The Effect of Sweet-tasting Foods Addiction on Appetite-related Hormones among Obese Adolescents

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ABSTRACT

Background: Food ingestion and energy spending are organized through a complicated neurological system that involves both hypothalamic centers and peripheral satiety regulation (gastrointestinal and pancreatic hormones).

Objectives: To assess the effects of sugar addiction on appetite-related hormones and metabolic hormones.

Materials and methods: The study was done in two main hospitals in Anbar governorate, Iraq from April 2020 to November 2020. Concentration of fasting blood glucose (FBG), insulin, hormone insulin resistance (HOMA-IR), leptin, ghrelin, lipid profile, TSH, T3, and T4 were measured in the 54 obese adolescents and were compared with 54 normal-weight adolescents.

Results: There was a significant increase in the concentrations of FBG, insulin, HOMA-IR, leptin, total cholesterol (TC), triacylglycerol (TAG), low-density lipoprotein cholesterol (LDL-C), and TSH in obese adolescents as compared to normal-weight adolescents (P-value <0.05). While there was a significant (P < 0.05) decreased in the concentrations of ghrelin, high-density lipoprotein cholesterol (HDL-C), T3, and T4 in obese adolescents compared with normal-weight adolescents. The results also showed that there is a significant positive correlation between the concentration of leptin and each of BMI, FBG, insulin, and HOMA-IR, while there was a significant negative association between leptin level with HDL-C and ghrelin.

Conclusion: Sweet-tasting meals are a major source of stimulation, which leads to overeating and thus leads to obesity.

Keywords: Leptin; Ghrelin; Sugar; Obesity; Adolescents; Insulin resistant.

INTRODUCTION

Sweet, bitter, salty, sour, and umami (taste of glutamate or amino acids) are the five taste categories in humans, in addition to the sixth taste, which is fatty acids, this fact supporting by strong evidence of the previous study [1]. Sugar is a public idiom use to characterize a dissolvable category of molecules named carbohydrates which gives a sweet taste when be eaten. Sugar can be obtained from a variety of sources, including natural sweeteners (glucose, fructose, sucrose, and maltose), artificial sweeteners (saccharin, aspartame, and cyclamate), sweet amino acids (D-tryptophan, D-phenylalanine, and D-serine), and sweet proteins (monellin, brazzein, and thaumatin) [2].

Sweet foods include gooey cookies, crisp sweets, velvety cakes, as well as ice cream-filled waffle cones. They can be found in a wide range of foods and beverages, including high-fructose corn syrup, fruit juice, raw sugar, and honey. In addition to candies and sweets, sugar also is found in a range of meals, including tomato sauce, yogurt, dried fruit, flavored drinks, and granola bars [3]. Our sense of taste is a primary predictor of our like for sweet foods and their excessive consumption. The detection of sweet foods provides information on caloric and macronutrient contents ingested in foods. Sweet tastes are detecting by stimulating taste receptors in the tongue. Sweet-taste receptors are expressed not only in the mouth but also in a variety of non-taste organs such as the gastrointestinal system, pancreas, bladder, and adipose tissues. The brain receptors direct a signal up to several areas of the forebrain, so, stimulate a brain's reward system [4].

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Reward system (dopamine movement) is a mysterious idiom that involves at least three factors hedonics (liking), reinforcement (learning), and motivation (wanting). Reflecting on this idea, both short- and long-term sugar intake impacts gene expression and neuroplasticity in the brain [5]. The mesocorticolimbic distribution of dopaminergic neurons is part of this pathway. The prefrontal cortex (PFC), amygdala (AMG), ventral tegmental area (VTA), and nucleus accumbens are the neuronal areas of the reward system [6], as shown in Figure 1.

The reward pathway is closely related to the flow of dopamine, which is the main currency of the reward system. The importance of dopamine lies in maintaining the motivational state or desire for a particular behavior or substance (for example drugs, sexual behavior, social media, or food). This pathway could be overstimulated through candy or drug [7].

