


⇒ Research Article



Effect of Arginine Supplementation and High Intensity Training on Appetite Hormones and Body Composition of Obese Boys

Tohid Mabhut Moghadam¹ , Mehrdad Fathi^{2*}, Sayed Reza Attarzadeh Hosseini², Mohammad Mosaferi Ziaaldini², Amir Rashidlamir²

¹Department of Sport Sciences, Khavaran Institute of Higher Education, Mashhad, Iran

²Department of Sport Sciences, Ferdowsi University of Mashhad, Mashhad, Iran

Abstract

Background: There is little information about the effects of high intensity aerobic exercise training (HIT) and L-arginine supplementation on appetite-regulating hormones among obese male adolescents. We aimed to determine the effect of eight weeks of HIT and L-arginine supplementation on appetite-regulating hormones and body composition indices in obese adolescent boys.

Methods: Twenty obese adolescents were randomly divided into two groups of HIT and placebo (P-HIT, n=10) and HIT with supplementation of L-arginine (A-HIT, n=10). The HIT protocol was treadmill running with ventilation threshold (VT) intensity and training sessions were isoenergetic and energy consumption were set to 350 kcal per session for each participant, which were evaluated indirectly by calorimetry. The A-HIT group received 3 g of L-arginine per day for 8 weeks. Before the interventions and 48 hours after the last exercise session, anthropometric indices and levels of appetite-regulating hormones were measured.

Results: There was no significant changes between the groups with respect to leptin, agouti, and PYY3-36 peptide levels. There were significant changes in weight reduction between the groups ($P \leq 0.05$). However, body mass index (BMI) and percent body fat (PBF) changes were not significant in between groups ($P \geq 0.05$).

Conclusion: Our findings suggest that co-supplementation of L-arginine with HIT training had no further effects on appetite regulatory hormones and body composition of obese male adolescents.

Keywords: L-arginine, Leptin, Agouti, PYY3-36, High intensity training, Obesity

*Correspondence to

Mehrdad Fathi,

Email: mfathei@um.ac.ir



Received July 5, 2020, Accepted: December 20, 2021, Published Online: December 29, 2021

Background

Obesity is one of the main health problems of people in many countries (1). Child obesity, as one of the most severe public challenges in the 21st century, affects global population growth (2). Several peptides released by peripheral tissues interact with specific regions of the brain and release neurons secreting anti-appetite and appetite neuropeptides that are involved in controlling nutritional behavior and energy patterns (3). Recent studies have focused on the effect of physical activity on appetite and energy intake (4). In this regard, many studies have suggested that physical activity is a robust non-pharmaceutical strategy for the prevention and management of obesity and the beneficial effects of exercise may not be merely through influencing energy consumption, but by regulating appetite, which can in turn affect the energy equilibrium equation (5). Appetite-reducing and stimulating hormones, such as peptide PYY3-36, leptin, and Agouti-related protein (AgRP) play an important role in appetite regulation (6-8). Studies have shown that among the appetite-regulating hormones, PYY3-36 peptide has attracted the most attention and plays a more important role in suppressing

appetite and hunger (9). Moreover, the contradictory results of some studies concerning leptin as an anti-appetite neuropeptide show that decrease the levels of leptin in response to physical activity in children and adolescents with (10-12) or without (13) has been weight loss. Some results also indicate the insignificant effects of exercise on leptin levels (14-16). Even in some cases that changes in levels of leptin may not be tangible in the blood, a regular physical activity can induce the effects of anorexia and thermogenesis by increase in the binding of leptin receptors and the expression of the leptin gene (17).

