

THE ROLE OF GHRELIN AND PANCREATIC POLYPEPTIDES IN DEVELOPMENT OF HIGH FAT DIET (HFD) - INDUCED OBESITY IN ADULT ALBINO RATS

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ABSTRACT

Background: Sex difference in eating behavior is well documented. Development of diet-induced obesity in males and females is mediated by distinct mechanisms. Therefore, understanding the key molecular mechanisms involved in the pathogenesis of obesity could be beneficial for the development of a therapeutic approach.

Objective: Assessing whether high fat diet (HFD) induced obesity is sex-specific and the possible effect of pancreatic polypeptide (PYY) and ghrelin on the HFD induced obesity in albino rats.

Material and Methods: Sixty four rats of a local strain were divided into 4 equal groups. Each group was divided into male and female subgroups: group I(control group), group II (HFD received rats), group III (HFD- PYY treated rats at a dose of 50 µg/kg twice daily by i.p injection), and group IV(HFD- ghrelin treated rats at a dose of 10 nmol/ day by intraperitoneal injection).

Results: There were extensive differences between the sexes in the development of obesity by using high fat diet at the end of 4th and 5th weeks. Body weight was significantly lower in females as compared to males. Administration of PYY caused significant decrease in body weight compared to HFD, whereas ghrelin administration caused significant increase in body weight compared to HFD in all groups.

Conclusion: Despite extensive similarities in the brain responses to hunger and satiety between male and female, there were sex- differences in the development of obesity and body weight gain. PYY administration reduced HFD induced obesity, while a ghrelin administration exaggerated the degree of obesity.

Keywords: high fat diet, obesity, Ghrelin, pancreatic polypeptide PYY, albino rats.

INTRODUCTION

Obesity is a major public health problem, Most of the world's population lives in countries where overweight and obesity kill more people than underweight. According to the World Health Organization (WHO), episode of obesity has more than doubled since 1980. In 2014, over 1.9 billion adults, 18 years and older were overweight (WHO;

Obesity and Overweight, 2016). Body weight is tightly regulated by complex homeostatic mechanisms. Obesity is a state in which energy intake chronically exceeds energy expenditure. Even a subtle mismatch (less than 0.5%) in caloric intake over expenditure is sufficient to cause weight gain (Hagan and Niswender, 2012). There are certain diseases such as type 2 diabetes,

hypertension, cardiovascular disease, and several forms of cancer which were found to be associated with obesity. Therefore, understanding the mechanisms involved in the pathogenesis of obesity could be beneficial for the therapeutic approach. Hormones such as ghrelin, peptide YY (PYY), pancreatic polypeptide (PP), have an intense impact on energy balance and maintenance of homeostasis by inducing satiety and meal termination (**Rasmussen et al., 2012**).

The gut–brain axis refers to the bidirectional communication between the gut and the brain. Four information carriers (vagal and spinal afferent neurons, immune mediators such as cytokines, The members of the neuropeptide Y (NPY) family of biologically active peptides, NPY, peptide YY (PYY) and pancreatic polypeptide (PP), are expressed by cell systems at distinct levels of the gut–brain axis. PYY and PP are exclusively expressed by endocrine cells of the digestive system, whereas NPY is found at all levels of the gut–brain and brain–gut axis (**Peter et al., 2012**).

Pancreatic polypeptide (PP) is a family of peptides including neuropeptide Y (NPY) and peptide YY (PYY). PP is produced in PP cells of pancreatic islets of Langerhans and released into circulation after ingestion of food. Effects of PP are thought to be mediated by directly through the Y4 receptor in the brainstem and hypothalamus. In addition, it may act also via the vagus nerve, as the anorectic effects of PP are abolished by vagotomy in rodents (**Keisuke et al., 2010**). Plasma PP levels show diurnal variations: lowest levels are observed in the early morning and highest in the evening. The release of postprandial PP is biphasic.