Bodyweight is controlling via a complex system involving genetic and peripheral agents in addition to hormones. Leptin and ghrelin are two hormones that have crucial role in the organization of food ingest and body weight, as well as it affects dopaminergic transition in brain reward areas and food-seeking behavior in animals and stimulates brain reward areas in the humans [8]. Leptin is a hormone that plays an important role in the energy consumption and regulation of its consumption, which means leptin is a moderator of the long-term regulation of energy balance [9]. Leptin is also known as the hunger or satiety hormone; because it is the hormone responsible for sending some notifications to the brain that the individual is feeling full, and that he has taken the sufficient amount of calories that his body needs. Or to work in reverse, that is, the individual still needs more calories [9]. The gastrointestinal tract secretes the hormone ghrelin when the stomach is empty, indicating that the body needs food (energy), then this hormone travels through the blood to the hypothalamus in the brain to cause hunger and enhance the desire to intake food, causing a person to consume more calories. The lateral hypothalamus understands the metabolic balance through glucose, ghrelin, and leptin concentrations [10].

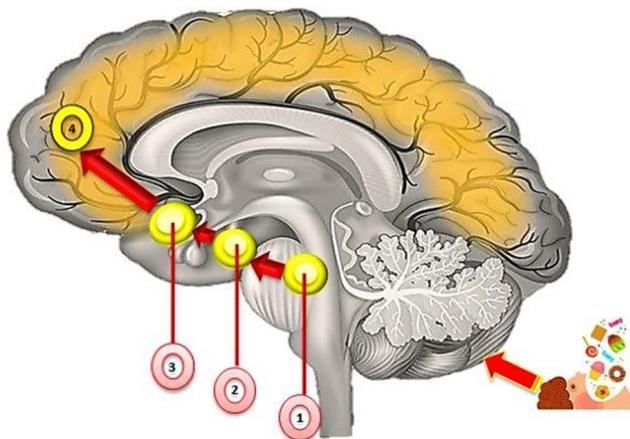To our best knowledge, there are no local studies that tackle

Figure 1. Reward pathway (Dopamine movement) including 1-Ventral Tegmental Area (VTA), 2-Amygdala (AMG), 3-Nucleus Accumbens (NAc), 4-Prefrontal Cortex (PFC).

the effect of sweet-tasting foods addiction on appetite-related hormones among obese adolescents, hence the current study was performed. We aimed to investigate the effect of sugar addiction on appetite-related hormones and metabolic hormones.

MATERIALS AND METHODS

Participants

This cross-sectional comparative study was conducted in the two main hospitals in the Anbar governorate, Iraq (Maternity and Children Teaching Hospital and Al-Ramadi Teaching Hospital in Ramadi city). The study was covered the period from the 1st of April 2020 to the end of November 2020. A total of 84 subjects, 54 (27 boys and 27 girls) obese and 54 (27 boys and 27 girls) normal-weight adolescents were enrolled in this study. The individuals participating in the study were close to the ages from 11-17 years. People who participate in any active exercise and who follow a healthy diet were excluded. Also, those who suffer from heart disease, diabetes, renal disease, and pituitary or thyroid gland diseases.

The Ethical Approval Committee of the Anbar Health Directorate was approved in the present study. Informed consent was taken from all individuals.

Studying food behavior

The questionnaire was included questions based on the dietary habits of adolescents aged 1117 years. The questionnaire was included the following questions:

1. How many meals do you usually consume daily?
2. What types of food do you usually consume during the weekdays?
3. How many servings for every type of food that consumed per week?

Food frequency consumption for 21 products and 6 beverages are: high-fat foods group (Cream cheese, French fries, Corn Chips), sweet foods group (Chocolate cake, Candy, Chocolate Cookies, Ice cream, Pancake, Doughnut), carbohydrates/starches group (Whitebread, Pasta, Rice), fast foods group (Burger, Pizza, Fried chicken), fruit and vegetables group (Banana, Apple, Orange, Date, Strawberry), soft drinks, juice, and sweet drinks group (Coca-Cola, 7-Up, Soda, Fanta Strawberry, Rani orange, Original orange drink) were with the following responses and scores: from 3 - 16 times a week (Figure 2).

