P-ISSN 1991-8941
E-ISSN 2706-6703
Vol. 20, No. 2 (2026)

Journal of University of Anbar for Pure Science
(JUAPS)

journal homepage: juaps.uoanbar.edu.iq

Open Access

Original Paper

Dynamic modulation changes of POMC in the arcuate nucleus and neuroendocrine adaptation in response to lifestyle intervention in obese adults

Nour Shakir Rezaieg[1*], **Muthanna M. Awad**[1]

[1]Department of Biology, College of Education for Pure Sciences, University of Anbar, Anbar, Iraq

ARTICLE INFO

Received: 02/09/2025
Revised: 31/10/2025
Accepted: 13/11/2025
Available online: 30/07/2026
August Issue
10.37652/juaps.2025.164462.1647

Cite @ JUAPS

Corresponding author
Nour Shakir Rezaieg
nou23u1003@uoanbar.edu.iq

ABSTRACT

Obesity occurs as a result of long-term positive energy balance, in which energy intake exceeds energy expenditure. This anabolic condition can lead to impaired hypothalamic neuronal activity involved in nutrient sensing and nutrient-signaling responses. Proopiomelanocortin (POMC) is a neuropeptide that plays a pivotal role in regulating appetite and neuroendocrine responses to energy balance. From this perspective, the study aimed to assess the impact of 6 months of lifestyle intervention on neurohormonal and inflammatory indicators, including POMC, leptin, and IL-17A, in participants with obesity. A quasi-experimental longitudinal controlled study involved 100 adults of both sexes: 50 individuals with obesity (30 males and 20 females) and 50 healthy controls (37 males and 13 females), classified based on body composition analysis using the InBody device. Participants with obesity received personalized instructions on healthy diet and physical activity throughout the 6-month intervention period. Neuroendocrine and inflammatory markers were assessed at baseline in both groups and reassessed after the intervention in participants with obesity. At baseline, participants with obesity showed significantly higher neuroendocrine and inflammatory marker levels compared with healthy controls. After 6 months of lifestyle intervention, these parameters decreased significantly among participants with obesity compared with their baseline values; however, they remained elevated compared with healthy controls. Lifestyle modification for 6 months significantly improved neuroendocrine and inflammatory markers in adults with obesity. To the best of our knowledge, this is the first study to investigate the impact of lifestyle intervention on POMC in adults with obesity, highlighting the neuroendocrine response to weight loss.

Keywords: *ARC, IL-17A, Leptin, Obesity, POMC*

1 INTRODUCTION

To coordinate the physiological and behavioral responses required to maintain energy balance, the central nervous system rapidly and accurately integrates information received from the body in response to changing environmental and internal conditions [1]. This integration occurs through bidirectional communication between the body and the brain, in which hormones and nutrients transmit signals to the hypothalamus (HT) to regulate appetite, metabolism, and energy balance [2].

The hypothalamic nuclei are involved in the regulation of vital functions, including stress, sexual behavior, and energy balance [3]. Among these nuclei, the arcuate nucleus (ARC) is particularly important because of its connection to the median eminence, which has a partially permeable blood–brain barrier (BBB). This anatomical feature enables the ARC to sense hormonal changes and peripheral signals from the blood [4].

The ARC contains two critical neuronal populations that continuously monitor signals reflecting energy status and stimulate appropriate behavioral and metabolic responses to changes in energy demand [5]. The first group of ARC neurons promotes food intake and is known as appetite-stimulating neurons. These cells express neuropeptide Y (NPY) and agouti-related peptide (AgRP). AgRP is expressed mainly in the ARC of the hypothalamus, and AgRP-producing neurons co-secrete NPY [6]. The second group reduces food intake by secreting cocaine- and amphetamine-regulated transcript (CART) and proopiomelanocortin (POMC), which represent opposing branches of the melanocortin signaling pathway [7].

POMC is a multifunctional precursor protein that gives rise to several peptides involved in energy homeostasis and appetite control, including α-melanocyte-stimulating hormone (α-MSH). POMC-producing neurons are found mainly in two brain regions: the ARC of the hypothalamus and the nucleus tractus solitarius (NTS) in the brainstem [8]. These neurons respond to peripheral metabolic signals and project to hypothalamic neurons, as well as to neurons in the brainstem and spinal cord [9].

Hunger and satiety are regulated through complex interactions between neural and hormonal signals. When satiety signals are elevated, the melanocortin pathway is activated by the release of α-MSH from POMC-producing neurons, leading to appetite suppression and increased energy expenditure [10]. In contrast, NPY/AgRP neurons promote appetite and inhibit POMC action, thereby increasing hunger and decreasing energy expenditure [11].

Hormonal signals reach the arcuate nucleus through two main routes. The first route is through blood circulation, because of the ARC's proximity to areas with a partially permeable BBB. The second route is through neural signals transmitted by visceral nerves, especially the vagus nerve, to brainstem nuclei such as the NTS [12]. These nuclei then send inputs to the hypothalamus, where they are integrated with blood-derived signals in the ARC. After processing this information, output neurons, such as POMC and AgRP neurons, send signals to other hypothalamic nuclei, including the lateral hypothalamic area (LHA) and the paraventricular nucleus (PVN), which contribute to the regulation of appetite, metabolic rate, and eating behavior [13].

In obesity, regulation of energy balance through the ARC no longer follows normal physiological patterns because of central resistance to hormonal signals, such as leptin, insulin, and ghrelin. This hormonal resistance not only disrupts responses within AgRP/NPY and POMC/CART circuits but also leads to dysfunctional activity in these neural pathways. Some appetite-suppressing neurons may appear more active, while appetite-stimulating neurons may appear less active; however, this does not necessarily translate into an actual reduction in food intake [14].

This discrepancy may be explained by defects in signal reception within neural pathways or impaired function of melanocortin 4 receptors (MC4Rs), in addition to obesity-associated inflammatory changes within the arcuate nucleus, which alter its neuronal environment. Thus, obesity is a complex condition that arises not only from increased energy intake but also from an intricate interaction among disrupted hormonal signaling, neural activity, and inflammation [15].

Although the role of POMC neurons in appetite regulation and energy homeostasis has been extensively studied in animal models, little is known about circulating POMC concentrations in humans. To the best of our knowledge, no prior study has examined serum POMC concentrations in individuals with obesity, especially in response to a healthy lifestyle intervention. Therefore, this study aimed to investigate the relationship between central appetite-regulating peptides and metabolic-inflammatory markers by assessing serum POMC, leptin, and IL-17A levels in participants with obesity before and after intervention.

