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Positive correlation of galanin with insulin resistance and triglyceride levels in obese children

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Background/aim: Galanin is a neuropeptide that is shown to be involved in the regulation of food intake and glucose homeostasis. The objective of this study was to evaluate the relation of serum galanin levels with anthropometric and metabolic parameters in obese and healthy children.

Material and methods: The cross-sectional study consisted of 38 obese children (mean age: 11.9 ± 3.0 years) and 30 healthy children (mean age: 11.4 ± 2.0 years). Clinical and biochemical parameters [glucose, insulin, homeostasis model assessment-insulin resistance (HOMA-IR), lipids, galanin, and leptin levels] were assessed.

Results: Serum galanin and leptin levels were significantly higher in obese children. In obese children, galanin levels were positively correlated with fasting glucose ($r = 0.398$, $p = 0.013$), insulin ($r = 0.383$, $p = 0.018$), HOMA-IR ($r = 0.375$, $p = 0.020$), and triglycerides ($r = 0.391$, $p=0.015$). Multivariate backward regression analysis revealed that galanin levels were significantly associated with fasting glucose, insulin, HOMA-IR, and triglyceride, which explained 42.0% of the variance ($r^2 = 0.483$, $P < 0.001$).

Conclusions: Serum galanin levels were significantly higher in obese children than healthy controls and positively correlated with insulin resistance and triglycerides in obese children. This study suggests that galanin is associated with glucose homeostasis and lipid metabolism in childhood obesity.

Key words: Childhood obesity, galanin, glucose homeostasis, insulin resistance, leptin

1. Introduction

Obesity, with a worldwide increasing prevalence, is an important health problem that causes significant mortality and morbidity (1). It is a complex condition that is mostly caused by an imbalance between food intake and energy expenditure as well as sedentary lifestyle (1). Recent studies have shown that appetite is regulated by a complex network of peptides that are synthesized in the peripheral and central nerve system (2,3). Most peptides mediate their effects in hypothalamus, leading to stimulation or inhibition of food intake (1–3).

Galanin, a 29/30 amino acid peptide, was first identified in 1983 from the porcine intestine by Tatemoto et al. (4). Galanin is synthesized in several tissues including the central and peripheral nervous systems and is believed to be involved in the regulation of eating behavior. Increased galanin concentration stimulates food intake and increases the risk of obesity via activating galanin receptor 1 (GalR1), one of the three receptors of galanin, that is mainly distributed in the hypothalamus (5–9). On the other hand, food consumption was demonstrated to be decreased in galanin knockout mice and in rats that were given intracerebroventricular galanin antagonist (M40 and C7 molecules) (10,11). Higher concentrations of plasma galanin have been found in adult patients with obesity, impaired glucose tolerance, type 2 diabetes mellitus, and gestational diabetes mellitus (8,12–15). In addition, serum galanin levels are lower in lean women than normal controls, suggesting that galanin concentrations are higher in subjects with greater amounts of adipose tissue (16). Moreover, a limited number of studies investigating galanin concentrations have been conducted in children with type 1 diabetes and epilepsy receiving valproate, and significantly higher concentrations of galanin than in healthy subjects were demonstrated (17,18). Some studies have indicated that the galanin neuropeptide contributes to the regulation of glucose and insulin homeostasis by increasing insulin sensitivity (5,6,15,19,20). To the best

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of our knowledge, no prior study has investigated the relationship between galanin levels and childhood obesity. The aim of this study was to evaluate the levels of galanin and its relation with anthropometric and metabolic parameters in obese children.

2. Materials and methods

The current study consisted of 38 obese children with a current body mass index (BMI) greater than or equal to the 95th percentile, according to the Centers for Disease Control and Prevention (CDC-2000), and 30 age- and sex-matched healthy children with a BMI between the 3rd and 85th percentiles. The BMI of each case was calculated by dividing weight in kilograms by height in squared meters. For calculation of percentiles and standard deviation scores (SDSs) of all anthropometrics according to CDC data, the Child Metrics online calculator program (http://www.childmetrics.com) was used (21,22).

