	51.49 ± 3.62	56.9 ± 2.77$^{*\#}$	49.28 ± 3.62	60.88 ± 5.72$^{**\#\#}$	0.65	1.03	0.37
RPE	–	–	8.3 ± 0.42	7.95 ± 0.28	7.9 ± 0.43	7.5 ± 0.4	–	–	1.15
Mean of distance (km)	–	–	1.353 ± 0.211	2.63 ± 0.366	1.327 ± 0.164	2.504 ± 0.357	–	–	0.12

(*): significant sign with similar stage of another group.
(#): significant sign with pretest.
(θ): effect size.

Table 4
Correlations between serum OXA variations and the other parameters.

variable		Weight (kg)	BMI (kg/m2)	fat percentage (%)
Orexin-A (ng/ml)	Pearson Correlation	-.464[b]	-.359[a]	-.449[b]
	Sig. (2-tailed)	0.005	0.026	0.006

[a] Correlation is significant at the 0.05 level.
[b] Correlation is significant at the 0.01.

ITAE group was higher (12.8%). Also, body-fat percentage, weight, and BMI in POAE group and ITAE group decreased significantly. (−10.6% VS -3.2%, −7.6% VS -4.1%, and −7.8% VS -4.6% respectively). The VO_2 MAX also increased in both training groups significantly (5.8% VS 7.8%) (Fig. 1).

Several mechanisms are involved in this regard. Evidence suggests that following obesity, hyperglycemia, and decreased insulin sensitivity affect the orexin neurons in the LHA and reducing the pre-pro orexin gene expression (Yamamoto et al., 1999). Also, obesity with the effect on cannabinoid receptors in the LHA inhibits orexinergic neurons and reduces the amount of orexin secretion (Flores et al., 2013). Also, orexin neurons are sensitive to various metabolic parameters and various synaptic inputs. There is the possibility that the metabolism and overall energy profile will filter the pure net output of orexin neurons and independently alter the main outflow of orexin neurons (Perez-Leighton et al., 2014). Therefore, it is likely that the observed reduction of orexin-A in obese subjects is due to this reason.

In the current study, we observed an increase in serum levels of OXA after aerobic exercise intervention in male obese adolescent boys. It seemed that increased orexin levels after aerobic exercise intervention was due to the increased motor activities and other factors such as irisin derived from muscle during exercise (Ferrante et al., 2016), lactate secretion (Hao et al., 2016), heart's natriuretic peptides (Harms and Seale, 2013), CO2 homeostasis (Williams et al., 2007), glucose metabolism (Messina et al., 2014a, 2014b), and Cannabinoid receptors (Flores et al., 2013) has been affected on the secretion of orexin in the central nervous system. Consistent with the findings of this study, it has been reported that after exercise serum OXA increased significantly (Hao et al., 2016; Messina et al., 2016; Chieffi et al., 2017a, 2017b). Mohammad Hassani and et al. in studying the effect of eight weeks of endurance and high-intensity interval training (HIIT) on plasma OXA and some anthropometric indices in obese adolescent boys, reported that despite the decreasing trend of OXA in the control and HIIT group and the increasing trend in endurance training group, the difference of OXA between control and exercise groups was no significant (Mohammadhassani et al., 2015) which is inconsistent with the findings of this study. Although the source of peripheral orexin is still unclear some researchers proposed that orexin A might be directly released from the pituitary into the blood circulation (Tsunematsu and Yamanaka, 2012), since orexin-immunoreactive fibers are present in the median eminence and pituitary or leaked from the cerebrospinal fluid. Furthermore, orexin-A may rapidly cross the blood-brain barrier from brain tissue to reach blood by the process of simple diffusion (Chieffi et al., 2017a, 2017b).

Also, it has been reported that OXA trough the alteration in spontaneous physical activity (SPA) and peripheral tissue thermogenesis is associated with total daily energy expenditure (TDEE) (Seale, 2011; Zink et al., 2018). Orexin terminals innervate noradrenergic locus coeruleus neurons that project to the prefrontal cortex, which may influence SPA and energy expenditure (Teske et al., 2013). Also, neuromodulation of orexin neurons in the hypothalamus, as well as adrenergic agonists released from the sympathetic neurons, cause to an increase in mitochondrial biogenesis and enhanced peripheral tissue thermogenesis (Nixon et al., 2012; Abdel-Magid, 2016; Zink et al., 2018). Therefore, probably, this body-fat percentage, weight, and BMI reduction following exercise appear to be linked with the OXA improvement in response to the exercise. In this study, the significant correlations observed between serum OXA variations and the other parameters such as weight, BMI and fat percentage confirmed this effect (Table 4).

