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ORIGINAL ARTICLE

Environmental Factors and Beta2-Adrenergic Receptor Polymorphism: Influence on the Energy Expenditure and Nutritional Status of Obese Women

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Abstract Our aim was to evaluate the influence of the Gln27Glu polymorphism of the β_2-adrenergic receptor (ADRβ_2) gene, fat intake and physical activity on the energy expenditure (EE) and nutritional status of obese women. Sixty obese women (30–46 years) participated in the study and were assigned to three groups depending on the genotypes: Gln27Gln, Gln27Glu and Glu27Glu. At baseline and after nutritional intervention, the anthropometric and body composition (bioelectrical impedance), dietary, EE (indirect calorimetry) and biochemical variables were measured. All women received a high-fat test meal to determine the postprandial EE (short-term) and an energy-restricted diet for 10 weeks (long term). The frequencies of Gln27Gln, Gln27Glu and Glu27Glu were 36.67, 40.0 and 23.33 %, respectively. Anthropometric and biochemical variables and EE did not differ between groups, although women who had no polymorphism demonstrated decreased carbohydrate oxidation. On the other hand, the Glu27Glu genotype showed a positive relation with EE in physical activity and fat oxidation. The environmental factors and Gln27Glu polymorphism did not influence the nutritional status and EE of obese women, but physical activity in obese women with the polymorphism in the ADRβ_2 gene can promote fat oxidation. The results suggest that encouraging the practice of physical exercise is important considering the high frequency of this polymorphism in obese subjects.

Keywords Obesity · ADRβ_2 gene · Fat intake · Physical activity · Energy expenditure · Nutritional status

Abbreviations

ADRβ_2	β_2 Adrenergic receptor
BEE	Basal energy expenditure
BCHOX	Basal carbohydrate oxidation
BFATOX	Basal fat oxidation
BMI	Body mass index
Bp	Base pairs
EE	Energy expenditure
IRMA	Immunoradiometric
Mets	Metabolic equivalent index
MUFA	Monounsaturated fatty acid
NPBRQ	Non-protein basal respiratory quotient
NPPPRQ	Non-protein postprandial respiratory quotient
NPRQ	Non-protein respiratory quotient
PCR	Polymerase-catalyzed chain reaction
PPEE	Postprandial energy expenditure
PPCHOX	Postprandial carbohydrate oxidation
PPFATOX	Postprandial fat oxidation
PPARgamma2	Peroxisome proliferator-activated receptor gamma 2
PUFA	Polyunsaturated fatty acids
RQ	Respiratory quotient
SD	Standard deviation
SFA	Saturated fatty acis
S/U	Relation saturated/unsaturated fatty acid
TEF	Thermogenic effect of food

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TBF	Total body fat
UNAV	University of Navarra
VO_2	Oxygen consumption
VCO_2	Carbon dioxide production
WC	Waist circumference
W/H	Waist-hip circumference ratio

Background

Obesity is a multifactorial disease that is currently considered a global epidemic [1, 2]. In addition to unhealthy lifestyles, it has been argued that the gene-environment interaction is involved in the onset of obesity; however, assessing genetic influences is complex because they are determined by the interplay of many genes with dietary and physical activity patterns [3, 4].

Efforts to identify candidate genes for obesity have concentrated on adipose tissue, since thermogenesis regulation through the sympathetic nervous system carried out by brown adipose tissue is mediated by the β_2 adrenergic receptor ($ADR\beta_2$) [5].

Genes involved in the regulation of catecholamine function may be important in obesity because of the role catecholamines play in energy expenditure (EE) and lipolysis [6, 7]. $ADR\beta_2$ is a mediator of the lipolytic effects of catecholamines [6] participating in energetic homeostasis because they stimulate the reduction of glycogen use and increase of lipid mobilization [7]. Abdominal fat has a higher density of ADRβ2; therefore, in obese individuals with a larger waist circumference (WC), ADRβ2 gene activity levels are higher [6].

Large *et al*. [8] detected three genetic variations in the $ADR\beta_2$ gene, Arg16Glu, Gln27Glu and Thr164Ile. The frequency of obese women who possessed the Glu27 variant was higher (48 %) compared with those of normal weight (30 %). The opposite occurred with the Gln27 allele being more frequent in normal-weight women.