The mean daily calorie consumption or energy intake was calculated based on Nutritional Guidelines for Americans (2015) (https://hnrca.tufts.edu/myplate/tips-extra-info/2015-dietary-guidelines-for-americans/), which be made up13 subcomponents that produce a total score of 0 to 100, with a higher number indicating better dietary quality.

Methods

The bathroom scale and height measuring tape were used to estimate the anthropometric measurements, which involved estimating both weight and height and were estimated to the nearest 0.1 kg cm or 0.1 cm, respectively. Obesity is defined as a body mass index (BMI) percentile more than or equal to the 95th percentile, while overweight is defined as a BMI percentile greater than or equal to the 85th percentile, according

Table 1. WHO classification of the BMI [11]

Classification	BMI (kg/m^2)	Risk of comorbidities
Underweight	<18.5	Low (but the risk of other clinical problems increased)
Normal range	18.524.9	Average
Overweight (pre-obese)	25.029.9	Mildly increased
Obese	$\geq$ 30.0	
Class I	30.034.9	Moderate
Class II	35.039.9	Severe
Class III	$\geq$ 40.0	Very severe

Figure 2. The number of servings for every type of food per week that consumed by obese adolescents.

to WHO guidelines for adult obesity data. BMI was calculated according to the formula (CDC Growth Charts, 200), and classifying the individuals as shown in Table 1.

$$BMI(kg/m^2) = \text{Body weight (kg)/ height}(m)^2$$

RESULTS

Concentrations of serum leptin were estimated by DRG (ELISA kit) [12]. Ghrelin hormone was measured used ELIZA kit from Phoenix Pharmaceuticals, INC an in vitro quantitative assay). Using the Randox Diagnostic kit, the lipid profile total cholesterol (TC), triacylglycerol (TAG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were estimated. The enzymatic colorimetric method (GOD-POD) was used to determine fasting blood glucose (FBG), while insulin concentration by a commercially available DRG ELISA kit. Serum T3, serum T4, and serum TSH were measured by ELISA kit. The homeostasis model assessment (HOMA-IR) was used to determine the degree of insulin resistance; the resistance can be calculated from the fasting glucose and insulin concentrations by the below formula:

(HOMA-IR) = [fasting insulin (μ U/ml) $\times$ fasting glucose (mg/dl)]/405

(The constant 405 should be replaced by 22.5 if glucose is expressed in S.I. units).

Statistical Analysis

The data were analyzed by SPSS version 18 (Statistical Package for the Social Sciences). student t-test was used to compare the mean values in comparison groups. The correlation coefficient (r) testwas used to describe the association between the variables studied parameters. P< 0.05 was considered statistically significant.

Figure 2 showed the question responses on the questionnaire, which there were high cravings on sweets, carbohydrates/starches, soft drinks, sugar-sweetened drinks and fast foods, high-fat foods, and that did not include fruit/vegetable cravings.

Table 2 summarized the characteristics of the obese and normal-weight adolescent groups. Body mass index (BMI), fasting blood glucose (FBG), insulin, HOMA-IR, leptin, total cholesterol (TC), triacylglycerol (TAG), low-density lipoprotein cholesterol (LDL-C), TSH, and energy intake were significantly (P<0.05) increased in obese adolescents when compared to the normal-weight adolescents, whereas there was a
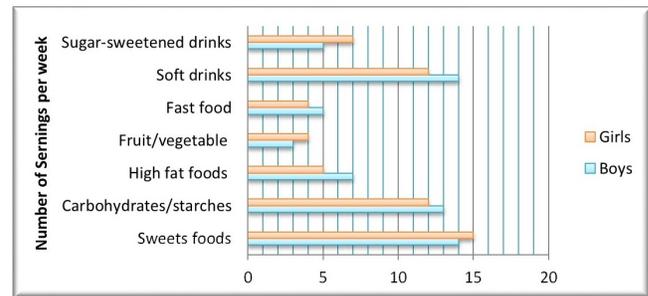
significant decrease in the concentration of ghrelin and high-density lipoprotein cholesterol (HDL-C), T3 and T4 serum in adolescents obese when compared with the normal-weight adolescents.