Furthermore, the hypothalamus integrates a number of peripheral signals which modulate food intake and energy expenditure. Gut hormones, such as peptide YY, pancreatic polypeptide, glucagon-like peptide-1, oxyntomodulin, and ghrelin, are modulated by acute food ingestion (**Keisuke et al., 2012**).

Ghrelin is an endogenous ligand for the growth hormone secretagogue receptor. It activates the release of growth hormone from the pituitary (**Mora et al., 2013**).

Ghrelin is a multifaceted gut hormone which activates its receptor, growth hormone secretagogue receptor (GHS-R). Ghrelin's hallmark functions are its stimulatory effects on food intake, fat deposition and growth hormone release. Ghrelin is famously known as the “hunger hormone” (**Geetali et al., 2013**).

There are also differences in fasting and postprandial ghrelin concentrations in nondiabetic populations between lean and obese persons. Postprandial plasma ghrelin is suppressed proportional to meal calorie content in normal weight but not in obese subjects, which suggest that food intake fails to suppress ghrelin levels in obese humans (**Higgins et al., 2007**).

Ghrelin effects on hypothalamic neurons (ghrelin blocks leptin's action through the activation of the hypothalamic NPY/Y1 receptor pathway) has been suggested to be one of the important mechanisms for control food intake and body weight (**Khatib et al., 2016**).

The expression of gastric ghrelin was decreased in PP-over expressing mice. Repeated administrations of PP decreased body weight gain and ameliorated insulin resistance and hyperlipidemia in obese

mice (Keisuke et al., 2012). The aim of this study is to determine the sex difference in development of obesity as a result of high fat diet in rats and further to focus on the role of pancreatic polypeptide and ghrelin in HFD induced obesity of adult albino rats.

MATERIAL AND METHODS

The current study was conducted at Departments of Physiology, Faculty of Medicine, October'6 University since May till September 2016. The study protocol was approved by the Local Ethical Committee, October'6 Faculty of Medicine.

Sixty four adult albino rats of both sexes (32 males and 32 females) with body weight ranging from 180-200 g. were randomly divided into four equal groups. Rats were fed with normal chows or HFD after weaning until 10–12 month old, and their body weights and diet consumption were monitored. The rats were housed in separate cages (45cmx25cmx20cm), 4 rats /cage. The rats were kept at room temperature with natural light /dark cycles for one week acclimatization to lab conditions. All animal procedures undertaken were approved by October 6th University, Animal Care and Use Committee.

Experimental groups:

Group 1 (control group): Rats were subdivided into:(1-a) Control male group and (1-b) Control female group. These rats were allowed standard rat chow diet for 5 weeks without treatment and received intraperitoneal injection with saline (0.5 ml /rat) during the 5th week of the experiment.

Group 2 High fat diet (HFD) non treated group: Rats were subdivided into: (2-a) HFD non- treated male group, and (2-b) HFD non-treated female group.

These rats were allowed to receive HFD for 5 weeks without treatment and received intraperitoneal injection with saline (0.5 ml /rat) during the 5th week of the experiment.

Group 3 High fat diet group PYY treated group: Rats were subdivided into: (3-a) HFD PYY treated male group and (3-b) HFD PYY treated female group. These rats were allowed to receive HFD for 5 weeks. The rats were accustomed to the injection procedure by intraperitoneal injection with saline (0.5 ml /rat) for 2 days before polypeptide administration then PYY was received at a dose of 50 µg/kg twice daily dissolved in saline during the 5th week (Boggiano et al., 2005).

Group 4 High fat diet group ghrelin treated group: Rats were subdivided into: (4-a) HFD ghrelin treated male group and (4-b) HFD ghrelin treated female group. These rats were allowed to receive HFD for 5 weeks. The rats were accustomed to the injection procedure by intraperitoneal injection with saline (0.5 ml /rat) for 2 days before ghrelin administration then ghrelin was received intraperitoneally at a dose of 10 nmol/ day dissolved in 0.5 ml saline during the 5th week (Alison et al., 2001).