A comprehensive physical examination was performed for all subjects, including both the obese and control subjects, before the outset of the current study. Children with any acute infection, chronic systemic diseases (respiratory, neurologic, cardiovascular, or gastrointestinal), a history of drug use (antiepileptics, antipsychotics, and steroids), endocrinological disease (hypothyroidism or Cushing syndrome), or suspected obesity-related syndromes (Prader–Willi, Bardet–Biedl, and Alstrom syndromes) were excluded from the current study.

A Harpenden stadiometer with sensitivity of 0.1 cm was used for measurement of height. Body weight measurement was performed using a scale with sensitivity of 0.1 kg (SECA, Hamburg, Germany). BMI was calculated by dividing weight in kilograms by height in square meters. The body weight of each participant was measured while wearing light clothing. Waist circumference (WC) was measured using a nonstretchable tape between the midpoint of the lowest rib cage and the iliac crest without clothing, to the nearest 0.1 cm, at the end of a gentle expiration (23). WC SDS was calculated according to the data for Turkish children (24). Bioelectrical impedance analysis (Tanita BC-418, Tokyo, Japan) was used for measuring percent body fat (PBF) and fat mass (kg) in all subjects.

Pubertal development of each participant was assessed according to Tanner's staging (25). Testicular volume of ≥4 mL in boys and breast development of stage 2 and above in girls were considered as pubertal findings.

The homeostasis model assessment of insulin resistance (HOMA-IR) index was used to assess the status of insulin resistance. Different cut-off values according to pubertal phases were employed to define the insulin resistance status (prepubertal >2.5, pubertal >4.0) (26).

Blood pressure measurements were performed using a calibrated sphygmomanometer by the same investigator using a validated protocol. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice on the right arm after 10 min of rest in the supine position.

This study was approved by the ethical committee of the Dokuz Eylül University School of Medicine in İzmir, Turkey, in accordance with the Declaration of Helsinki. All of the children and their parents gave their written informed consent before the study.

Blood samples for analyzing glucose, lipid profile, insulin, galanin, and leptin levels were taken after 10–12 h of overnight fasting. Venous blood samples were taken in the morning and centrifuged at 1200 × *g* 10 min, and the serum samples were collected into Eppendorf tubes using plastic Pasteur pipettes and they were stored at –80 °C until analysis. Fasting serum glucose, triglyceride (TG), total cholesterol (TC), and high-density lipoprotein (HDL-C) levels were measured enzymatically using the DP Modular Systems (Roche Diagnostic Corp., Indianapolis, IN, USA). Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald formula when plasma TG levels were <400 mg/dL. Serum insulin levels were measured by electrochemiluminescence immunoassay method using an automated immunoassay analyzer (Immulite 2500 Insulin, Diagnostic Products Corporation, Los Angeles, CA, USA). Serum galanin (Cat No.: S-1347, Peninsula Laboratories, San Carlos, CA, USA) and leptin (Cat No.: EK0437, Boster Biological Technology Co. Ltd., Wuhan, China) were measured by an enzyme-linked immunosorbent assay (ELISA) kit based on the principle of sandwich enzyme immunoassay. The microplate in the kit is precoated with an antibody specific to the analyte. The standard is reconstituted and prepared by serial dilution with the sample diluent. Serum samples are diluted with sample diluent at ratios of 1:10 for leptin and 1:1 for galanin assays. The ELISA tests for galanin and leptin respectively had a sensitivity of 0.022 ng/mL and <10 pg/mL, a detection range of 0.313–10 ng/mL and 0.625–40 ng/mL, and intraassay CV of <10% and interassay CV of <15%.

Statistical analyses of the data were performed using SPSS 20.0 for Windows (IBM Corp., Armonk, NY, USA). Distribution of data was evaluated using the Kolmogorov–Smirnov test. For numerical comparisons, Student's t-test or Mann–Whitney U- tests were used to assess differences between two groups according to the normal distribution of the measured parameters. The chi-square test was used to compare the categorical variables. Spearman's rho correlation was used to identify the associations between variables. Variables with a P-value of <0.05 in bivariate correlation analysis were included in the multivariate linear regression analysis model to

evaluate the independent determinants of serum galanin levels. Data were presented as mean ± standard deviation (SD) or median and interquartile range (IQR, 25th–75th percentile). In all statistical tests, $P < 0.05$ was considered as statistically significant.