The effects of physical activity on the AgRP as an appetite peptide that can affect nutritional behavior, weight adjustment, and energy homeostasis are contradictory to some extent but most of the results indicate an increase in agouti in both the plasma and gene expression (18, 19). Several studies have shown that aerobic exercise has not led to an acute and recognizable increase in energy in children (15) and adolescents (20) with obesity. On the other hand, increasing evidence from studies shows the special effects of L-arginine on obesity, while the clinical study on the effects of L-arginine on obesity

is insufficient (21). The mechanism of action of the physiological levels of L-arginine stimulates the oxidation of glucose and long-chain fatty acids while reducing the repeated synthesis of glucose and triacylglycerols (22). Besides, the use of L-arginine supplements increases lipolysis and inhibits lipogenesis by regulating the expression and function of the key enzymes involved in the antioxidant response and lipid metabolism in insulin-sensitive tissues (23). In recent years, various studies have shown that the use of L-arginine supplements has been beneficial in reducing obesity and improving insulin sensitivity in multiple animal models and some human samples (12). However, the results of some studies suggest that high-intensity physical activity significantly reduces the amount of energy consumed within 24 hours after activity in adolescent boys (24). The apparent point of this study is the isoenergetic nature of the training sessions so that the subjects burn a certain number of calories during each session of the exercise. This may prevent the impact of different energy consumption between the groups. This technique is commonly used in studies that attempt to evaluate the effect of exercise intensity (12). The synergetic effect of L-arginine consumption and high intensity training (HIT) is not clearly understood. In this study we investigated the effect of eight weeks of L-arginine supplementation along with HIT training on appetited regulatory hormones and body composition of obese adolescent boys.

Materials and Methods

Subjects

In this quasi-experimental study, 20 adolescent boys were selected and assigned into two groups randomly as high-intensity aerobic exercise and placebo (P-HIT, 10 subjects) and high-intensity aerobic exercise group with supplementation of L-arginine (A-HIT, 10 subjects) for eight weeks. The inclusion criteria were homogeneity of subjects' weight, not having a history of specific diseases such as cardiovascular disease, high blood pressure, diabetes mellitus, and lack of perceptual impairment, or any disorder that affects one's ability to perform the protocol. All parents and students were introduced to the purpose and manner of conducting the research and

related coordination regarding the study was made. Then, the consent form was received from the student and the parents and then the necessary permissions were obtained from the Ethics Committee of the Ferdowsi University of Mashhad. The characteristics of the participants are shown in Table 1.

Blood Sampling and Measurement of Biochemical Variables

Before and 24 hours after the eight-week intervention, 10 cc blood samples were collected from the antecubital vein under fasting conditions (> 12 hours). The blood samples were centrifuged for 20 minutes at 3600 rpm and stored at -80°C until analysis. Levels of leptin, AgRP and PYY3-36 (Hangzhou East Biopharm, code No CK-E10738, CK-E11648, CK-E92030 respectively) were measured using enzyme-linked immunosorbent assay (ELISA).

Exercise Protocol

The design of the HIT protocol primarily required the assessment of peak oxygen consumption (VO₂ peak) and ventilation threshold (VT) of the participants. To do this, participants performed an incremental test to volitional exhaustion on a treadmill (Italy-K4b2 model). Oxygen uptake was measured (Cosmed) throughout the test and the greatest 15s average was defined as VO₂ peak. VT was determined as the point where a systematic increase in the ratio of ventilation to consumed oxygen (VE/VO₂) occurred without an increase in the ventilation to carbon dioxide ratio (VE/VCO₂).

After evaluating VO₂ peak and VT of each participant, the HIT protocol was designed on the treadmill for three times per week during the eight weeks of study. The running speed in the training session was based on the speed at which the participants achieved their VT. The training sessions were isoenergetic and energy consumption was set to 350 kcal per session for each participant, which was evaluated indirectly by calorimetry (12). To apply progressive load of exercise, every two-week the VT of each subject were evaluated and the new speed was applied for treadmill running. To determine the approximate duration of the training session, the following equation were used:

Table 1. Body Composition Characteristics of the Participants Before and After HIT Training and L-Arginine Intervention

Variable	Groups	Mean ± SD		Intragroup Changes		Intergroup Changes	
		Before Intervention	After Intervention	T Value	P Value	T Value	P Value
Weight (kg)	P-HIT	71.85 ± 11.79	69.12 ± 10.74	3.17	0.011*	5.19	<0.01*
	A-HIT	76.80 ± 5.93	73.72 ± 6.47	8.50	0.01*		
BMI (kg/m ²)	P-HIT	28.60 ± 2.95	27.25 ± 2.04	2.98	0.017*	0.279	0.783
	A-HIT	30.02 ± 1.77	28.56 ± 1.2	9.64	<0.01*		
PBF (%)	P-HIT	43.37 ± 4.89	40.29 ± 3.75	2.25	0.050*	0.577	0.047*
	A-HIT	41.61 ± 5.59	36.80 ± 2.06	2.45	0.036*		

BMI: body mass index; PBF: percent body fat; P-HIT: placebo and high intensity training; A-HIT: L-arginine and high intensity training.