In addition, findings show that these reductions in body compassion and weight loss were higher in the POAE group than the ITAE group. This effect appears to be linked with the more OXA improvement in the POAE group relative to the ITAE group. In this regard, Novak et al. reported that daily intra-paraventricular OXA treatment induces weight loss in rats (Novak and Levine, 2009). They indicated that OXA-treated rats lost significantly more weight than their vehicle-injected counterparts without a significant difference in food intake. These results support this concept that orexinergic agents have a potential role to produce negative energy balance through increasing physical activity. On the other hand, Morrison et al. (Tupone et al., 2011) in their study stated that an orexinergic pathway from the perifornical lateral hypothalamus to the rostral raphe pallidus has been demonstrated to increase the gain of the excitatory drives to medullary sympathetic premotor neurons controlling brown adipose tissue sympathetic outflow and its thermogenesis. Thus, the result that observed in this study probably related to the OXA improvement after exercise intervention.

On the other hand, Orexin neurons receive a broad variety of signals related to environmental, physiological, metabolic and emotional stimuli and project broadly to the entire CNS (Chieffi et al., 2017a, 2017b). Therefore orexin neurons are “multi-tasking” neurons regulating a set of vital body functions, including sleep/wake states, energy expenditure, and cognition (Chieffi et al., 2017a, 2017b). In the present study, during playing in form of outdoor aerobic exercise, the serum OXA in POAE group was higher than the ITAE and control group. In this regard, the interest of subjects participating in the study to do exercise in this form may justify the role of environmental stimuli in more OXA secretion. As in the current study, the estimated Rating of perceived exertion (RPE) in POAE group was significantly lower than ITAE group (Fig. 1). It seems that outdoor aerobic exercise in natural and outdoor environments may provide some of the different signals from indoor treadmill exercise. Some variable such as natural light, playing field, changing weather conditions, communication with others, pleasure, joy, and emotional stimuli during outdoor play, prefer the outdoor aerobic exercise from indoor treadmill exercise. So, the uniformity of indoor treadmill exercise with the coercion and without pleasure and the above mentioned in the closed area may justify its lesser effectiveness of indoor treadmill exercise on the research variables.

Also, although in the literature review there was no study that surveys the effect of exercise intensity on OXA, in order to minimize this effect, target exercise heart rate and distance traveled by the subjects in both groups analyzed each Session and equalized next session. as shown in Fig. 1, there was no significant difference between the mean distance traveled by the experimental groups.

In supporting of this finding and the crucial role of the orexin system in physiological system Chieffi and et al. found a selective loss of orexin neuron in maintaining wakefulness and arousal in narcolepsia (Chieffi et al., 2017a, 2017b). It has been demonstrated that OXA undetectable in the cerebrospinal fluid (CSF) of the patients with narcolepsy (Nishino et al., 2000). Also, Wang et al. stated that in the children with type 1 narcolepsy BMI increased rapidly and decreased BMR is an important cause underlying rapid weight gain (Wang et al., 2016). In this regard, in the POAE group improvement in body composition parameter was better than ITAE group. Although the findings of some studies inconsistent with the findings (Brownell and Conti, 2010) but others are consistent (Zink, 2015; Messina et al., 2016; Blais et al., 2017; Chieffi et al., 2017a, 2017b). This disparity may be attributed to the subjects involved in the research process, gender (Brownell and Conti, 2010), and measurement method.

In connection with the VO_2 Max improvement that has occurred in this research, in general, it can be said that aerobic exercise that exerts cardiovascular system and energy requirements in form of oxidative phosphorylation, can affect the components of oxygen supply for muscle contractions. So, aerobic exercise with an effect on the cardiovascular and respiratory system performance, as well as the development of cellular and molecular alteration within the muscles, increase the maximum oxygen consumption (Heyward and Gibson, 2014). For this reason, after aerobic exercise intervention, the VO2MAX of these subjects increased significantly.

Also, in relation to the body fat percentage reduction in the subjects, physical activity, especially aerobic exercise, which provides most of its

energy from carbohydrate and fat phosphorylation in mitochondria (Ahmad and Imam, 2015), and OXA medullation effect on mitochondrial biogenesis (Perez-Leighton et al., 2014) can be helpful in energy expenditure and body fat percentage reduction. Also, the body weight loss observed in this study followed the training period (−10.6% VS -3.2%) was not exception to this rule.