Standard diet was composed of fat 5% (corn oil 5%), carbohydrates 65 % (corn starch 15% and sucrose 50%), proteins 20.3% (casein 20 % and DL methionine 0.3 %) fiber 5%, salt mixture 3.7% and vitamins 1% (Davidson et al., 2012).

High fat diet was composed of 20% fat [19% butter oil and 1% soybean oil] (Yang et al., 2015). Rats were allowed HFD for 5 weeks during which body weight measured every week.

Chemicals used: Pancreatic polypeptide YY₃₋₃₆ was obtained from Sigma Aldrich USA Ghrelin powder was obtained from Sigma Aldrich USA.

The body weights were measured at the first day before initiation of administration, and weekly from initial administration day to termination day using an automatic electronic balance (Precisa Instrument, Switzerland). At initiation and termination days, all experimental animals were fasted overnight (water was provided; about 12 h) to reduce any differences from feeding. At sacrifice, the weights of fat pads of the liver and kidney were measured, and relative body weight was calculated using the body weight and the absolute organ weight according to the formula (absolute organ weight/body weight) × 100 (Chung et al., 2013).

Lee index was used to determine obesity in rats using body weight and naso-anal length. It was measured at the beginning of the study and after 4 and 5 weeks. Lee index equals cube root of body weight x10/naso-anal length. Obesity was considered if Lee index >0.3 (Novelli et al., 2007).

At the end of 5 weeks, rats were sacrificed after an overnight fasting by decapitation, and blood samples were collected. These were allowed to clot at room temperature, and then centrifuged at 3000 rpm for 15 minutes in Hettich centrifuge. Serum was then withdrawn

into identified Eppendorf tubes, and stored at – 20 °C for biochemical assay.

The head was dissected, then the brain was removed and the hypothalamus was isolated for determination of neuropeptide Y (NPY) concentration. The hypothalamus was homogenized by ultrasonic in 500µl of 0.5 mol/L acetic acid (El Nasser Pharmaceutical Chemical Company) completed to 1000 ml by adding distilled water, then the tissue was centrifuged at 10000 rpm for 10 min. at 4 °C . Determination of hypothalamic NPY: the NPY immunoassay kit (Sigma Aldrich USA- cat No RAB0387) is an in vitro quantitative assay based on the principle of competitive enzyme immunoassay (Kuo et al., 2007).

- Serum ghrelin was measured using the commercially available kit (Linco Research Inc. St. Charles, 63304 MO and USA) (Peterli et al., 2009).
- Total serum cholesterol was measured using enzyme assay system (Bio-diagnostic EGYPT-CAT. NOCH 12 20) (Richmond, 1973).
- Serum triglycerides were measured using enzyme assay system (Bio-diagnostic EGYPT-CAT. NO CH 20 30) (Fassati and Prencipe, 1982).
- Serum LDL cholesterol was measured using enzyme assay system (Bio-diagnostic EGYPT-CAT. No CH 12 31).
- Serum HDL cholesterol was measured using Spekol 11 spectrophotometer (Wieland and Seidel, 1983).

Statistical analysis was conducted using SPSS for Windows (Release 6.1.3., SPSS Inc., and Chicago, IL, USA). All values

were expressed as mean ± SD. One way ANOVA was used for the statistical analysis, and Fischer’s LSD as a post hoc test using Sigma Stat 3.5 (Systat Software, Richmond, VA, USA). The data were analyzed followed by multi-comparison test. Significant difference was considered when P value was less than 0.05.

RESULTS

Body weight changes in different groups:

The mean of the initial body weights were insignificant among different groups at the beginning of the study in both sex. High fat diet caused significant increase in body weight from the second week till the

5th week as compared to the control groups. Administration of PYY caused significant decrease in body weight compared to HFD, whereas, ghrelin injection caused significant increase in body weight compared to HFD in all groups. There was significant increase in body weight in ghrelin treated group in comparison to PPY treated group.

There was no significant difference in body weight between males and females at the beginning of the study in all groups, but at the end of 4th and 5th weeks, the body weight was significantly lower in females as compared to males in all groups (Table 1).