2 MATERIALS AND METHODS

2.1 Study type

The study was designed as a quasi-experimental longitudinal controlled study and was conducted at the University of Anbar, Anbar, Iraq, from December 1 to July 30. The study aimed to assess the impact of an intervention based on a healthy diet and regular exercise program on neurological (POMC), hormonal (leptin), and inflammatory (IL-17A) markers in participants with obesity. It also examined the extent to which this intervention could improve energy homeostasis and stimulate sustainable long-term weight loss.

2.2 Participants

The study included 100 participants aged 21–40 years, divided into two groups. The obesity group included 50 participants with obesity, consisting of 30 males and 20 females. Obesity was diagnosed based on body

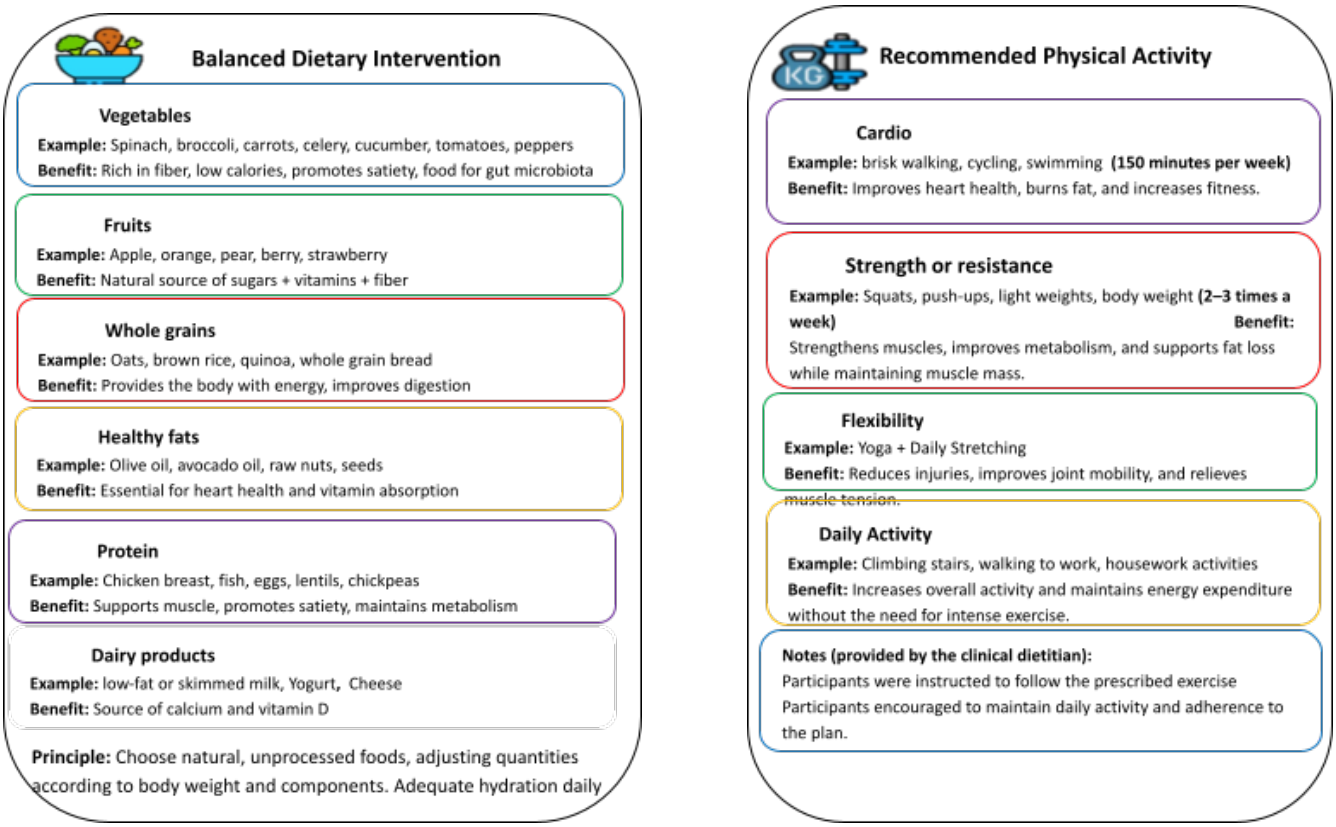

Fig. 1 The intervention protocol : a- Ddietary protocol , b- exercise program (Designed by researcher).

composition measurements using the InBody device, with careful review by a nutritionist at private nutrition clinics in Anbar. The healthy control group included 50 participants, consisting of 37 males and 13 females. These participants had no chronic diseases or hormonal disorders, and their normal weight and body composition were confirmed using the InBody device.

2.3 Study hypothesis

Based on previous studies indicating that consumption of unhealthy foods disrupts hunger and satiety signals in the hypothalamus, promotes addictive eating behavior, and contributes to the development of obesity and hormonal and immune disorders related to appetite and metabolism regulation [16], this study hypothesized that adopting a healthy lifestyle would modify POMC, leptin, and IL-17A levels, thereby promoting restoration of energy balance.

2.4 Intervention protocol

The study protocol included a 6-month dietary intervention designed according to the condition of each participant with obesity, taking into account body composition measured by the InBody device and specific nutritional needs. Although the diet followed a general framework based on calorie reduction and improved nutritional quality, the daily nutritional details were tailored to each participant.

The exercise component included a moderate-intensity exercise program, such as brisk walking or aerobic exercise, for no less than 150 min per week, distributed over 3–5 sessions.

The dietary protocol and exercise program used in this study were designed by dietitians at therapeutic nutrition clinics, where participants with obesity attended for weight management and weight loss. To facilitate reader understanding and ensure study replicability, the researcher summarized the original dietary protocol and exercise program and organized them visually in Figure 1.

2.5 Study plan

Figure 2 shows the study plan.

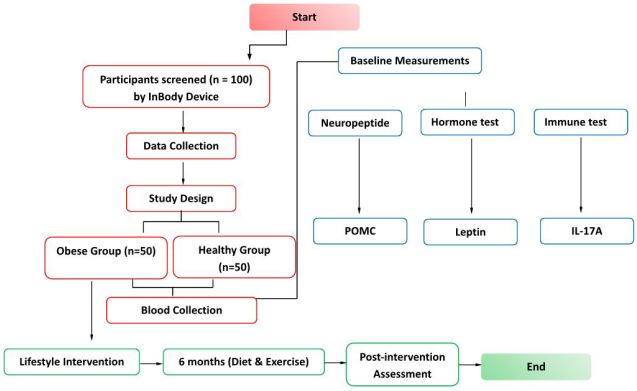

Fig. 2 Study plan.