3. Results

The present study included 38 obese children (mean age: 11.9 ± 3.0 years) and 30 healthy children (mean age: 11.4 ± 2.0 years). The clinical, anthropometric, and laboratory characteristics are shown in Tables 1 and 2. There was no significant difference between the two groups in terms of age, sex, and pubertal status (Table 1). However, significant differences were found between obese and healthy children regarding BMI, BMI-SDS, WC, WC SDS, fat mass, PBF, HOMA-IR, SBP, DBP, serum insulin, TG, TC, LDL-C, HDL-C, leptin, and galanin levels (Tables 1 and 2). Additionally, age, pubertal status, WC, BMI, fat mass, HOMA-IR, insulin, and TG levels were significantly different among subjects with and without insulin resistance (Table 3).

In the obese children, galanin was positively correlated with fasting glucose ($r = 0.398$, $p = 0.013$), insulin ($r = 0.383$, $p = 0.018$), HOMA-IR ($r = 0.375$, $p = 0.020$), and TG ($r = 0.391$, $p = 0.015$) (Table 4; Figures 1 and 2). On the other hand, no such correlation was found between galanin levels and anthropometric and metabolic parameters. Multivariate backward regression analysis in obese children revealed that galanin levels ($r^2 = 0.483$, $P < 0.001$) were significantly associated with fasting glucose (β-coefficient = 0.478, $P = 0.003$), insulin (β-coefficient = 2.319, $P = 0.001$), HOMA-IR (β-coefficient = –2.255, $P = 0.002$), and TG (β-coefficient = 0.382, $P = 0.005$), which explained 42.0% of the variance (Table 5).

4. Discussion

In the present study, in which serum galanin levels were investigated in obese children for the first time, significantly higher levels of galanin were found in obese children than in healthy children. These results are consistent with the previous studies conducted in adults (12,16,20,27). Studies conducted by Baranowska et al. (12,16) showed higher serum galanin levels in obese women, especially in those with BMI >31, than in healthy controls. In these studies, increased serum galanin levels were found to be associated with increased BMI and adipose tissue. In a study conducted by Meczekalski et al. (27), significantly higher levels of serum galanin were observed in adult obese women compared to controls. In another study, serum galanin levels in nondiabetic adult obese male subjects were reported to be significantly higher at baseline and during the oral glucose tolerance test (OGTT) compared to healthy controls (20). The results of our study extend these finding by indicating that galanin levels are associated with obesity in children and adolescents as well.

Several studies investigating the effects of galanin peptide on insulin and glucose metabolism have reported that galanin enhances insulin sensitivity and increases

Table 1. The clinical characteristics of obese and healthy children.

	Obese children (n = 38)	Healthy children (n = 30)	P
Age (years)	11.9 ± 3.0	11.4 ± 2.0	0.404[a]
Sex (male/female)	24/14	18/12	0.790[c]
Pubertal/prepubertal	20/18	19/11	0.376[c]
BMI (kg/m^2)	31.3 ± 5.2	18.8 ± 2.2	<0.001[a]
BMI SDS	2.3 ± 0.2	0.04 ± 0.7	<0.001[a]
WC (cm)	101.3 ± 12.6	66.8 ± 9.5	<0.001[a]
WC SDS	3.78 ± 0.55	0.54 ± 0.65	<0.001[a]
Fat mass (kg)	28.8 (22.1–39.1)	6.4 (5.3–13.2)	<0.001[b]
PBF (%)	38.7 ± 5.2	18.6 ± 5.0	<0.001[a]
SBP (mmHg)	115 (110–125)	100 (95–110)	<0.001[b]
DBP (mmHg)	70 (70–80)	60 (55–66.3)	<0.001[b]

[a]Student's t-test, [b]Mann–Whitney U test, [c]chi-square test; data are given as mean ± SD or median (IQR 25th–75th percentile).
BMI: Body mass index, BMI-SDS: standard deviation score of body mass index, WC: waist circumference, WC SDS: standard deviation score of waist circumference, PBF: percent of body fat, SBP: systolic blood pressure, DBP: diastolic blood pressure.

Table 2. The laboratory characteristics of obese and healthy children.