Table (1): Differences in body weight (mean ± SD) between male and female in all groups.

Group \ Body Weight	Control		HFD		HFD, PYY treated		HFD, ghrelin treated	
	♂	♀	♂	♀	♂	♀	♂	♀
Initial	187±1.2	189±1.7	186±2.1	188±1.8	186±2.3	187±1.8	178±2.1	189±1.6
1 st week	203±2.5	201±2.4	207±2.8	205±4.1	208±3.03	206.5±1.8	208±1.2	209±1.9
2 nd week	220±0.8	214±2.7	231±2.2@	221±1.8@	230±1.6@	223±1.2@	234±2.3@	227±0.9@
3 rd week	224±0.7	215±2.8	232±1.1@	224±2.1@	233±1.5@	225±1.05@	237±1.4@	228±1.2@
4 th week	225± 1.3	216±1.4 ^c	235±3.1@	226±3.4@ ^{\$}	236±2.7@	226±1.4@ ^Y	238±3.3@	230±2.3@ ^g
5 th week	228±2.3 [#]	218±3.3 ^{#c}	237±1.6@ [#]	227±0.9@ ^{##}	230±2.4 ^{##}	221±2.1 ^{##Y}	243±1.7@ ^{##*}	235±0.8@ ^{##g*}

@ Significant difference from control group of same sex.
 f Significant difference from HFD group of same sex.
 # Significant difference from the initial value.
 c Significant difference compared to control male group.
 \$ Significant difference compared to HFD male group.
 Y Significant difference compared to HFD PYY treated male group.
 g Significant difference compared to HFD ghrelin treated male group.
 * Significant difference compared to HFD PYY treated group of the same sex.

Lee index changes in different groups:

Lee index in control rats at the end of the experiment was less than 0.3 (non

obese). HFD rats had Lee index higher than 0.3 at the 4th and 5th week, and were considered obese, in which Lee index

significantly increased compared to control groups. Injection of PYY at 5th week did not decrease the Lee index below 0.3 and rats still obese. The value of Lee index in PYY treated rats was significantly decreased as compared to HFD groups and non significant as compared to control groups. The lee index was significantly higher in ghrelin treated groups at the end of 5th week as compared

to control groups. There were no significant differences in Lee index between males and females were observed at the beginning of the study up to the 4th week in all groups. At the end of 5th week the Lee index was significantly lower in HFD females than males with non significant differences between males and females in other groups (Table 2).

Table (2): Differences in lee index (mean \pm SD) between male and female in all groups.

Groups Lee Index	Control		HFD		HFD, PPY treated		HFD, ghrelin treated	
	♂	♀	♂	♀	♂	♀	♂	♀
Initial	0.289 \pm 0.002	0.287 \pm 0.005	0.291 \pm 0.003	0.268 \pm 0.007	0.290 \pm 0.002	0.289 \pm 0.003	0.288 \pm 0.001	0.287 \pm 0.006
4 th week	0.2914 \pm 0.001	0.291 \pm 0.003	0.312 \pm 0.007 [@]	0.310 \pm 0.005 [@]	0.314 \pm 0.004	0.290 \pm 0.001	0.327 \pm 0.008	0.324 \pm 0.002
5 th week	0.293 \pm 0.003	0.292 \pm 0.001	0.316 \pm 0.003 [@]	0.311 \pm 0.002 [@] ^{\$}	0.315 \pm 0.006 ^f	0.308 \pm 0.006 ^f	0.329 \pm 0.003 ^{@f}	0.325 \pm 0.004 ^{@f}

@ Significant difference from control group of same sex.

f Significant difference from HFD group of same sex.

\$ Significant difference compared to HFD male group.

Lipid profile changes in different groups.

In HFD group, there was significant increase in serum level of TC, LDL-c and TGs with a significant decrease in serum level of HDL-c as compared to control group of same sex. Injection of PYY had no significant effect on serum lipid profile in comparison to HFD group. In ghrelin treated group the serum level of TC, LDL-c and TGs were significantly higher than the control group with a significant lower serum level of HDL-c but no significant

difference compared to HFD or PPY treated groups of same sex.