2.6 blood collection

Blood samples were collected from all participants in the morning after a 10–12 h fast to reduce the effect of diurnal variation on parameter concentrations. Blood samples were collected from participants with obesity before and after the 6-month intervention, whereas samples from the healthy control group were collected only once.

The samples were then centrifuged at 3500 rpm for 15 min. Serum samples prepared for hormonal and immunological assays were stored at 2–8 °C until analysis, according to the manufacturer's instructions.

2.7 Materials and instruments

Table 1 presents the chemical agents, instruments, and suppliers used for biomarker evaluation in this study.

Table 1 Chemicals and equipment in the current study

No.	Chemical material(Kits)	Instrument	Company	Country
1	Human POMC ELISA kit	-	Shanghai	China
2	Human Leptin ELISA kit	-	Reed Biotech	China
3	Human IL-17A ELISA kit	-	Proteintech	U. S. A.
4	-	Reader Eliza	Biotek	U. S. A.
5	-	Washer Eliza	Biotek	U. S. A.
6	-	Printer Eliza	Biotek	U. S. A.
7	-	InBody 270	InBody Co., Ltd	South Korea
8	-	Centrifuge	Hermle, Z 207 A,	Germany

2.8 Methods

POMC concentrations were assessed using an ELISA kit (Shanghai, China) according to the manufacturer's protocol. Leptin concentrations were determined using a commercial ELISA sandwich kit (Reed Biotech, China) according to the manufacturer's instructions.

Serum IL-17A concentrations were measured using an ELISA kit (Proteintech, China), as described in the supplied protocol [17]. All measurements were performed in duplicate to ensure reliability, and final concentrations were calculated according to the manufacturers' procedures.

For all ELISA assays, a standard curve was generated using serial dilutions of the provided standards. Optical density was measured at 450 nm using a microplate reader (BioTek Instruments, USA), and concentrations were calculated using four-parameter logistic (4-PL) regression.

2.9 Statistical analysis

Statistical analysis was performed using SPSS version 24 and GraphPad Prism version 9. Comparisons among study groups were performed using one-way analysis of variance (ANOVA) followed by the LSD post hoc test. Pearson's correlation analysis was used to assess associations between variables, and logistic regression analysis was used to identify predictors. Receiver operating characteristic (ROC) curve analysis and area under the curve (AUC) analysis were used to evaluate the discriminative ability of POMC, IL-17A, and leptin. A p value <0.05 was considered statistically significant.

3 RESULTS AND DISCUSSION

3.1 Demographic characteristics

Participants were divided into two groups: an obesity group and a healthy control group, with 50 participants in each group. The mean age was 30.06 ± 5.9 years in the obesity group and 29.9 ± 5.9 years in the healthy control group. The sex distribution was 30 males and 20 females in the obesity group and 37 males and 13 females in the healthy control group.

Regarding place of residence, participants were distributed between urban areas and rural areas in both groups. Participants were also classified into four age groups: 20–25, 26–30, 31–35, and 36–40 years. No significant differences were observed between the two groups in age distribution (Table 2).

3.2 Biochemical parameters

Table 3 summarizes the mean ± SD serum concentrations of POMC, leptin, and IL-17A in healthy controls and participants with obesity before and after the intervention. One-way ANOVA followed by the LSD post hoc test showed significant differences among the three groups for all parameters. After the intervention, the mean POMC concentration decreased from 26.09 ± 11.5 to 22.1 ± 8.58 pg/mL, the mean leptin concentration decreased from

40.09 ± 7.24 to 30.50 ± 5.95 ng/mL, and the mean IL-17A concentration decreased from 31.08 ± 4.83 to 24.76 ± 3.59 mg/dL ($p < 0.05$).

Table 2 Mean ± standard deviation of demographic characteristics in healthy controls, obese participants pre-intervention, and 6 months post-intervention

Variables		Healthy Controls	Obese Group		X2 F	p-value
			Pre-intervention	Post-intervention		
Age (Years)	Mean±SD	29.9±5.9	30.06±5.9	30.06±5.9	0.007	0.993 N.S
Age periods (Years) n (%)	20 – 25	16	13	13	3.92	0.685 N.S
	26 – 30	9	15	15		
	31 – 35	15	10	10		
	36 – 40	10	12	12		
Sex n (%)	Male	37	30	30	2.85	0.239 N.S
	Female	13	20	20		
Region n (%)	Urban	31	33	33	0.174	0.917 N.S
	Rural	19	17	17		

Note. Significant differences (p-value less than 0.05), Abbreviation: SD: Standard deviation.
Min.: Minimum, Max.: Maximum, N.S: No significant difference between groups

Table 3 Mean ± standard deviation of POMC, Leptin and IL-17A inhealthy controls, obese participants pre-intervention, and 6 months post-intervention

Variables		Healthy Control (n=50)	Obese group (n=50)		F	p-value
			Post-intervention	Pre-intervention		
POMC (Pg/ml)	Mean±SD	13.67±6.87 a	26.09±11.5b	22.1±8.58 c	23.70	0.0001
	Min. – Max.	7.11 – 52.16	8.92 – 55.68	7.99 – 41.20		
Leptin (ng/ml)	Mean±SD	14.53±2.04 a	40.09±7.24 b	30.50±5.95 c	271.6	0.0001
	Min. – Max.	11.02 – 19.67	25.1 – 57.1	20.9 – 43.21		
IL-17A (mg/dl)	Mean±SD	13.91±4.68 a	31.08±4.83 b	24.76±3.59 c	194.3	0.0001
	Min. – Max.	8.21 – 29.54	23.54 – 41.2	19.94 – 35.0		

Note. Significant differences (p-value less than 0.05), Abbreviation: a: control group, b: Obese group before, c: Obese group after, Different superscript letters (a, b, c) indicate statistically significant differences between groups, SD: Standard deviation, Min.: Minimum, Max.: Maximum, POMC: Pro-opiomelanocortin

3.3 Graphical representation of study parameters

Figures 3 – 5 show the concentrations of POMC, leptin, and IL-17A in healthy controls and participants with obesity before and after the intervention. Differences among groups were analyzed using one-way ANOVA followed by the LSD post hoc test. After the intervention, the mean POMC concentration decreased from 26.09 ± 11.5 to 22.1 ± 8.58 pg/mL, the mean leptin concentration decreased from 40.09 ± 7.24 to 30.50 ± 5.95 ng/mL, and the mean IL-17A concentration decreased from 31.08 ± 4.83 to 24.76 ± 3.59 mg/dL ($p<0.05$).