	Obese children (n = 38)	Healthy children (n = 30)	P
Glucose (mg/dL)	84.3 ± 5.4	83.8 ± 4.8	0.819[a]
Insulin (μIU/mL)	17.1 (10.9–23.6)	5.4 (3.4–10.4)	<0.001[b]
HOMA-IR	3.4 (2.1–5.7)	1.1 (0.7–1.5)	<0.001[b]
TG (mg/dL)	112.0 (96.8–165.0)	64.0 (53.0–86.5)	<0.001[b]
TC (mg/dL)	165.0 (151.7.5–193.5)	154.0 (138.8–163.3)	0.001[b]
LDL-C (mg/dL)	97.5 (89.5–117.3)	87.0 (75.5–97.5)	0.002[b]
HDL-C (mg/dL)	46.1 ± 8.1	59.4 ± 12.5	<0.001[a]
Galanin (ng/mL)	1.12 (0.93–1.37)	0.98 (0.85–1.11)	0.010[b]
Leptin (ng/mL)	10.1 (4.3–13.7)	1.2 (0.8–3.5)	<0.001[b]

[a]Student's t-test, [b]Mann–Whitney U test; data are given as mean ± SD or median (IQR 25th–75th percentile). HOMA-IR: Homeostasis model assessment-insulin resistance, TG: triglyceride, TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol.

Table 3. The clinical and laboratory characteristics of obese patients with and without insulin resistance.

	IR (-) group (n = 14)	IR (+) group (n = 24)	P
Age (years)	10.3 (8.9–12.2)	13.1 (10.4–14.8)	0.016[a]
Sex (male/female)	10/4	14/10	0.700[b]
Pubertal/prepubertal	3/11	17/7	0.001[b]
BMI (kg/m^2)	28.7 (25.8–30.3)	32.2 (29.7–35.4)	0.002[a]
BMI SDS	2.3 ± 0.2	2.4 ± 0.2	0.117[c]
WC (cm)	93.5 (84.8–102.3)	105.2 (97.7–113.0)	0.006[a]
WC SDS	3.5 (2.9–4.2)	4.0 (3.5–4.2)	0.058[a]
Fat mass (kg)	23.8 ± 7.5	35.0 ± 11.9	0.003[c]
PBF (%)	36.7 ± 4.4	39.9 ±5.4	0.073[c]
Glucose (mg/dL)	79.5 (75.5–91.0)	86.5 (84.2–92.5)	0.071[a]
Insulin (μIU/mL)	8.1 (6.9–11.1)	22.6 (16.7–31.5)	<0.001[a]
HOMA-IR	1.6 (1.4–2.2)	5.1 (3.5–6.3)	<0.001[a]
TG (mg/dL)	100 (89.3–105)	135.5 (108.3–198.8)	0.004[a]
TC (mg/dL)	154.5 (150–169.3)	178.5 (153.8–195.0)	0.062[a]
LDL-C (mg/dL)	95 (86.5–100.8)	102 (92.3–124.8)	0.106[a]
HDL-C (mg/dL)	47 (39–56.3)	44.5 (38.3–52.3)	0.410[a]
Galanin (ng/mL)	0.95 ± 0.4	1.27 ± 0.4	0.228[c]
Leptin (ng/mL)	10.9 (2.6–14.19)	8.98 (5.3–12.8)	0.893[a]

[a]Mann–Whitney U test, [b]chi-square test, [c]Student's t-test; data are given as median (IQR 25th–75th percentile). IR: Insulin resistance, BMI: body mass index, BMI-SDS: standard deviation score of body mass index, WC: waist circumference, WC-SDS: standard deviation score of waist circumference, PBF: percentage of body fat, HOMA-IR: homeostasis model assessment-insulin resistance, TG: triglyceride, TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein-cholesterol.

Table 4. Correlation coefficients between galanin levels and anthropometric and laboratory parameters.

Parameters	Obese children (n = 38)		Healthy children (n = 30)	
	r*	P	r*	P
Age (years)	0.169	0.310	0.134	0.479
BMI (kg/m^2)	0.160	0.337	0.141	0.458
BMI SDS	0.103	0.537	0.115	0.545
WC (cm)	0.116	0.487	0.168	0.374
WC SDS	–0.124	0.457	0.069	0.716
Fat mass (kg)	0.138	0.339	–0.004	0.981
PBF (%)	0.191	0.318	–0.153	0.345
SBP (mmHg)	0.202	0.312	–0.092	0.683
DBP (mmHg)	0.208	0.226	–0.011	0.960
Glucose (mg/dL)	0.398	0.013	0.088	0.644
Insulin (μIU/mL)	0.383	0.018	–0.110	0.564
HOMA-IR	0.375	0.020	–0.024	0.901
TG (mg/dL)	0.391	0.015	–0.074	0.699
TC (mg/dL)	0.218	0.183	0.068	0.690
LDL-C (mg/dL)	0.229	0.166	–0.045	0.812
HDL-C (mg/dL)	0.025	0.879	0.243	0.196
Leptin (pg/mL)	–0.061	0.715	–0.182	0.335