P < 0.05 was considered significant.

$$\text{Exercise session time (min)} = 350 / (v_{o_2} \times 496)$$

The speed and duration of running were proportional to the VT and VO₂ peak gained by the subjects themselves. Nevertheless, to apply the additional load because of a possible improvement in performance, VT and VO₂ peak of all subjects were re-assessed at the end of the fourth week and became the criteria for determining the duration of the training session and treadmill speed in the next four weeks.

Arginine Supplementation Protocol

A-HIT received 3 g of L-arginine a day for 8 weeks (tablet, 99.9% purity, Karen, Iran) by dissolving the tablet and mixing with drinking water. P-HIT group received dextrin in similar manner with A-HIT group (25).

Statistical Analysis

SPSS, version 22.0 (SPSS Inc., USA) was used to determine the effect of 8-week HIT training and L-arginine supplementation. An independent *t* test between the groups or a paired *t* test between times were applied. All values are expressed as mean ± standard deviation (SD). *P* < 0.05 were considered significant.

Results

Body Composition

The results show a significant reduction in weight in both P-HIT and A-HIT groups after 8 weeks (*P* = 0.011 and *P* = 0.000, respectively). Also, body weight reduction in the A-HIT group was significantly higher than P-HIT group after eight weeks of intervention (*P* = 0.000). We found a significant change in BMI indicis in both groups (*P* = 0.017, *P* = 0.015, P-HIT and A-HIT respectively). However, no significant difference were shown between groups. There was a significant reduction in PBF after eight weeks of study in both groups of P-HIT and A-HIT (*P* = 0.050, *P* = 0.036 respectively). However, the A-HIT group experimented higher reduction then P-HIT group (*P* = 0.047; Table 1).

The Regulatory Appetite Hormones

The results showed that after 8 weeks of training and

taking arginine supplementation, the changes of leptin, Agouti and PYY3-36 levels did not change significantly compared with the pre-test (*P* > 0.05). Also, no significant difference was observed in any of the hormones between the two groups (*P* = 0.681, 0.742, and 0.858 respectively, Table 2).

Discussion

The purpose of this study was to investigate the effect of 8 weeks of HIT training and L-arginine supplement under isoenergetic conditions on appetite-regulating hormones and anthropometric indices in obese adolescent boys. We found that the levels of leptin, AgRP, and peptide PYY3-36 after the protocol were not significantly different from the pre-protocol values in both groups of P-HIT and A-HIT. In this regard, the intergroup analysis also showed a non-significant difference in changes in levels of leptin, AgRP, and peptide PYY3-36 between the P-HIT and A-HIT groups (Table 2).

Saghebjoos and colleagues recently investigated effect of six weeks of high-intensity interval training and L-arginine supplementation on serum levels of adiponectin and lipid profile in overweight and obese young men. They found no significant changes in serum adiponectin levels, lipid profile, body mass index, and fat percentage after high-intensity interval training and/or L-arginine intake (26).

The physiological stress resulting from exercise is a potential leptin secretion regulator. Changes associated with the flow of fuel, circulating hormonal concentrations and energy costs may affect leptin concentrations (27). Despite the expectations that regular physical activity can induce effects of anorexia and thermogenesis of leptin by increasing the binding of receptors of leptin and the expression of the leptin gene, in some cases, these effects do not change leptin levels in the blood (17). In the present study, after eight weeks of HIT under isoenergetic conditions in the P-HIT and A-HIT groups, the comparison of the values between the two groups was not significant. In line with this study, Letizia and colleagues examined the effect of exercise and caloric intake on obesity, weight adjustment, and hypothalamic neuropeptides' and agouti presentation in obese mice. Their results showed that exercise significantly reduced