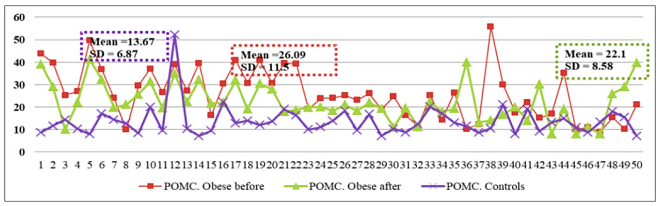

Fig. 3 Serum concentrations of POMC across study groups

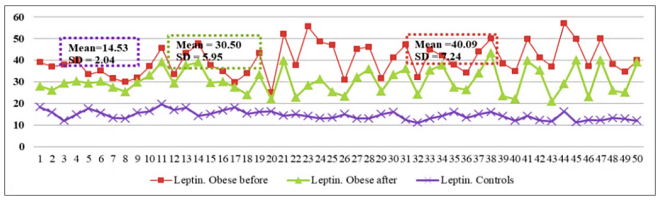

Fig. 4 Serum concentrations of leptin across study groups

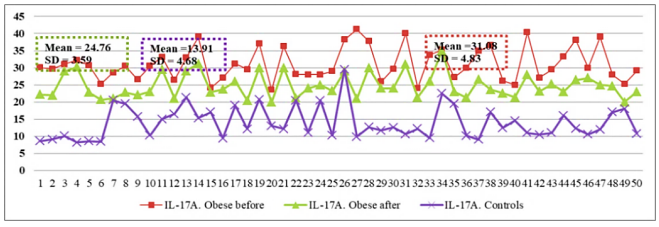

Fig. 5 Serum concentrations of IL-17A across study groups

3.4 Associations of parameters with age and sex

Figures 6-8 show the associations of POMC, leptin, and IL-17A with participants' age and sex in the study groups. Regarding age, no significant differences in POMC concentrations were observed among the four age groups: 20-25 years, 26.96 ± 11.13; 26-30 years, 24.78 ± 6.67; 31-35 years, 20.37 ± 9.00; and 36 – 40 years, 23.33 ± 10.79. Regarding sex, the mean POMC concentration was significantly higher in males (26.78 ± 10.87) than in females (20.12 ± 8.03) ($p < 0.05$).|

Regarding age, no significant differences in leptin concentrations were observed among the four age groups: 20 – 25 years, 36.52 ± 7.40; 26 – 30 years, 35.59±9.57; 31−35 years, 33.14±7.56; and 36−40 years, 35.39 ± 7.78. Regarding sex, the mean leptin concentration was significantly higher in females (40.41 ± 7.27) than in males (31.89 ± 6.89)($p < 0.05$).

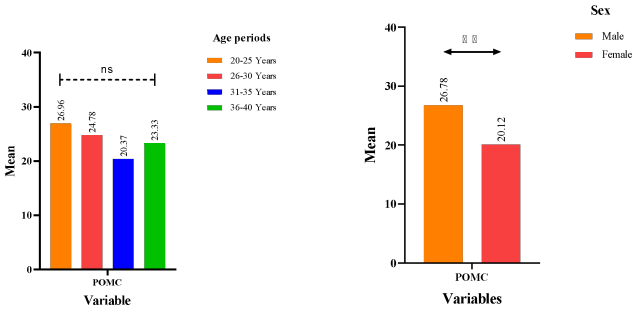

Fig. 6 Relation of POMC concentrarions with (a-age) and (b-sex). ns: No significant difference between groups, **: Significant difference between groups

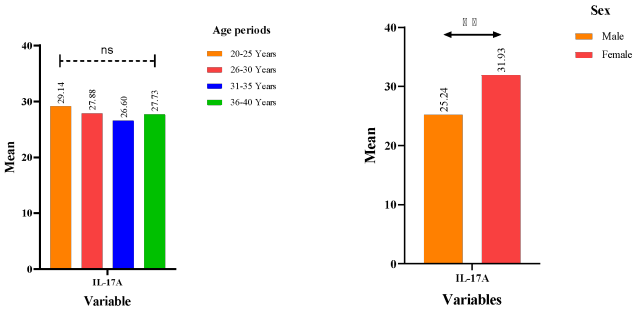

Fig. 8 Relation of IL-17A concentrarions with (a-age) and (b-sex). ns: No significant difference between groups, **: Significant difference between groups

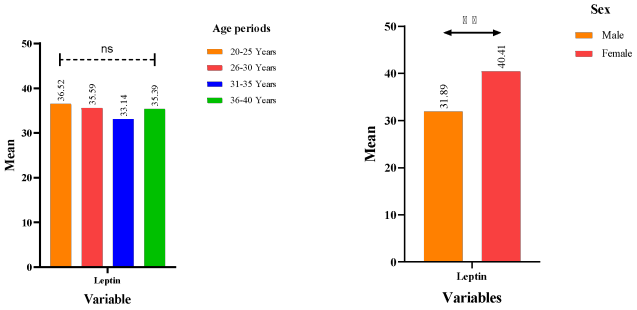

Fig. 7 Relation of leptin concentrations with (a-age) and (b-sex). ns: No significant difference between groups, **: Significant difference between groups

Regarding age, no significant differences in IL-17A concentrations were observed among the four age groups: 20-25 years, 29.14 ± 5.93; 26-30 years, 27.88 ± 5.83; 31-35 years, 26.60 ± 4.30; and 36 – 40 years, 27.73 ± 4.30 . Regarding sex, the mean IL-17A concentration was significantly higher in females (31.93 ± 5.25) than in males (25.24± 3.25) ($p < 0.05$).

3.5 roc curve analysis of the parameters

POMC levels before and after the intervention showed AUC values of 0.840 and 0.819, cutoff values of 21.08 and 17.52, sensitivity values of 66% and 78%, specificity values of 96% and 82%, and p values of 0.0001, respectively (Figure 9).

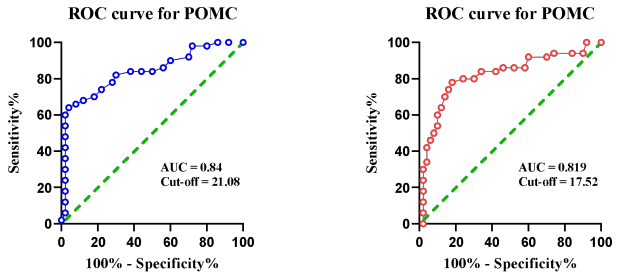

Fig. 9 ROC curves for POMC in obese participants (a-pre-intervention) and (b-post-intervention)

Leptin levels before and after the intervention showed AUC values of 1.000 and 1.000, cutoff values of 22.40 and 20.285, sensitivity values of 100% and 100%, specificity values of 100% and 100%, and p values of 0.0001, respectively (Figure 10).