In addition, there were no significant (P<0.05) differences between boys and girls who are obese and of normal-weight adolescents for all the mentioned characteristics, as shown in table 2. Except for leptin levels, there was a significant (P<0.05) increase in leptin levels in females when compared to males in both cases.

DISCUSSION

A complex brain network controls food intake and energy expenditure, and the hypothalamus has been recognized as the axis of homeostatic organization. Therefore, Sweet-tasting foods can compromise normal appetite regulation. Sweet-tasting foods alter appetite management and inducing pleasure and reward resulting in excessive ingestion of appetizing energy-dense food. Thereafter, a deep state of reward hyposensitivity, similar to that seen in drug abuse, can lead to overeating [13]. This is consistent with the behavior of obese adolescents in this study.

The present study demonstrated a statistically increased FBG, Insulin, and HOMA-IR levels in obese adolescents in comparison to the normal-weight adolescents, these results were consistent with the study done by Arcidiacono and his colleagues [14]. The high levels of FBG, insulin, and HOMA-IR, as was observed in obese adolescents, may increase food cravings instead of suppressing them. Also, this leads to stimuli in dopamine reward areas like the ventral tegmental area (VTA), nucleus accumbens, and dorsal striatum [15].

Insulin resistance occurs due to obesity and thus increases insulin levels in the blood, and overtime and continued weight gain leads to a decrease in insulin sensitivity and thus weakens the pancreatic β-cell function [16].

Addiction to sweet-tasting foods leads to overproduction of intrahepatic trioses-phosphate, which is firstly responsible for the development of hepatic insulin resistance (IR), intrahepatic fat aggregation, and elevated blood triglyceride concentrations. Over time, these effects might leads to the expansion of cardiovascular diseases and obesity [17].

Researches have mentioned that consuming a high amount of sweet-tasting foods leads to minus energy reparations for its failure to decrease suitable homeostatic replies in satiety and appetite hormones. These hormonal responses are very coordinated [18]. They either inhibit the intake of more energy into the body such as leptin or increase the entry of

Table 2. Comparison of all variables between obese and normal-weight adolescents (Mean $\pm$ SE)[*].

Variables	Obese Group (n = 54)		Normal Group (n = 54)		P-value
	Male	Female	Male	Female	
Age	12.54±0.65	13.09±	13.19±0.23	13.98±0.43	N.S
BMI (Kg/m^2)	32.25±0.43	34.7±0.26	22.1±0.41	23.32±0.44	0.0001
Kilocalories	2,221±0.12	2,189±0.42	1,315±0.39	1,309±0.21	0.001
FBG (mg/dl)	105.76±0.37	110.54±0.61	91.43±0.32	93.43±0.17	0.009
Insulin (μU/ml)	15.43±0.55	18.01±0.62	6.71±0.71	5.98±0.68	0.001
HOMA-IR	4.01±0.54	4.89±0.43	3.54±0.51	3.64±0.30	0.001
Leptin (ng/ml)	28.91±0.13	36.41±0.11	19.01±0.29	24.43±0.91	0.0001
Ghrelin(pg/ml)	447.14±0.60	450.25±0.16	557.3±0.33	570.89±0.19	0.001
TC (mg/dl)	188.56±0.22	185.11±0.19	172.98±0.61	177.6±0.55	0.001
TAG (mg/dl)	149.43±0.12	150.11±0.91	130.81±0.28	131.54±0.45	0.001
HDL-C (mg/dl)	40.32±0.34	42.63±0.43	55.81±0.13	56.11±0.34	0.004
LDL-C (mg/dl)	104.28±0.63	102.47±0.26	70.77±0.70	72.69±0.21	0.008
T3 (ng/ml)	1.05±0.23	0.99±0.31	1.16±0.54	1.14±0.18	0.001
T4(μg/dl)	5.03 ±0.87	5.24±0.92	7.54±0.44	7.32±0.31	0.001
TSH(μIU/ml)	2.71±0.63	2.51±0.69	1.61±0.43	1.59±0.37	0.0001

[*] P-value < 0.05 is significant, SE: Standard Error , N.S: NotSignificant

energy into the body, such as ghrelin by sending messages to the hypothalamus and brain stem regarding obesity and an acute nutritional condition [19].