In females control group, there was significant higher level of HDL-c as compared to males with insignificant differences in serum level of TC, TGs, and LDL-c. In HFD, HFD PYY treated group and HFD ghrelin treated groups, the serum level of TC and TGs were significantly lower in female groups compared to male groups associated with non significant changes in LDL-c and HDL-c serum level between males and females (Table 3).

Table (3): Differences in lipid profile (mean ± SD) between male and female in all groups.

Lipid profile \ Groups	Control		HFD		HFD, PPY treated		HFD, ghrelin treated	
	♂	♀	♂	♀	♂	♀	♂	♀
TC (mg/dl)	132.4± 2.4	134.7±1.5	157.1±1.4 [@]	140.1±0.7 ^{@\$}	152.9±2.6 [@]	139.1±0.3 ^{@Y}	156.8±0.7 [@]	140.1±2.6 ^{@g}
TGs (mg/dl)	96.2±0.8	97.2±1.3	166.8±2.3 [@]	129.7±2.4 ^{@\$}	165.8±1.5 [@]	128.1±3.7 ^{@Y}	167±1.2 [@]	128.3±3.2 ^{@g}
LDL-c (mg/dl)	69.1± 1.3	66.9±0.8	74.±0,4 [@]	72.8±±1.2 [@]	73.1±0.9 [@]	70.2±1.3 [@]	75.1 ±0.8 [@]	73.6±0.9 [@]
HDL-c (mg/dl)	47.1±0.6	57.1±1.6 ^C	37.6±0.9 [@]	39.7±0.6 [@]	38.4±0.7 [@]	38.6±0.8 [@]	39.2±1.5 [@]	38.9±1.3 [@]

@ Significant difference from control group of same sex.
 c Significant difference compared to control male group.
 \$ Significant difference compared to HFD male group.
 Y Significant difference compared to HFD PPY treated male group.
 g Significant difference compared to HFD ghrelin treated male group.

Hypothalamic NPY and S. Ghrelin changes between different groups:

The hypothalamic NPY significantly decreased in HFD groups compared to control groups. Injection of PYY caused a significant lower in hypothalamic NPY level in HFD-PYY treated group as compared to control group. In ghrelin treated HFD groups there were significant increase in hypothalamic NPY compared to HFD groups. The female control groups showed significant lower in the hypothalamic NPY concentration as compared to males with no significant difference in HFD group, PPY treated group and ghrelin treated group.

There was significant increase in serum ghrelin level in HFD groups as compared to control groups. Injection of PYY caused a significant lower in serum ghrelin level in HFD -PYY treated group as compared to HFD group, while in ghrelin treated HFD groups there were significant increase in serum ghrelin level as compared to HFD groups and HFD -PYY treated group. Ghrelin concentration was significantly lower in females as compared to males in control groups, with no significant difference in HFD group, PPY treated group and ghrelin treated group between males and females (table 4).

Table (4): Differences in Hypothalamic NPY S. Ghrelin (mean ± SD) between male and female in all groups.

Hormones \ Groups	Control		HFD		HFD, PPY treated		HFD, ghrelin treated	
	♂	♀	♂	♀	♂	♀	♂	♀
Hypoth.NPY (pg/ml)	21.8± 0.6	17.1±0.8 ^c	13.5±1.2 [@]	13.3±1.7 [@]	10.3±0.9 [@]	10.3±0.7 [@]	22.3±0.4 ^{f*}	21.5±0.6 ^{f*}
S. Ghrelin (pg/ml)	301±1.4	263±0.7 ^C	342±0,3 [@]	317±1.1 [@]	294±0.9 ^f	281±2.1 ^f	398±1.7 ^{f*}	371±2.1 ^{f*}

@ Significant difference from control group of same sex.
 f Significant difference from HFD group of same sex.
 c Significant difference compared to control male group.
 * Significant difference compared to HFD PPY treated group of the same sex.