*Spearman's correlation analysis; serum galanin level as dependent variable.
BMI: Body mass index, BMI-SDS: standard deviation score of body mass index, WC: waist circumference, WC SDS: standard deviation score of waist circumference, PBF: percent of body fat, SBP: systolic blood pressure, DBP: diastolic blood pressure, HOMA-IR: homeostasis model assessment-insulin resistance, TG: triglyceride, TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol.

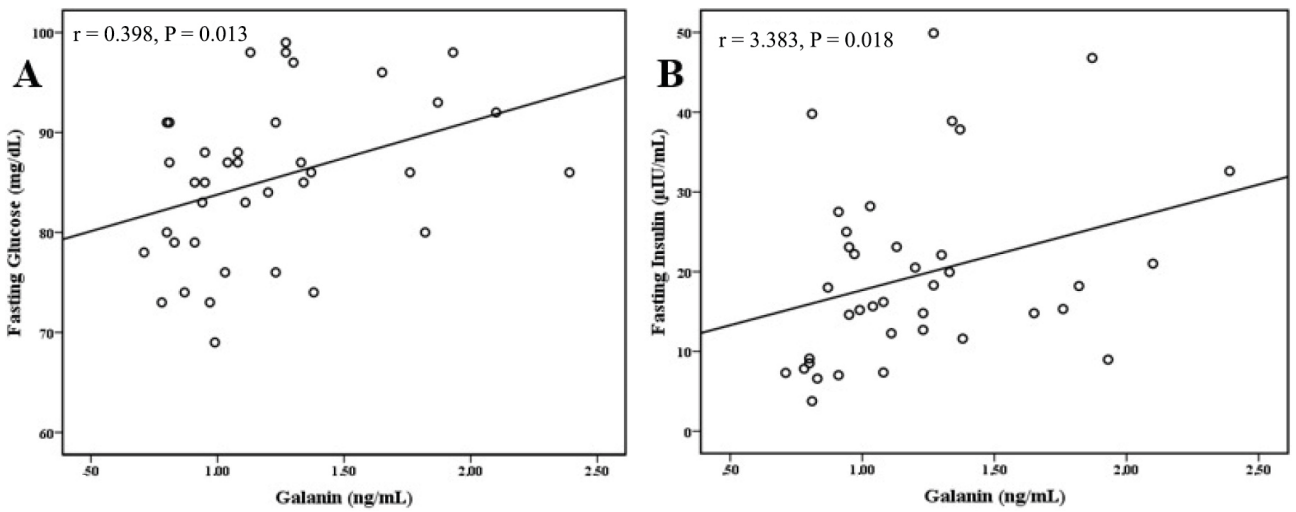

Figure 1. The positive correlations of galanin levels with fasting glucose (A) and insulin (B) in obese children.