In the end, it is worth noting there were some limitations in this research, which could provide guidance for future research. First, orexin secretion can be influenced by many factors such as lifestyle, circadian rhythm, stress, nutrition, physical activity, environmental variables as well as medications that can indirectly influence the effect of this neurohormone on the body. Therefore, the study of the orexin system with attention to this factor will be interesting. Second, in this study, RPE as a Rating of perceived exertion was used. If combined with RPE physical activity enjoyment of participants were measured the justification of the results was more acceptable.

5. Conclusion

Overall, the findings in this study suggest that body composition and weight loss improvement following aerobic exercise appear to be linked with the OXA improvement in response to the exercise. However, these improvements were higher in the POAE group that increased more OXA than ITAE group. So, we believed that instead of training in closed environments, such as indoor treadmill exercises, obese and overweight children, who are less willing to do exercise in this environment, outdoor exercise combined with a variety and enjoyable games to be used.

Conflicts of interest

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

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the Helsinki declaration on the use of human subjects for research. Written parental and individual consent was obtained before participation in the project.

Authors' contributions

EM drafted the manuscript and statistical analysis; ZM helped to draft the manuscript and conceived of the study, participated in its design and coordination; BK conceived of the study, participated in its design and coordination, and helped to draft the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Acknowledgments

This work was supported by grants from Physical Education and Sports Science College, Payam Noor University, Tehran, Iran. The authors are thankful for the subjects involved in the research process and their parents for their contributions to this research.

References

Abdel-Magid, A.F., 2016. Antagonists of orexin receptors as potential treatment of sleep disorders, obesity, eating disorders, and other neurological and psychiatric disorders. ACS Med. Chem. Lett. 7 (10), 876–877. https://doi.org/10.1021/acsmedchemlett.6b00325.

Ahmad, S.I., Imam, S.K., 2015. Obesity: A Practical Guide. Springer.

Blais, A., Drouin, G., Chaumontet, C., Voisin, T., Couvelard, A., Even, P.C., Couvineau, A., 2017. Impact of orexin-A treatment on food intake, energy metabolism and body weight in mice. PLoS One 12 (1), e0169908. https://doi.org/10.1371/journal.pone.0169908.

Brownell, S.E., Conti, B. J. N. l., 2010. Age-and gender-specific changes of hypocretin immunopositive neurons in C57Bl/6 mice. Neurosci. Lett. 472 (1), 29–32. https://doi.org/10.1016/j.neulet.2010.01.048.

Chieffi, S., Carotenuto, M., Monda, V., Valenzano, A., Villano, I., Precenzano, F., Tafuri, D., Salerno, M., Filippi, N., Nuccio, F., 2017a. Orexin system: the key for a healthy life. Front. Physiol. 8, 357–366. https://dx.doi.org/10.3389/fphys.2017.00357.

Chieffi, S., Messina, G., Villano, I., Messina, A., Esposito, M., Monda, V., Valenzano, A., Moscatelli, F., Esposito, T., Carotenuto, M., 2017b. Exercise influence on hippocampal function: possible involvement of orexin-A. Front. Physiol. 8 (85), 1–8. https://doi.org/10.3389/fphys.2017.00085.

Ferrante, C., Orlando, G., Recinella, L., Leone, S., Chiavaroli, A., Di Nisio, C., Shohreh, R., Manippa, F., Ricciuti, A., Vacca, M., Brunetti, L., 2016. Central inhibitory effects on feeding induced by the adipo-myokine irisin. Eur. J. Pharmacol. 791, 389–394. https://doi.org/10.1016/j.ejphar.2016.09.011.

Flores, Á., Maldonado, R., Berrendero, F., 2013. Cannabinoid-hypocretin cross-talk in the central nervous system: what we know so far. Front. Neurosci. 7 (256), 1–17. https://dx.doi.org/10.3389/fnins.2013.00256.

Gorostegi-Anduaga, I., Corres, P., MartinezAguirre-Betolaza, A., Pérez-Asenjo, J., Aispuru, G.R., Fryer, S.M., Maldonado-Martín, S., 2018. Effects of different aerobic exercise programmes with nutritional intervention in sedentary adults with overweight/obesity and hypertension: EXERDIET-HTA study. Eur J Prev Cardiol 25 (4), 343–353. https://doi.org/10.1177/2047487317749956.

Hao, Y.Y., Yuan, H.W., Fang, P.H., Zhang, Y., Liao, Y.X., Shen, C., Wang, D., Zhang, T.T., Bo, P., 2016. Plasma orexin-A level associated with physical activity in obese people. Eat. Weight Disord. 19 (1), 69–77. https://doi.org/10.1007/s40519-016-0271-y.