Table 2. Appetite Hormonal Response to 8 Weeks of Intervention in P-HIT and A-HIT Groups

Variable	Groups	Mean ± SD		Intragroup Changes		Intergroup Changes	
		Before Intervention	After Intervention	T Value	P Value	T Value	P Value
Leptin (ng/mL)	P-HIT	529.76 ± 156.64	529.32 ± 134.96	0.01	0.989	-0.42	0.681
	A-HIT	437.50 ± 54.04	450.03 ± 55.14	1.18	0.269		
Agouti (ng/mL)	P-HIT	147.52 ± 52.05	146.86 ± 52.54	0.13	0.900	-0.33	0.742
	A-HIT	122.70 ± 9.34	132.92 ± 12.99	-0.40	0.693		
PYY ₃₋₃₆ (pg/mL)	P-HIT	36.49 ± 13.09	37.09 ± 11.18	-0.25	0.805	0.18	0.858
	A-HIT	32.66 ± 3.45	32.84 ± 4.60	-0.19	0.850		

P-HIT: placebo and high intensity training; A-HIT: L-arginine and high intensity training.

body weight, but did not significantly affect the AgRP (18).

Markofski and colleagues reported a 4.3% significant increase in AgRP compared with the control group following a long-term aerobic protocol (28). AgRP was introduced as an appetite-boosting signal in the classification of environmental signals (9), and negative energy balance was a major contributor to AgRP which can be affected by physical activity (28). The negative energy balance to stimulate appetite and increase food intake can depend on intensity, duration, exercise, the initial amount of fuel sources and nutritional status (19, 28) which could lead to negative energy balance and AgRP peptide values (29, 30). Therefore, in the present study it seems that because of the isoenergetic nature of the nutritional diet of the subjects, the opportunity to supply excess energy resulting from an increase in appetite after exercise is limited. In a similar study using the HIT protocol for 12 weeks on obese adolescents, PYY3-36 levels increased. Prado and colleagues compared the effect of low and high-intensity aerobic exercise training program on obese adolescent girls and found that 12 weeks of high-intensity training led to improved levels of PYY3-36 and may have reduced eating in obese adolescents. Changes in PYY3-36 levels were associated with the HIT group (31). The mechanism of PYY increase was vague, but one of the causes seems to be changing in the nervous system that increases with the intensity of exercise (32). Other possible causes of the absence of differences in PYY3-36 values in this study were that in other studies, most of the exercise protocols were long-term or aerobic and the measurements included total PYY values of human samples (16, 33) and perhaps the contradiction in PYY values in studies is a reflection of the type of total PYY measurement and change rather than the serum blood levels. One of the reasons for the increase in PYY3-36 levels is the decreased appetite and nutrition following high-intensity aerobic exercises (31).

Along with the present study, in most studies with or without supplementation in which long-term aerobic exercise protocols were used, the changes in physical characteristics of the subjects were tangible (12, 34). For example, Prado et al showed that following an intervention of 12 weeks of high and low intensity training in 36 adolescent boys and girls, the physical features such as weight, BMI and PBF after the protocol significantly reduced compared to pre-protocol conditions so that this decrease was more significant in the HIT group (12). In another randomized clinical study on the specific effects of arginine on obesity over 21 days, 8.3 g/d arginine (approximately 80 mg/kg body weight per day) and placebo were given to 33 obese people (mean BMI = 39.1 kg / m²) with a low calorie diet (1000 calories per day), a regular exercise program (45 minutes, twice daily, 5 days a week). The participants were randomly divided

into two HIT + arginine and HIT + placebo groups, the body indices such as weight, BMI, and PBF significantly improved with the completion of the research compared with baseline values. It should be noted that these changes in the arginine group were greater than the placebo group (34). The factors contributing to the supplemental role of L-arginine as a factor in reducing obesity are probably a complex mechanism at cellular-molecular levels and the whole body so that the mitochondrial biogenesis stimulation and regulating gene expression and metabolic pathways via L-arginine are expected. Therefore, the use of L-arginine supplementation for obese people induces fat loss and prevents the reduction of body mass during weight loss (34).