DISCUSSION

Body weight is known to be regulated by many mediators and regulatory pathways in the brain and periphery (**Natalie and Hans-Rudolf, 2009**). Sex differences in eating behavior are well documented. The development of diet-induced obesity in males and females might be mediated by distinct mechanisms warranting different treatment approaches. In previous studies, a high sucrose diet induced excessive weight gain in female but not in male Sprague-Dawley rats (**Olga et al., 2011**). Many peptides, including NPY, orexin, melanin-concentrating hormone, α -MSH, CRF, and leptin, have been shown to affect energy balance (**Carmen et al., 2014**).

Our study was designed to detect sex differences in HFD induced obesity in rats. Induction of obesity was performed through feeding with HFD for five weeks and the role of PPY and ghrelin in adult male and female albino rats. The occurrence of obesity was confirmed by the lee index where lee index ≥ 0.3 indicated obesity (**Long et al., 2015**). Our results revealed that HFD induced significant increase in body weight and this agreed with **Sour et al., 2015**. The mechanisms of increased body weight involved fat accumulation and this was compatible with the study of **Miras et al. (2014)**. Furthermore, in control groups, the body weight and hypothalamic NPY concentration were significantly higher in males than females associated with significantly lower serum level of HDL-c. This was explained by **Renato Pasquali, (2012)** who stated that the higher

hypothalamic NPY concentration in males may be related to different sex hormone because testosterone has stimulatory effect. The difference in sex hormones may also be the cause of higher HDL-c in females, due to the protective effect of estrogen which causes higher HDL-c level (**Ihedioha et al., 2013**). Another study detected that normal androgen level in males were found to have suppressive effect on HDL-c (**Vodo et al., 2013**).

Previous study detected that NPY dysfunction may lead to decrease in Y1R gene expression. In addition, the decreased expression of Y1 receptors was only observed in male mice suggesting the susceptibility of male mice to develop obesity. However, the hypothalamic NPY mRNA increase /or remain unchanged in diet induced obesity dependant on genetic background (**Zammaretti et al., 2007**).

In the current study, the intake of HFD also caused hyperlipidemia as evident by significant increase in TC, TGs and LDL-c and significant decrease in HDL-c in comparison to control groups. This was in agreement with **Zhukova et al. (2014)**. These disturbances in lipid profile could be attributed to greater visceral fat accumulation. The reduction in HDL -c with HFD may be due to hypertriglyceridemia, because the hepatic lipase hydrolyses the TG of HDL-c and, due to the very small size, the HDL particles can be filtered in the kidney (**Klop et al., 2013**).

Peripheral administration of PYY after induction of obesity significantly lowered body weight, Lee index and hypothalamic NPY. This was in agreement with

Mittapalli and Roberts, (2014). Within the CNS, PYY exerts its anorectic effect via actions in ARC hypothalamic nucleus. The ARC nucleus is in close to the BBB deficient area of the median eminence of the hypothalamus. This allowed that region to respond rapidly to the released gut hormones in the circulation including PYY (**Bougszewsk and van der Lely, 2015**). The broad distribution of the Y receptor subtypes both centrally and peripherally with the antagonistic effects of stimulation of different subtypes and the fact that PYY could act both centrally and peripherally. The higher hypothalamic NPY concentration in males may be the cause of increased food intake and body weight in males (**Lalitha et al., 2014 and Fukushima et al., 2015**).

However, another study showed that food intake was equal in both sexes (**Hwanq et al., 2010**). On contrary, a study reported that food intake was higher in males than female with no difference in weight (**Ohta et al., 2014**). On the other hand, previous study reported that there was an insignificant difference in serum lipid profile in both sexes (**Choi et al., 2012**). These different results may be related to different strains of used rats.

In our study, concerning the HFD groups, body weight, lee index, TC; TGs were significantly higher in males than females. Previous studies suggested that HFD may alter endogenous sex hormones metabolism in males (**Silva, 2014**). Certain study reported that plasma estradiol was increased in females with HFD (**Fuente et al., 2013**).