Hara, J., Beuckmann, C.T., Nambu, T., Willie, J.T., Chemelli, R.M., Sinton, C.M., Sugiyama, F., Yagami, K.-i., Goto, K., Yanagisawa, M., 2001. Genetic ablation of orexin neurons in mice results in narcolepsy, hypophagia, and obesity. Neuron 30 (2), 345–354. https://dx.doi.org/10.1016/S0896-6273(01)00293-8.

Harms, M., Seale, P., 2013. Brown and beige fat: development, function and therapeutic potential. Nat. Med. 19 (10), 1252–1263. https://dx.doi.org/10.1038/nm.3361.

Heyward, V.H., Gibson, A., 2014. Advanced Fitness Assessment and Exercise Prescription, seventh ed. Human kinetics.

Hughes-Austin, J.M., Larsen, B.A., Allison, M.A., 2013. Visceral adipose tissue and cardiovascular disease risk. Curr Cardiovasc Risk Rep 7 (2), 95–101. https://doi.org/10.1007/s12170-013-0298-9.

Jackson, A.S., Pollock, M.L., Sportsmedicine, 1985. Practical assessment of body composition. Physician Sportsmed. 13 (5), 76–90. https://doi.org/10.1080/00913847.1985.11708790.

Kastin, A.J., Akerstrom, V., 1999. Orexin A but not orexin B rapidly enters brain from blood by simple diffusion. J. Pharmacol. Exp. Ther. 289 (1), 219–223.

Kotz, C., Nixon, J., Butterick, T., Perez-Leighton, C., Teske, J., Billington, C., 2012. Brain orexin promotes obesity resistance. Ann. N. Y. Acad. Sci. 1264, 72–86. https://doi.org/10.1111/j.1749-6632.2012.06585.x.

Marinov, B., Kostianev, S., Turnovska, T., 2003. Modified treadmill protocol for evaluation of physical fitness in pediatric age group comparison with Bruce and Balke protocols. Acta Physiol. Pharmacol. Bulg. 27 (2–3), 47–51.

Messina, G., Dalia, C., Tafuri, D., Palmieri, F., Dato, A., Russo, A., 2014a. Orexin A controls glucose metabolism. J Diabetes Metab 5 (398), 2. https://dx.doi.org/10.4172/2155-6156.1000398.

Messina, G., Di Bernardo, G., Messina, A., Dalia, C., Chieffi, S., Galderisi, U., Monda, M., Studies, D., 2014b. Brief exercise enhances blood hypocretin-1 in sedentary men. J. Sports Med. Doping Stud. 4 (5), 149. https://doi.org/10.4172/2161-0673.1000149.

Messina, G., Di Bernardo, G., Viggiano, A., De Luca, V., Monda, V., Messina, A., Chieffi, S., Galderisi, U., Monda, M., 2016. Exercise increases the level of plasma orexin A in humans. J. Basic Clin. Physiol. Pharmacol. 27 (6), 611–616. https://doi.org/10.1515/jbcpp-2015-0133.

Mohammadhassani, F., Esfandiarinezhad, A., Jafari, A., 2015. The effects of endurance training and high intensity interval training on orexin-A and anthropometric parameters in obese adolescent boys. J. Sch. Public Health Inst. Public Health Res. 13 (1), 99–112.

Nishino, S., Ripley, B., Overeem, S., Lammers, G.J., Mignot, E.J.T.L., 2000. Hypocretin (orexin) deficiency in human narcolepsy. Lancet 355 (9197), 39–40. https://doi.org/10.1016/S0140-6736(99)05582-8.

Nixon, J.P., Kotz, C.M., Novak, C.M., Billington, C.J., Teske, J.A., 2012. Neuropeptides controlling energy balance: orexins and neuromedins. Handb. Exp. Pharmacol. 209, 77–109. https://doi.org/10.1007/978-3-642-24716-3_4.

Novak, C.M., Levine, J.A.J.O., 2009. Daily intraparaventricular orexin-A treatment induces weight loss in rats 17 (8), 1493–1498. https://doi.org/10.1038/oby.2009.91.

Ohno, K., Sakurai, T., 2008. Orexin neuronal circuitry: role in the regulation of sleep and wakefulness. Front. Neuroendocrinol. 29 (1), 70–87. https://doi.org/10.1016/j.yfrne.2007.08.001.