In the current study, obese adolescents were showed a significant increase in leptin levels, with a higher level in the girls than boys. These results were similar to a prior study by Tajiri and his colleagues [20]. Numerous scientific studies have proven that leptin levels increase with puberty. Therefore, girls often reach puberty nearly two years before boys. Besides, the results were showed that in normal-weight adolescents, the leptin levels in boys were lower than in girls, this might be partially described through the suppressive effects of the androgen [21].

In physiological situations, normal leptin end food ingestion through stimulation of anorexigenic neurons. It is implicated in immune processes, reacts with the sleep-wake cycle, and regulates sexual conduct side by side with genital function. Raise in leptin levels has been connected with weight gaining produced by non-nutritious foods rich in calories [22].

There is a problem in obese individuals, which is the leptin secretion increases. This increase is unable to link to its receptor. The brain in this process is unable to understand that the body has an excess of fat, resulting in fat accumulation and leads to obesity [23]. This condition is named leptin resistance and appears as a main biological anomaly in the obese status. This result was in agreement with a previous study [24].

Obesity is linked to several negative changes in lipid metabolism, including a significant increase in serum total cholesterol, LDL, and TG, as well as a significant decrease in serum HDL concentrations, findings of the current study, were similar to the study by Lonnie [25].

Hypertriglyceridemia is frequently linked to lower HDL levels, implying a metabolic connection between these two lipid types. The key to this relationship could be that the increase of fat deposition in obese individuals is linked to insulin resistance, which leads to increased TG-rich lipoprotein production in the liver [26].

A possible explanation for the low ghrelin concentration in obese adolescents is a contest between the agents that increase ghrelin concentration (insulin deficiency) and agents that decrease ghrelin concentration (obesity, glucose, and hyperinsulinemia), What confirms this explanation is the high rate of insulin resistance in obese adolescents in the results of this study and another study [27].

Thyroid hormones (T3 triiodothyronine and T4 thyroxine) act on nearly every cell in the body. They act as regulatory agents, are involved in energy balance, increasing the basal metabolic rate and lipolysis, regulate the metabolism of protein, carbohydrates and vitamins, and suppress the thyroid-stimulating hormone (TSH) concentrations [28]. The levels of the thyroid hormones (T3 and T4) were significantly lower in the obese group than the control group, while the reverse was true regarding the TSH. As a result of the TSH elevation, there is an increment in the cardiovascular risk. Similar findings were detected by Ozcelik et al. [28].

Food control is a complicated mechanism including the organism's appetite, motivation, and energy demands, all of which are influenced by food availability [29]. The central nervous system detects several peripheral neuronal and humoral indicators. The endocrine and hormonal inputs are received by this complex neural network. Hormones, like leptin, insulin, and ghrelin coordinate food ingestion by notices and amendments in orexigenic and anorexigenic neurons. In turn, these cues, including taste (the key factor in making decisions about feeding behavior, and the olfaction), reflect both the functions of the digestive system and the body's energy needs [30].

There is more intake of the sources and levels of sweet-tasting food in the urban than rural dwellers. However, the current study didn't consider this variance and this was considered as one of the shortcomings of the study. Besides, the study did not compare between the sexes regarding the consumption of sweet-tasting food. Lastly, the sample size was small due to a lot of cases were refused to participate in the study.

CONCLUSION

The results of the present study indicated that there was an increase in leptin, FBG, insulin, HOMA-IR, lipid profile

excepted HDL and TSH level in the obese adolescent group. While there was a decrease in ghrelin, T3, and T4 hormone levels when compared with non-obese ones.

RECOMMENDATION

We need to perform further studies to gain a better understanding of the brain circuit mechanisms underlying the

vitally important topic of eating regulation, which is crucial to human health.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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