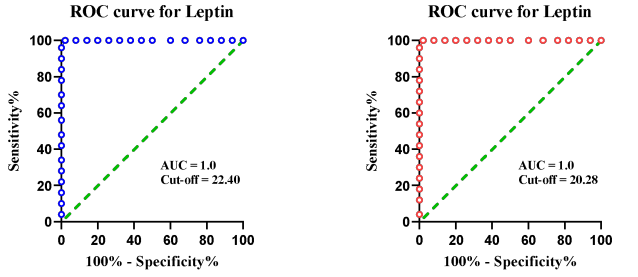

Fig. 10 ROC curves for leptin in obese participants (a-pre-intervention) and (b-post-intervention)

IL-17A levels before and after the intervention showed AUC values of 0.991 and 0.969, cutoff values of 23.02

and 20.875, sensitivity values of 100% and 92%, specificity values of 98% and 94%, and p values of 0.0001, respectively (Figure 11).

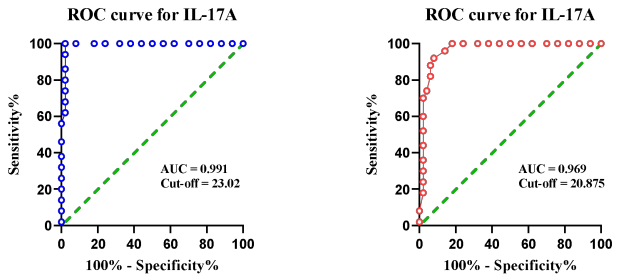

Fig. 11 ROC curves for IL-17A in obese participants (a-pre-intervention) and (b-post-intervention)

3.6 logistic regression analysis

Table 4 shows the logistic regression analysis for participants with obesity. POMC, leptin, and IL-17A were significantly associated with the dependent variable. The coefficient (B), p value, odds ratio (OR), and 95% confidence interval (CI) for each variable were as follows: POMC ($B = 0.113, p = 0.010, OR = 1.119, 95\%CI : 1.027 - 1.219$), leptin ($B = 0.186, p = 0.040, OR = 1.204, 95\%CI : 1.009 - 1.438$), and IL − 17 A($B = 0.364, p = 0.015, OR = 1.439, 95\%CI : 1.073$-1.931).

Table 4 Logistic regression analysis of obesity predictors pre- and post-interventiom

Variable	Coefficient (B)	P value	O.R	95% CI
POMC(pg/ml)	0.113	0.010	1.119	1.027 – 1.219
Leptin(ng/ml)	0.186	0.040	1.204	1.009 – 1.438
IL-17A(mg/dl)	0.364	0.015	1.439	1.073 – 1.931

Our genes face an important challenge in the modern environment, which is characterized by the abundance of hyperpalatable foods, high-calorie foods that are affordable and easily accessible, and reduced physical activity resulting from an unhealthy modern lifestyle. This mismatch is one of the major causes of obesity [18].

Adopting a healthy lifestyle led to significant improvements in neuropeptide, hormonal, and inflammatory markers. Notably, the results of the current study indicate the central role of the hypothalamus in adapting to a healthy and active lifestyle. These findings confirm the effectiveness of the applied program and contribute to expanding scientific knowledge about the mechanisms involved in improving health, reducing unhealthy food intake, and promoting a more active lifestyle.

The results in Table 2 showed no statistically significant differences in age, age groups, sex, or geographical distribution between the groups. Scientific studies [19] have emphasized the importance of achieving demographic balance between study groups to reduce the influence of confounding factors and ensure the reliability of the results.

The effect of overfeeding is not limited to increased energy intake; it also extends to functional changes in neural networks within the hypothalamus, especially in the arcuate nucleus (ARC), which is a major center for sensing and regulating appetite-stimulating and appetite-inhibiting signals [20].

In obesity resulting from chronic overeating, especially hyperpalatable foods, the dopaminergic reward system interacts with appetite-regulating hypothalamic circuits, reinforcing eating behavior through mechanisms similar to neuronal addiction [21]. This neural interaction causes disturbance in the homeostasis of inhibitory and excitatory appetite signals in the ARC. This occurs because of central resistance to several peripheral hormonal signals that regulate appetite, such as leptin, ghrelin, and insulin, as well as synaptic reprogramming that changes the sensitivity of these neural circuits. These changes encourage a neural pattern that promotes overeating and obesity [22].

This was reflected in the current study results. Before the intervention, the obesity group showed increased POMC concentrations compared with healthy controls. After the intervention, POMC concentrations decreased, although they remained higher than those of healthy controls (Table 3, Figure 3). Although POMC is known to suppress appetite through the production of α-MSH, which activates melanocortin 4 receptors (MC4Rs), the recorded increase in POMC concentration in participants with obesity may reflect a state of hyperstimulation or an initial compensatory response within a high-calorie nutritional environment [23]. Nevertheless, this increase in POMC concentration may not result in appetite suppression because of resistance of POMC neurons to inhibitory hormonal signals, such as leptin and insulin, leading to weakened melanocortin receptor activation and reduced functional α-MSH activity. As a result, overeating may continue.

Despite the wealth of information on the role of POMC in appetite regulation from animal models, direct human data remain limited. The current results suggest that

evaluating POMC concentrations in the context of dietary and lifestyle interventions may open a new dimension for deeper understanding of the neuroendocrine mechanisms associated with obesity and their compensatory responses, highlighting the need for further clinical studies.

Despite the marked decrease in POMC concentrations after the intervention, as shown in Table 2 and Figure 2, concentrations remained higher than those of healthy controls. This may be explained by the heterogeneity of POMC neurons, which consist of distinct subpopulations with different receptor profiles, neurotransmitter systems, and projection targets that may recover their function at different rates. As a result, total melanocortin signaling may remain partially elevated [24].

In addition, hypothalamic inflammation and endoplasmic reticulum stress may restrict rapid restoration of leptin/STAT3 sensitivity. Persistent impairments in leptin transport across the blood–brain barrier (BBB) by tanycytes, together with slowly reversible epigenetic changes in the POMC promoter, may further delay full normalization. Therefore, more gradual improvement may be expected with longer follow-up periods exceeding 6 months [25].

The current results showed that males with obesity had significantly higher POMC concentrations than females (Figure 6B). This increase may be attributed to the physiological effect of testosterone through androgen receptor (AR) signaling in the central nervous system, which plays an important role in promoting skeletal muscle mass and regulating energy metabolism [26].