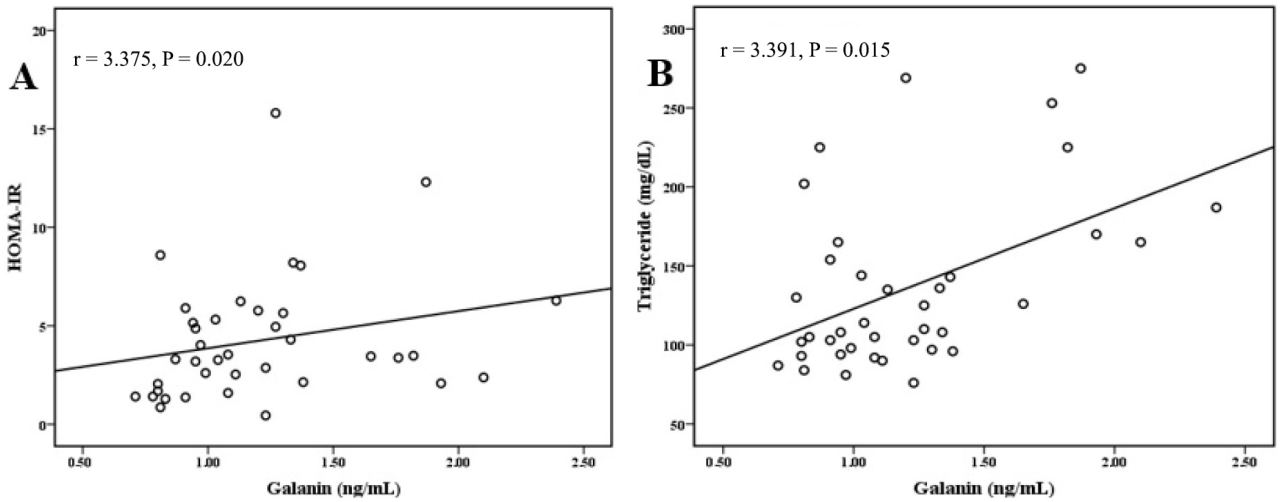

Figure 2. The positive correlations of galanin levels with HOMA-IR (A) and triglyceride (B) in obese children.

Table 5. Multivariate backward linear regression analysis.

Variable	B (95% CI)	SRC (β)	t	P-value
Glucose (mg/dL)	0.021 (0.007 / 0.034)	0.478	3.028	0.003
Insulin (μIU/mL)	0.059 (0.026 / 0.093)	2.319	3.579	0.001
HOMA-IR	–0.229 (–0.0367 / –0.091)	–2.255	–3.369	0.002
TG	0.005 (0.002 / 0.009)	0.382	3.028	0.005

HOMA-IR: Homeostasis model assessment-insulin resistance, TG: triglyceride, B: coefficient of regression, SRC: standardized regression coefficient ($r^2 = 0.483$, $P < 0.001$, Durbin–Watson = 1.922).

glucose uptake (5,6,20,27,28). Similarly, OGTT and hyperinsulinemic-euglycemic clamp studies demonstrated that galanin knockout mice and galanin antagonist (M35)-administered rats exhibited impaired glucose metabolism and increased insulin resistance, whereas increased insulin sensitivity was shown in transgenic mouse models (5,28–32). Bu et al. (33) showed that galanin administration in rats increases glucose utilization via activation of GLUT4, which is significantly expressed in fat and muscle tissue. On the other hand, administration of the galanin antagonist (M35) decreased GLUT4 channel expression and affected insulin-glucose metabolism (5,34). In other studies in adults with impaired glucose tolerance, type 2 diabetes, and gestational diabetes mellitus, serum galanin levels were reported to be significantly higher compared to healthy controls and correlated positively with glucose levels (13,14). Moreover, Sandoval-Alzate et al. (20) reported a positive correlation between serum galanin levels and HOMA-IR, BMI, and insulin levels at all OGTT time points and with glucose levels at 60- and 120-min time points of the OGTT in nondiabetic obese adults. Similarly, in the present study, serum galanin levels were significantly correlated with fasting glucose, fasting insulin, and HOMA-IR in obese subjects, which seems to be conflicting with the positive effect of galanin on glucose metabolism. This can be explained by the galanin receptor resistance due to impairment in the galanin system, which helps in maintaining the glucose level within the normal range, similar to the role of insulin or leptin resistance in obesity (13,35). Furthermore, one study also noted that there may be an association between insulin resistance and galanin resistance in obesity (35). In line with this hypothesis, a positive correlation was also demonstrated between serum galanin levels and HOMA-IR in the present study. Additionally, in our study, serum galanin levels in obese subjects with insulin resistance were higher than in those without insulin resistance (1.27 vs. 0.95 ng/mL); however, statistical significance could not be determined due to a low number of subjects in subgroup analyses.