Perez-Leighton, C.E., Billington, C.J., Kotz, C.M., 2014. Orexin modulation of adipose tissue. Biochim. Biophys. Acta 1842 (3), 440–445. https://doi.org/10.1016/j.bbadis.2013.06.007.

Raedeke, T.D., 2007. The relationship between enjoyment and affective responses to exercise. J. Appl. Sport Psychol. 19 (1), 105–115.

Sakurai, T., Pandi-Perumal, S., Monti, J.M., 2015. Orexin and Sleep: Molecular, Functional and Clinical Aspects. Springer.

Scammell, T.E., Winrow, C.J., 2011. Orexin receptors: pharmacology and therapeutic opportunities. Annu. Rev. Pharmacol. Toxicol. 51, 243–266. https://doi.org/10.1146/annurev-pharmtox-010510-100528.

Seale, P., 2011. Orexin turns up the heat on obesity. Cell Metabol. 14 (4), 441–442. https://doi.org/10.1016/j.cmet.2011.09.007.

Teske, J.A., Perez-Leighton, C.E., Billington, C.J., Kotz, C.M., 2013. Role of the locus coeruleus in enhanced orexin A-induced spontaneous physical activity in obesity-resistant rats. Am. J. Physiol. Regul. Integr. Comp. Physiol. 305 (11), R1337–R1345. https://doi.org/10.1152/ajpregu.00229.2013.

Tsunematsu, T., Yamanaka, A., 2012. The Role of Orexin/hypocretin in the Central Nervous System and Peripheral Tissues, vol. 89. Vitamins & Hormones, Elsevier, pp. 19–33.

Tupone, D., Madden, C.J., Cano, G., Morrison, S.F., 2011. An orexinergic projection from perifornical hypothalamus to raphe pallidus increases rat brown adipose tissue thermogenesis. J. Neurosci. 31 (44), 15944–15955. https://doi.org/10.1523/JNEUROSCI.3909-11.2011.

Wang, Z., Wu, H., Stone, W.S., Zhuang, J., Qiu, L., Xu, X., Wang, Y., Zhao, Z., Han, F., Zhao, Z. J. S. m., 2016. Body weight and basal metabolic rate in childhood narcolepsy: a longitudinal study, vol. 25. pp. 139–144. https://doi.org/10.1016/j.sleep.2016.06.019.

Wensveen, F.M., Valentić, S., Šestan, M., Turk Wensveen, T., Polić, B., 2015. The "Big Bang" in obese fat: events initiating obesity-induced adipose tissue inflammation. Eur. J. Immunol. 45 (9), 2446–2456. https://doi.org/10.1002/eji.201545502.

Williams, R.H., Jensen, L.T., Verkhratsky, A., Fugger, L., Burdakov, D., 2007. Control of hypothalamic orexin neurons by acid and CO2. Proc. Natl. Acad. Sci. U. S. A. 104 (25), 10685–10690. https://doi.org/10.1073/pnas.0702676104.

Wu, M.-F., Nienhuis, R., Maidment, N., Lam, H., Siegel, J., 2011. Cerebrospinal fluid hypocretin (orexin) levels are elevated by play but are not raised by exercise and its associated heart rate, blood pressure, respiration or body temperature changes. Arch. Ital. Biol. 149 (4), 492–498. https://doi.org/10.4449/aib.v149i4.1315.

Yamamoto, Y., Ueta, Y., Date, Y., Nakazato, M., Hara, Y., Serino, R., Nomura, M., Shibuya, I., Matsukura, S., Yamashita, H., 1999. Down regulation of the prepro-orexin gene expression in genetically obese mice. Brain Res Mol Brain Res 65 (1), 14–22. https://doi.org/10.1016/S0169-328X(98)00320-9.

Yeh, H.-P., Stone, J.A., Churchill, S.M., Brymer, E., Davids, K., 2017. Physical and emotional benefits of different exercise environments designed for treadmill running. Int. J. Environ. Res. Public Health 14 (7), 752. https://doi.org/10.3390/ijerph14070752.

Zink, A., 2015. Neuromodulation of orexin neurons in the lateral hypothalamus regulates spontaneous physical activity, energy expenditure, and diet-induced obesity. http://hdl.handle.net/11299/183317.

Zink, A.N., Bunney, P.E., Holm, A.A., Billington, C.J., Kotz, C.M., 2018. Neuromodulation of orexin neurons reduces diet-induced adiposity. Int. J. Obes. 42 (4), 737–745. https://dx.doi.org/10.1038/ijo.2017.276.