Animal models of diet-induced obesity support the concept that leptin resistance does not occur uniformly throughout the brain, with the ARC and ventral tegmental area (VTA) being more affected than other regions. These findings indicate that leptin resistance represents a complex adaptive response involving cellular and molecular alterations that are partially reversible when dietary fat intake is reduced [27]. This mechanism is consistent with the current study, which demonstrated significantly elevated leptin concentrations in individuals with obesity before the intervention compared with healthy controls. After the intervention, leptin concentrations decreased but remained higher than those observed in healthy controls (Table 3, Figure 4).

Several previous studies have explained elevated leptin concentrations in individuals with obesity by the presence of central leptin resistance, mainly through three mechanisms: impaired leptin transport across the BBB, increased expression of suppressor of cytokine signaling 3 (SOCS3), which inhibits the JAK2/STAT3 pathway, and low-grade hypothalamic inflammation [28]. The decrease in leptin concentration after the intervention may be attributed mainly to reduced total body energy stores resulting from lower energy intake and increased energy expenditure through physical activity [29]. Because fat mass is the primary source of leptin secretion, any significant reduction in fat mass is reflected in decreased circulating leptin concentrations.

Wang et al. [30] reported that physical activity improves hypothalamic sensitivity to leptin signals, reducing the need for high leptin levels to maintain appetite control. This decrease may represent an adaptive response aimed at adjusting satiety signals and supporting restoration of energy homeostasis.

The current results are consistent with previous studies on obese adults, in which a 24-week milk-based low-energy liquid diet led to decreased leptin concentrations and improved metabolic markers [31]. Other studies have reported similar changes after bariatric surgery, including gastric bypass [32]. The leptin changes observed in the current study are generally consistent with findings from other interventions, including commercial meal-replacement programs [33].

Regardless of the type of intervention used, whether dietary or surgical, these results support the hypothesis that interventions creating a significant energy deficit lead to reduced leptin concentrations and contribute to improvements in metabolic mechanisms [34]. It is also worth noting that the observed decrease in leptin concentrations after the intervention may be attributed to improved insulin sensitivity in adipose and muscle tissues, which reduces leptin production from white adipose tissue. This decrease may reflect improved leptin signaling in the hypothalamus through POMC/AgRP neural pathways, promoting more efficient appetite and energy regulation. In addition, the reduction in adipocyte volume after the intervention contributes to reduced leptin production and may serve as an indicator of metabolic changes associated with healthy diet and physical activity [15, 30].

Elevated leptin concentrations in females with obesity (Figure 7B) are not only associated with increased fat mass but also with the stimulatory effect of estrogen on leptin secretion. Adipose tissue contains aromatase, an enzyme that converts androgens to estrogens, thereby stimulating local leptin production. This explains the complementary role of hormonal and adiposity-related factors in sex differences in leptin concentrations [35].

Table 3 and Figure 4 present the mean concentra-

tions of IL-17A across the three groups. Before the intervention, the obesity group showed increased IL-17A concentrations. After the intervention, IL-17A concentrations decreased, although they remained higher than those of healthy controls.

The high concentrations of IL-17A may be due to changes in the immune environment and metabolism of adipose tissue [36]. Obesity leads to increased secretion of adipokines from adipose tissue, particularly leptin, along with the accumulation of saturated fatty acids. This environment reprograms immune responses and promotes differentiation of Th17 cells, including $\gamma\delta$ T cells, thereby increasing interleukin production [37]. At the molecular level, leptin receptor activation enhances the STAT3/RORγt pathway, which is responsible for Th17 cell differentiation, while saturated fat promotes additional inflammatory signals. These mechanisms may explain the elevated IL-17A concentrations [38].

In addition to peripheral immune effects, previous studies have shown that obesity induces an inflammatory state in the hypothalamus through microglial activation, which leads to cytokine entry and neuroinflammation [39]. In this context, scientific evidence has shown that some neurons, including POMC neurons, may produce IL-17A, which directly affects circuits controlling appetite and energy balance [40]. This neuroimmune interaction partly explains the elevated IL-17A levels in individuals with obesity and links them to mechanisms of leptin resistance and imbalance between POMC/AgRP pathways [41]. The results of the current study support this connection, as they showed a strong positive correlation between leptin and IL-17A concentrations ($r = 0.53$, $p = 0.0001$).

Although IL-17A concentrations decreased after the intervention, they did not reach normal levels. This may be attributed to what is known as obesity memory. Obesity leaves a long-lasting inflammatory and epigenetic imprint on immune cells and adipose tissue, maintaining activity of the Th17/IL-17A pathway even after weight loss [42]. In addition, inflammatory memory supported by cellular and epigenetic reprogramming may delay full restoration of immune-metabolic homeostasis and explain the relatively high IL-17A concentrations that persist despite improvement. This has been reported in recent studies, including the study by Hinte et al. [43].

Receiver operating characteristic (ROC) curve analysis (Figures 9–11) was used to determine the potential predictive value of POMC, leptin, and IL-17A concentrations in distinguishing between participants with obesity and healthy controls before and after the intervention. According to the area under the curve (AUC) values, leptin was the strongest marker in this study, achieving the highest discriminatory ability between participants (AUC = 1.000), while POMC and IL-17A showed considerable but relatively lower discriminatory performance.

According to the logistic regression analysis (Table 4), IL-17A appeared to be the strongest independent predictor of obesity, highlighting the major role of chronic inflammation in obesity. Leptin also contributed substantially, reflecting impaired satiety signaling and altered hypothalamic regulation, whereas POMC may play a compensatory role within neuroendocrine pathways. These results indicate an interaction between inflammatory and neuroendocrine mechanisms in obesity risk, with inflammation, especially IL-17A, appearing to be the strongest factor in this cohort.

4 CONCLUSION

The results of this study indicate that obesity associated with an unhealthy lifestyle affects the neural circuits regulating energy homeostasis, leading to hormonal resistance and neuroinflammatory disturbances. To the best of our knowledge, this study is the first to assess serum POMC concentrations in participants with obesity before and after lifestyle intervention, highlighting its potential role in appetite regulation and energy balance.

ROC analysis showed that leptin was the strongest predictor of obesity, whereas IL-17A remained a significant indicator reflecting the inflammatory component of obesity. Therefore, these findings suggest a complex interaction among inflammatory, neural, and hormonal pathways and emphasize the importance of targeting these pathways in obesity prevention strategies. Further studies are required to confirm these findings and explore their potential therapeutic applications.