Conclusion

Our findings suggest that co-supplementation of L-arginine with HIT training had no further effects on appetite regulatory hormones and body composition of obese male adolescents. However, in future studies, nutritional habits of the participants should be monitored

Authors' Contribution

Study concept and design: TMM, MF and MMZ; analysis and interpretation of data: TMM, SRAH, MMZ, and AR; drafting of the manuscript: TMM, MF, SRAH and MMZ; critical revision of the manuscript for important intellectual content: TMM, MF, AR, SRAH and MMZ; statistical analysis: MMZ and SRAH.

Conflict of Interests

Authors have no financial interests related to the content of the manuscript.

Ethical Approval

Ethics Committee of the Ferdowsi University of Mashhad approved the study.

Funding/Support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. World Health Organization (WHO). Global Strategy on Diet, Physical Activity, and Health: Childhood Overweight and Obesity. Geneva: WHO; 2014.
2. Azab SF, Saleh SH, Elsaed WF, Elshafie MA, Sherief LM, Esh AM. Serum trace elements in obese Egyptian children: a case-control study. *Ital J Pediatr.* 2014;40:20. doi: [10.1186/1824-7288-40-20](https://doi.org/10.1186/1824-7288-40-20).
3. Schwarz NA, Rigby BR, La Bounty P, Shelmadine B, Bowden RG. A review of weight control strategies and their effects on the regulation of hormonal balance. *J Nutr Metab.* 2011;2011:237932. doi: [10.1155/2011/237932](https://doi.org/10.1155/2011/237932).
4. Russel RR, Willis KS, Ravussin E, Larson-Meyer ED. Effects of endurance running and dietary fat on circulating ghrelin and peptide YY. *J Sports Sci Med.* 2009;8(4):574-83.
5. Martins C, Morgan L, Truby H. A review of the effects of exercise on appetite regulation: an obesity perspective. *Int J Obes (Lond).* 2008;32(9):1337-47. doi: [10.1038/ijo.2008.98](https://doi.org/10.1038/ijo.2008.98).
6. De Silva A, Bloom SR. Gut hormones and appetite control: a focus on PYY and GLP-1 as therapeutic targets in obesity. *Gut*