Some studies have demonstrated that serum galanin levels are closely associated with increased fat consumption and serum TG levels (5,10,19,20,36–39). Significantly

higher fat-rich food consumption was observed in mice after an injection of galanin into the paraventricular nucleus or in galanin transgenic mice that led to overexpression of galanin (10,37). Additionally, it is well known that there is a close relationship between high-fat diet and serum TG (36). Taken together, it is noteworthy to say that there may be a close relation between the serum TG level and the galanin peptide, which increases the intake of fat-rich food. Poritsanos et al. (8) reported that TC and TG levels were significantly increased in transgenic mice that have 10-fold excess of galanin. Similarly, a positive association was demonstrated between serum galanin and TG levels in adult obese subjects by Fang et al. (19,38) and between serum galanin and TG and TC in nondiabetic obese adults by Sandoval-Alzate et a (20). In the present study, likewise, a positive correlation between serum galanin and TG levels was shown. This relationship suggests that galanin peptide, which causes an increase in food consumption, contributes to the development of obesity and its related effects, such as dyslipidemia. On the other hand, there are studies showing that a high-fat diet may cause changes in serum galanin levels (36,40). Leibowitz et al. (40) showed a 40% increase in galanin levels in the hypothalamus of high-fat-fed mice. In the same study, it was also reported that the level of TG in the hypothalamus was positively correlated with the mRNA transcript level of galanin; thus, the authors proposed that galanin levels may have increased in response to elevated serum TG. Taken together, these findings show that serum TG levels and galanin in obese subjects can be affected by nutrient contents such as fat. However, since the dietary habits of the patients were not taken into consideration, the effect of the nutritional pattern on galanin and TG were not investigated in the present study.

Another metabolic parameter that was evaluated in this study is leptin, which is mainly synthesized in the adipose tissue and inhibits food intake, contrary to galanin, which has an orexigenic effect (6,41). In experimental studies, a close association between ghrelin and leptin levels in the hypothalamus has been demonstrated (42). Leptin administration has been shown to reduce food intake and cause weight loss by reducing the expression of galanin in the hypothalamus, especially in the paraventricular nucleus (43,44). Moreover, it has been suggested that galanin exerts its effect on feeding behavior by inhibiting the effect of leptin (42,44). Moreover, galanin-knockout mice were reported to have higher leptin levels and increased leptin sensitivity, which in turn results in greater weight loss (42,45). Findings of another study indicated that these two hormones are involved in a common molecular interplay in the hypothalamus and that they modulate the effect of each other on feeding behavior (46). There is only one clinical study that has examined the relationship between serum galanin and leptin levels in obese subjects. Sandoval-Alzate et al. (20) reported a positive relationship between serum galanin and leptin levels in nondiabetic adults. However, in this study, obese and healthy subjects were evaluated together when the correlation was made, and that could have contributed to the positive relationship between serum galanin and leptin levels. In the present study, serum leptin and galanin levels were found to be significantly higher in obese subjects, but no relationship was found between them. There is a need for advanced molecular studies that can uncover the complex relationship between these two hormones, which interact with each other and modulate their effect on feeding behavior.

This study has some limitations. Even though higher serum galanin levels were found in obese subjects with insulin resistance than those without insulin resistance, this difference was not statistically significant due to the low number of subjects. Although we demonstrated significant associations regarding galanin in obese subjects, the sample size was not calculated before initiating the study and therefore we could not evaluate the effect of sample size on study results. In addition, subjects with probable type 2 diabetes or impaired glucose tolerance among obese subjects with insulin resistance could not be excluded as OGTT was not done. Furthermore, while clamp studies are regarded as the gold standard for determining insulin resistance, we used the HOMA model instead. However, a validation study demonstrated a strong association between HOMA and clamp techniques in young subjects; therefore, the HOMA model can be used to evaluate insulin resistance. (46). Lastly, we did not evaluate the dietary habits of subjects and therefore the relation of nutrition type with galanin could not be investigated.

In conclusion, the current study demonstrated that the serum galanin levels in obese children were significantly higher than in healthy controls and that galanin and TG levels are positively correlated. These findings suggest a role of galanin, an orexigenic peptide, in the development of obesity and related metabolic disorders. In addition, in obese subjects, serum galanin levels were demonstrated to be positively correlated with fasting insulin, fasting glucose, and HOMA-IR. The increase in galanin, which is known to have a regulatory role in insulin and glucose metabolism, could indicate a compensatory increase to increase insulin sensitivity in obese individuals with insulin resistance or an occurrence of galanin resistance in tissue, similar to leptin and insulin resistance. Further molecular studies to further study the concept of galanin resistance in obese subjects will provide a better understanding of the effect of galanin on insulin and glucose metabolism.

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