Author contributions

Nour Shakir Rezaieg PhD student designed the study, samples collected, and done the laboratory experiments. Also the student performed the statistical analyses and designed the figure in the manuscript. Prof. Dr. Muthanna M. Awad supervised the project, presented important guidance in study design and contributed in data explanation, and revised the manuscript.

Funding source

No funds received.

Data availability

N/A

DECLARATIONS

Conflict of interest

The authors declare no competing interests

Consent to publish

N/A

Ethical approval

The study was approved by the Ethical approval committee from University of Anbar, approval number (223), dated (24/2/2024). All participants signed an informed consent form after receiving a full explanation of the nature, procedures, and objectives of the study, and the confidentiality of participants' data and their identity were confirmed.

REFERENCES

[1] Bombassaro B, Araujo EP, Velloso LA. The hypothalamus as the central regulator of energy balance and its impact on current and future obesity treatments. Archives of Endocrinology and Metabolism. 2024;68(special issue). 10.20945/2359-4292-2024-0082

[2] Brüning JC, Fenselau H. Integrative neurocircuits that control metabolism and food intake. Science. 2023;381(6665). 10.1126/science.abl7398

[3] Chen X, Wang Y, Fu S, Wan Y, Mao J, Cui K, et al. The Integrated Function of the Lateral Hypothalamus in Energy Homeostasis. Cells. 2025;14(14):1042. 10.3390/cells14141042

[4] Song J, Choi SY. Arcuate Nucleus of the Hypothalamus: Anatomy, Physiology, and Diseases. Experimental Neurobiology. 2023;32(6):371–386. 10.5607/en23040

[5] Rezaieg NS, Awad MM. Neurophysiology and Endocrine Responses to Hunger and Satiety Mechanisms: The Brain-Gut Crosstalk. Karbala International Journal of Modern Science. 2025;11(3). 10.33640/2405-609x.3416

[6] Qi Y, Lee NJ, Ip CK, Enriquez R, Tasan R, Zhang L, et al. Agrp-negative arcuate NPY neurons drive feeding under positive energy balance via altering leptin responsiveness in POMC neurons. Cell Metabolism. 2023;35(6):979–995.e7. 10.1016/j.cmet.2023.04.020

[7] Hu H, Lu X, He Y, Li J, Wang S, Luo Z, et al. Sestrin2 in POMC neurons modulates energy balance and obesity related metabolic disorders via mTOR signaling. The Journal of Nutritional Biochemistry. 2024;133:109703. 10.1016/j.jnutbio.2024.109703

[8] Quiñones M, Hernández-Bautista R, Beiroa D, Heras V, Torres-Leal FL, Lam BYH, et al. Sirt3 in POMC neurons controls energy balance in a sex- and diet-dependent manner. Redox Biology. 2021;41:101945. 10.1016/j.redox.2021.101945

[9] Xing M, Li Y, Zhang Y, Zhou J, Ma D, Zhang M, et al. Paraventricular hypothalamic RUVBL2 neurons suppress appetite by enhancing excitatory synaptic transmission in distinct neurocircuits. Nature Communications. 2024;15(1). 10.1038/s41467-024-53258-6

[10] Clarke GS, Page AJ, Eldeghaidy S. The gut–brain axis in appetite, satiety, food intake, and eating behavior: Insights from animal models and human studies. Pharmacology Research & Perspectives. 2024;12(5). 10.1002/prp2.70027

[11] Rafiei N, Mitchell CS, Tedesco CR, Chen J, Choi EA, Roughley S, et al. Chemogenetic activation of arcuate nucleus NPY and NPY/AgRP neurons increases feeding behaviour in mice. Neuropeptides. 2024;107:102454. 10.1016/j.npep.2024.102454

[12] Liskiewicz A, Khalil A, Liskiewicz D, Novikoff A, Grandl G, Maity-Kumar G, et al. Glucose-dependent insulinotropic polypeptide regulates body weight and food intake via GABAergic neurons in mice. Nature Metabolism. 2023;5(12):2075–2085. 10.1038/s42255-023-00931-7

[13] Roh E, Choi KM. Hormonal Gut–Brain Signaling for the Treatment of Obesity. International Journal of Molecular Sciences. 2023;24(4):3384. 10.3390/ijms24043384

[14] Kim N, Kim S, Park S, Kim EK. Adenosine transmission from hypothalamic tanycytes to AGRP/NPY neurons regulates energy homeostasis. Experimental & Molecular Medicine. 2025;57(5):1047–1063. 10.1038/s12276-025-01449-6

[15] Liu W, Li N, Tang D, Qin L, Zhu Z. Multimodal Neuroimaging of Obesity: From Structural-Functional Mechanisms to Precision Interventions. Brain Sciences. 2025;15(5):446. 10.3390/brainsci15050446

[16] Rezaieg NS. Neurobiology of Sweet Cravings: The Brain's Reward System Response to Hedonic Eating. Kufa Medical Journal. 2024;20(2):135–146. 10.36330/kmj.v20i2.17199

[17] Song X, Qian Y. The activation and regulation of IL-17 receptor mediated signaling. Cytokine. 2013;62(2):175–182. 10.1016/j.cyto.2013.03.014

[18] Capocasa M, Venier D. A bio-cultural tale of the past, present and future of human nutrition. Journal of anthropological sciences. 2024;102:87-104

[19] Johnson-Mann CN, Cupka JS, Ro A, Davidson AE, Armfield BA, Miralles F, et al. A Systematic Review on Participant Diversity in Clinical Trials—Have We Made Progress for the Management of Obesity and Its Metabolic Sequelae in Diet, Drug, and Surgical Trials. Journal of Racial and Ethnic Health Disparities. 2022;10(6):3140–3149. 10.1007/s40615-022-01487-0

[20] Ariyani W, Yoshikawa C, Tsuneoka H, Amano I, Imayoshi I, Ichinose H, et al. Dopaminergic neurons in the paraventricular hypothalamus extend the food consumption phase. Proceedings of the National Academy of Sciences. 2025;122(13). 10.1073/pnas.2411069122

[21] Huwart SJP, Morales-Puerto N, Everard A. Gut microbiota-related neuroinflammation at the crossroad of food reward alterations: implications for eating disorders. Gut. 2025;74(10):1728–1740. 10.1136/gutjnl-2024-333397

[22] Hankir MK, Lutz TA. Novel neural pathways targeted by GLP-1R agonists and bariatric surgery. Pflügers Archiv - European Journal of Physiology. 2024;477(2):171–185. 10.1007/s00424-024-03047-3