- Liver. 2012;6(1):10-20. doi: [10.5009/gnl.2012.6.1.10](https://doi.org/10.5009/gnl.2012.6.1.10).
7. Konturek PC, Konturek JW, Cześnikiewicz-Guzik M, Brzozowski T, Sito E, Konturek SJ. Neuro-hormonal control of food intake: basic mechanisms and clinical implications. *J Physiol Pharmacol*. 2005;56 Suppl 6:5-25.
 8. Varela L, Horvath TL. Leptin and insulin pathways in POMC and AgRP neurons that modulate energy balance and glucose homeostasis. *EMBO Rep*. 2012;13(12):1079-86. doi: [10.1038/embor.2012.174](https://doi.org/10.1038/embor.2012.174).
 9. Jürimäe J. Ghrelin responses to acute exercise and training. In: *Endocrinology of Physical Activity and Sport*. Springer; 2020. p. 193-207.
 10. Gutin B, Ramsey L, Barbeau P, Cannady W, Ferguson M, Litaker M, et al. Plasma leptin concentrations in obese children: changes during 4-mo periods with and without physical training. *Am J Clin Nutr*. 1999;69(3):388-94. doi: [10.1093/ajcn/69.3.388](https://doi.org/10.1093/ajcn/69.3.388).
 11. Reinehr T, de Sousa G, Roth CL. Obestatin and ghrelin levels in obese children and adolescents before and after reduction of overweight. *Clin Endocrinol (Oxf)*. 2008;68(2):304-10. doi: [10.1111/j.1365-2265.2007.03042.x](https://doi.org/10.1111/j.1365-2265.2007.03042.x).
 12. Prado WL, Lofrano-Prado MC, Oyama LM, Cardel M, Gomes PP, Andrade ML, et al. Effect of a 12-week low vs. high intensity aerobic exercise training on appetite-regulating hormones in obese adolescents: a randomized exercise intervention study. *Pediatr Exerc Sci*. 2015;27(4):510-7. doi: [10.1123/pes.2015-0018](https://doi.org/10.1123/pes.2015-0018).
 13. Angelopoulos N, Goula A, Tolis G. Current knowledge in the neurophysiologic modulation of obesity. *Metabolism*. 2005;54(9):1202-17. doi: [10.1016/j.metabol.2005.04.005](https://doi.org/10.1016/j.metabol.2005.04.005).
 14. Lau PW, Kong Z, Choi CR, Yu CC, Chan DF, Sung RY, et al. Effects of short-term resistance training on serum leptin levels in obese adolescents. *J Exerc Sci Fit*. 2010;8(1):54-60. doi: [10.1016/s1728-869x\(10\)60008-1](https://doi.org/10.1016/s1728-869x(10)60008-1).
 15. Moore MS, Dodd CJ, Welsman JR, Armstrong N. Short-term appetite and energy intake following imposed exercise in 9- to 10-year-old girls. *Appetite*. 2004;43(2):127-34. doi: [10.1016/j.appet.2004.02.008](https://doi.org/10.1016/j.appet.2004.02.008).
 16. Jones TE, Basilio JL, Brophy PM, McCammon MR, Hickner RC. Long-term exercise training in overweight adolescents improves plasma peptide YY and resistin. *Obesity (Silver Spring)*. 2009;17(6):1189-95. doi: [10.1038/oby.2009.11](https://doi.org/10.1038/oby.2009.11).
 17. Patterson CM, Bouret SG, Dunn-Meynell AA, Levin BE. Three weeks of postweaning exercise in DIO rats produces prolonged increases in central leptin sensitivity and signaling. *Am J Physiol Regul Integr Comp Physiol*. 2009;296(3):R537-48. doi: [10.1152/ajpregu.90859.2008](https://doi.org/10.1152/ajpregu.90859.2008).
 18. Letizia C, Petramala L, Di Gioia CR, Chiappetta C, Zinamosca L, Marinelli C, et al. Leptin and adiponectin mRNA expression from the adipose tissue surrounding the adrenal neoplasia. *J Clin Endocrinol Metab*. 2015;100(1):E101-4. doi: [10.1210/jc.2014-2274](https://doi.org/10.1210/jc.2014-2274).
 19. Katzmarzyk PT, Malina RM, Bouchard C. Physical activity, physical fitness, and coronary heart disease risk factors in youth: the Québec Family Study. *Prev Med*. 1999;29(6 Pt 1):555-62. doi: [10.1006/pmed.1999.0592](https://doi.org/10.1006/pmed.1999.0592).
 20. Dodd CJ, Welsman JR, Armstrong N. Energy intake and appetite following exercise in lean and overweight girls. *Appetite*. 2008;51(3):482-8. doi: [10.1016/j.appet.2008.03.009](https://doi.org/10.1016/j.appet.2008.03.009).
 21. Lucotti P, Setola E, Monti LD, Galluccio E, Costa S, Sandoli EP, et al. Beneficial effects of a long-term oral L-arginine treatment added to a hypocaloric diet and exercise training program in obese, insulin-resistant type 2 diabetic patients. *Am J Physiol Endocrinol Metab*. 2006;291(5):E906-12. doi: [10.1152/ajpendo.00002.2006](https://doi.org/10.1152/ajpendo.00002.2006).