Our results showed that ghrelin injection after HFD induced obesity caused significant increase in body weight, serum lipid profile compared to PPY treated HFD group. This could be explained as Ghrelin mediated its orexigenic action via stimulation of NPY/agouti-related peptide (AgRP) coexpressing neurons within the ARC of hypothalamus. Peripheral administration of ghrelin increases c-fos expression in the ARC NPY/AgRP neurons, and ablation of both AgRP and NPY neurons completely abolishes the orexigenic effect of ghrelin (**Chen et al., 2004**) Both central and peripheral administration of ghrelin increase food intake and body weight along with a reduction in fat utilization in rodents (**Anthony et al., 2007**).

CONCLUSION

HFD induced obesity and weight gain, and Lee index had gender differences all of them were higher in male rats than females. PYY administration caused significant decrease in body weight and lipid profile in both sexes. On the other hand, adiposity increased after systemic ghrelin administration.

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دور الجريلين وبروتينات البنكرياس في حدوث السمنة الناتجة عن نظام غذائي عالي الدهون في الجرذان البيضاء البالغة

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خلفية البحث : تطور السمنة التي يسببها النظام الغذائي في الذكور والإناث يمكن أن تتم عن طريق آليات متنوعة. ولذلك ، فإن فهم الآليات الجزيئية الرئيسية المشاركة و المتسببة في السمنة يمكن أن تكون مفيدة لوضع نهج علاجي لهذه السمنة.

الهدف من البحث: تقييم ما إذا كانت السمنة المسببة نتيجة ارتفاع الدهون في النظام الغذائي المرتفع الدهون مختلفة بين الجنسين والتأثير المحتمل لبيبتيدات البنكرياس وهرمون جريلين على السمنة التي يسببها ارتفاع الدهون في الجرذان البيضاء.

مواد وطرق البحث : تم تقسيم الجرذان إلى ٤ مجموعات متساوية (العدد = ١٦ لكل مجموعة) ، و تم تقسيم كل مجموعة إلى مجموعتين فرعيتين من الذكور والإناث: المجموعة الأولى (مجموعة ضابطة)، والمجموعة الثانية (الجرذان ذات نظام غذائي عالي الدهون)، والمجموعة الثالثة (الجرذان ذات نظام غذائي عالي الدهون ومعالجة ببيبتيدات البنكرياس بجرعة ٥٠ ميكرو جم/ كغ مرتين يوميا عن طريق الحقن فى البطن داخل البريتون) ، والمجموعة الرابعة (الجرذان ذات نظام غذائي عالي الدهون ومعالجة بجريلين بجرعة من ١٠ نانومول / كغ عن طريق الحقن فى البطن داخل البريتون).

النتائج: لوحظت فروق ذات دلالات إحصائية بين الجنسين في تطوير البدانة باستخدام نظام غذائي مرتفع الدهون في نهاية الأسبوع الرابع والخامس، حيث كان ارتفاع وزن الجسم أقل لدى الإناث مقارنة بالذكور. كما أدى استخدام ببيبتيدات البنكرياس إلى انخفاض ملحوظ في وزن الجسم بالمقارنة مع الجرذان ذات نظام غذائي عالي الدهون، في حين أدى استخدام الجريلين إلى زيادة كبيرة في وزن الجسم بالمقارنة مع الجرذان ذات النظام الغذائي عالي الدهون في جميع المجموعات.

الاستنتاج: على الرغم من التشابه في استجابات المخ للجوع والشبع بين الذكور والإناث، فقد أظهرت الدراسة اختلافا بين الجنسين في تطور البدانة والزيادة في وزن الجسم. كذلك ثبت أن استخدام ببيبتيدات البنكرياس خفض السمنة التي يسببها النظام الغذائي عالي الدهون، في حين زاد استخدام الجريلين من درجة السمنة. وتوضح هذه الدراسة دور كل من ببيبتيدات البنكرياس والجريلين في السيطرة على وزن الجسم وتوازن الطاقة سواءً بالنقص أو بالزيادة.