[23] Min SH, Song DK, Lee CH, Roh E, Kim MS. Hypothalamic AMP-Activated Protein Kinase as a Whole-Body Energy Sensor and Regulator. Endocrinology and Metabolism. 2024;39(1):1–11. 10.3803/enm.2024.1922

[24] Quarta C, Claret M, Zeltser LM, Williams KW, Yeo GSH, Tschöp MH, et al. POMC neuronal heterogeneity in energy balance and beyond: an integrated view. Nature Metabolism. 2021;3(3):299–308. 10.1038/s42255-021-00345-3

[25] Al-Suhaimi EA, AlRubaish AA, Aldossary HA, Homeida MA, Shehzad A, Homeida AM. Obesity and Cognitive Function: Leptin Role Through Blood–Brain Barrier and Hippocampus. Molecular Neurobiology. 2025;62(12):16280–16301. 10.1007/s12035-025-05262-0

[26] Della Guardia L, Shin AC. Obesity-induced tissue alterations resist weight loss: A mechanistic review. Diabetes, Obesity and Metabolism. 2024;26(8):3045–3057. 10.1111/dom.15637

[27] Wulff BS, Kuhre RE, Selvaraj M, Rehfeld JF, Niss K, Fels JJ, et al. Improved leptin sensitivity and increased soluble leptin receptor concentrations may underlie the additive effects of combining PYY(3–36) and exendin-4 on body weight lowering in diet-induced obese mice. Heliyon. 2024;10(12):e32009. 10.1016/j.heliyon.2024.e32009

[28] Mitoiu BI, Nartea R, Miclaus RS. Impact of Resistance and Endurance Training on Ghrelin and Plasma Leptin Levels in Overweight and Obese Subjects. International Journal of Molecular Sciences. 2024;25(15):8067. 10.3390/ijms25158067

[29] Brandt-Heunemann S, Vogel M, Kiess W, Körner A, Blüher M, Meigen C, et al. Reference Values for Serum Leptin Levels in Children, Adolescents, and Adults With Normal Weight, Overweight, and Obesity. The Journal of Clinical Endocrinology & Metabolism. 2025;111(3):832–844. 10.1210/clinem/dgaf439

[30] Wang Y, Qi F, Li M, Xu Y, Dong L, Cai P. Traditional Chinese medicine modulates hypothalamic neuropeptides for appetite regulation: A comprehensive review. BioScience Trends. 2025;19(3):281–295. 10.5582/bst.2025.01087

[31] Rafey MF, Abdalgwad R, O'Shea PM, Foy S, Claffey B, Davenport C, et al. Changes in the Leptin to Adiponectin Ratio Are Proportional to Weight Loss After Meal Replacement in Adults With Severe Obesity. Frontiers in Nutrition. 2022;9. 10.3389/fnut.2022.845574

[32] Alic N, Ayaz A. Ghrelin and LEAP2: Their Interaction Effect on Appetite Regulation and the Alterations in Their Levels Following Bariatric Surgery. Medicina. 2025;61(8):1452. 10.3390/medicina61081452

[33] Sooriyaarachchi P, Jayawardena R, Pavey T, King NA. Meal Replacement as a Weight Loss Strategy for Night Shift Workers with Obesity: A Protocol for a Randomized Controlled Trial. Trials. 2022;23(1):860. 10.1186/s13063-022-06784-x

[34] Karczewska-Kupczewska M, Stefanowicz M, Nikołajuk A, Strączkowski M. Weight-Reducing Dietary Intervention Increases the Ability of Hyperinsulinemia to Suppress Serum Ghrelin Concentration in Individuals with Obesity. The Journal of Nutrition. 2024;154(5):1631–1639. 10.1016/j.tjnut.2023.12.043

[35] Belli R, Dattolo A, Sampogna F, Gubinelli E, Lulli D, Moretta G, et al. Leptin: a gender and obesity-related marker predictive of metabolic comorbidities and therapeutic response to anti-IL-23 biologic drugs in psoriatic patients. Frontiers in Immunology. 2025;16. 10.3389/fimmu.2025.1607312

[36] Polak-Szczybyło E, Tabarkiewicz J. IL-17A, IL-17E and IL-17F as Potential Biomarkers for the Intensity of Low-Grade Inflammation and the Risk of Cardiovascular Diseases in Obese People. Nutrients. 2022;14(3):643. 10.3390/nu14030643

[37] Alhamawi RM, Damfo S, Aloufi N, Almutawif YA, Suliman BA. Investigating the potential role of T helper 17 cells among women experiencing overweight and obesity and their possible therapeutic targeting of the RORγt molecule. Scientific Reports. 2024;14(1). 10.1038/s41598-024-81070-1

[38] Zi C, Wang D, Gao Y, He L. The role of Th17 cells in endocrine organs: Involvement of the gut, adipose tissue, liver and bone. Frontiers in Immunology. 2023;13. 10.3389/fimmu.2022.1104943

[39] Artemniak-Wojtowicz D, Kucharska AM, Stelmaszczyk-Emmel A, Majcher A, Pyrżak B. Changes of Peripheral Th17 Cells Subset in Overweight and Obese Children After Body Weight Reduction. Frontiers in Endocrinology. 2022;13. 10.3389/fendo.2022.917402

[40] Sun CY, Yang N, Zheng ZL, Liu D, Xu QL. T helper 17 (Th17) cell responses to the gut microbiota in human diseases. Biomedicine & Pharmacotherapy. 2023;161:114483. 10.1016/j.biopha.2023.114483

[41] JANICKA L, DAJNOWSKA A, ARCISZEWSKI MB. Role of Proopiomelanocortin (POMC) Derivatives in Body Weight Regulation: A Review of Current Knowledge and Significance in the Pathogenesis of Obesity in Mammals. Medycyna Weterynaryjna. 2025;81(5):221–230. 10.21521/mw.6998

[42] Douglas A, Stevens B, Lynch L. Interleukin-17 as a key player in neuroimmunometabolism. Nature Metabolism. 2023;5(7):1088–1100. 10.1038/s42255-023-00846-3

[43] Hinte LC, Castellano-Castillo D, Ghosh A, Melrose K, Gasser E, Noé F, et al. Adipose tissue retains an epigenetic memory of obesity after weight loss. Nature. 2024;636(8042):457–465. 10.1038/s41586-024-08165-7

How to cite this article

Rezaieg NS, Awad MM. Dynamic Modulation Changes of POMC in the Arcute Neuclus and Neuroendocrine Adaptation in Response to Lifestyle Intervention in Obese Adults . Journal of University of Anbar for Pure Science. 2026; 20(2):100-111. doi:10.37652/juaps.2025.164462.1647