 22. Jobgen W, Fu WJ, Gao H, Li P, Meininger CJ, Smith SB, et al. High fat feeding and dietary L-arginine supplementation differentially regulate gene expression in rat white adipose tissue. *Amino Acids*. 2009;37(1):187-98. doi: [10.1007/s00726-009-0246-7](https://doi.org/10.1007/s00726-009-0246-7).
 23. Jobgen W, Meininger CJ, Jobgen SC, Li P, Lee MJ, Smith SB, et al. Dietary L-arginine supplementation reduces white fat gain and enhances skeletal muscle and brown fat masses in diet-induced obese rats. *J Nutr*. 2009;139(2):230-7. doi: [10.3945/jn.108.096362](https://doi.org/10.3945/jn.108.096362).
 24. Thivel D, Isacco L, Montaurier C, Boirie Y, Duché P, Morio B. The 24-h energy intake of obese adolescents is spontaneously reduced after intensive exercise: a randomized controlled trial in calorimetric chambers. *PLoS One*. 2012;7(1):e29840. doi: [10.1371/journal.pone.0029840](https://doi.org/10.1371/journal.pone.0029840).
 25. Hurt RT, Ebbert JO, Schroeder DR, Croghan IT, Bauer BA, McClave SA, et al. L-arginine for the treatment of centrally obese subjects: a pilot study. *J Diet Suppl*. 2014;11(1):40-52. doi: [10.3109/19390211.2013.859216](https://doi.org/10.3109/19390211.2013.859216).
 26. Saghebjo M, Farrokhi-Fard M, Hedayati M, Sadeghi-Tabas S. The effect of high-intensity interval training and L-arginine supplementation on the serum levels of adiponectin and lipid profile in overweight and obese young men. *Obes Med*. 2019;16:100139. doi: [10.1016/j.obmed.2019.100139](https://doi.org/10.1016/j.obmed.2019.100139).
 27. Hulver MW, Zheng D, Tanner CJ, Houmard JA, Kraus WE, Slentz CA, et al. Adiponectin is not altered with exercise training despite enhanced insulin action. *Am J Physiol Endocrinol Metab*. 2002;283(4):E861-5. doi: [10.1152/ajpendo.00150.2002](https://doi.org/10.1152/ajpendo.00150.2002).
 28. Markofski MM, Carrillo AE, Timmerman KL, Jennings K, Coen PM, Pence BD, et al. Exercise training modifies ghrelin and adiponectin concentrations and is related to inflammation in older adults. *J Gerontol A Biol Sci Med Sci*. 2014;69(6):675-81. doi: [10.1093/gerona/glt132](https://doi.org/10.1093/gerona/glt132).
 29. Horowitz JF. Fatty acid mobilization from adipose tissue during exercise. *Trends Endocrinol Metab*. 2003;14(8):386-92. doi: [10.1016/s1043-2760\(03\)00143-7](https://doi.org/10.1016/s1043-2760(03)00143-7).
 30. Krashes MJ, Shah BP, Koda S, Lowell BB. Rapid versus delayed stimulation of feeding by the endogenously released AgRP neuron mediators GABA, NPY, and AgRP. *Cell Metab*. 2013;18(4):588-95. doi: [10.1016/j.cmet.2013.09.009](https://doi.org/10.1016/j.cmet.2013.09.009).
 31. Prado WL, Balagopal PB, Lofrano-Prado MC, Oyama LM, Tenório TR, Botero JP, et al. Effect of aerobic exercise on hunger feelings and satiety regulating hormones in obese teenage girls. *Pediatr Exerc Sci*. 2014;26(4):463-9. doi: [10.1123/pes.2013-0200](https://doi.org/10.1123/pes.2013-0200).
 32. Larson-Meyer DE, Palm S, Bansal A, Austin KJ, Hart AM, Alexander BM. Influence of running and walking on hormonal regulators of appetite in women. *J Obes*. 2012;2012:730409. doi: [10.1155/2012/730409](https://doi.org/10.1155/2012/730409).
 33. Kelly KR, Brooks LM, Solomon TP, Kashyap SR, O'Leary VB, Kirwan JP. The glucose-dependent insulinotropic polypeptide and glucose-stimulated insulin response to exercise training and diet in obesity. *Am J Physiol Endocrinol Metab*. 2009;296(6):E1269-74. doi: [10.1152/ajpendo.00112.2009](https://doi.org/10.1152/ajpendo.00112.2009).
 34. McKnight JR, Satterfield MC, Jobgen WS, Smith SB, Spencer TE, Meininger CJ, et al. Beneficial effects of L-arginine on reducing obesity: potential mechanisms and important implications for human health. *Amino Acids*. 2010;39(2):349-57. doi: [10.1007/s00726-010-0598-z](https://doi.org/10.1007/s00726-010-0598-z).