In a meta-analysis, Jalba *et al*. [9] verified that the presence of the Glu27 allele in the $ADR\beta_2$ gene appears to be a significant risk factor for obesity in Asians, Pacific Islanders and American Indians, but not in Europeans. Considering that the $ADR\beta_2$ gene polymorphism can alter lipolytic functions, it may be a candidate for obesity [10]. Large *et al*. [8] also found a positive association between the Gln27Glu polymorphism and obesity. However, Gjesing *et al*. [11] evaluated 7808 middle-aged obese white subjects in a case-control study and did not find consistent evidence for an association of this variant with obesity.

Hellström *et al*. [12] found a positive association between obesity in women and the $ADR\beta_2$ gene polymorphism, but did not in men, suggesting the effect of sex on the frequency of polymorphism. However, González Sánchez *et al*. [13] conducted a cross-sectional population-based study with 666 nonrelated adults, aged 35–64 years, and suggested the Glu 27 allele of $ADR\beta_2$ may be a risk factor in men, but not women, for the accumulation of visceral fat and for its association with the development of type 2 diabetes mellitus.

The influence of the $ADR\beta_2$ gene polymorphism on obesity may depend on environmental factors. Arner [14] verified that an interaction between the $ADR\beta_2$ gene polymorphism and body mass index (BMI) was observed in sedentary individuals, but not in those who performed physical activity. Gungor *et al*. [15] observed that with physical exercise, the individuals with the Glu allele in the $ADR\beta_2$ gene have a lower maximum volume of oxygen, suggesting a reduction of lipolysis and increase in the respiratory quotient (RQ).

In addition to the genetic factor, Williams [16] suggests that, in Western societies, obesity is greatly influenced by environmental factors, considering that subjects of the same community living in the same environment vary in body size and composition genetically determined as a response to the environment.

Dietary fat differs in fatty acid chain length, the degree of saturation, and the position and stoichiometric double-bound configuration, affecting their oxidation rates. Saturated fatty acids (SFAs) have a slower oxidation speed than polyunsaturated fatty acids (PUFAs); the former favor fat deposition. Monounsaturated fatty acids (MUFAs) favor fat deposition as an energy source in fat tissue compared with PUFA, thus exerting less control on appetite [17].

Rosado *et al*. [18] verified that obese women with peroxisome proliferator-activated receptor gamma 2 (PPARgamma2) and $ADR\beta_2$ gene polymorphism showed a higher postprandial EE after high-fat and SFA meals compared with obese women with only the PPARgamma2 polymorphism or absence of the polymorphism in both genes. Rosado *et al*. [19] recommended the control of the fats and SFA intake in obese women with Pro12Pro/Gln27Gln and Pro12Pro/Gln27Glu genotypes, and MUFA in Pro12Pro/Glu27Glu. In Pro12Ala/Gln27Glu, AGPI intake can result in greater body weight loss. Therefore, there is an interaction between genes.

Martínez *et al*. [20] verified that genotype-environment interactions may appear when the impact of lifestyle factors (e.g., diet) on a phenotype (e.g., BMI >30 kg/m^2) differs by genotype. A case-control study (obese subjects vs. normal weight controls) was conducted to assess a possible effect modification on the obesity risk of the Gln27Glu polymorphism for the $ADR\beta_2$ gene depending on dietary intake. The obesity incidence was not directly affected by the polymorphism. They found a positive association of carbohydrate intake with insulin among women carrying the Gln27Glu polymorphism. This gene-nutrient

interaction emphasizes the importance of examining the outcome of some obesity-related mutations depending on lifestyle (including diet) and may explain the heterogeneity of findings from previous studies.

The purpose of this article is to assess the influence of the interactions between the Gln27Glu polymorphism in the ADRβ_2 gene on EE and nutritional status according to dietary fat and physical activity in obese women.

Materials and Methods

Subjects

Sixty obese Spanish females (BMI = 37.66 ± 6.24 kg/m^2) ranging between 20 and 49 years of age (34.59 ± 7.56) were selected to participate in an interventional trial aiming at comparing both the acute and long-term effects of dietary fat intake on EE, body composition and biochemistry variables depending on the ADRβ_2 gene polymorphism. The study was performed at the Nutrition, Food Sciences and Toxicology Unit of the Clinic of the Navarra University (UNAV), Spain.

Women with a BMI ≥30 kg/m^2 and regular menstruation with no chronic diseases were included, and their clinical and biochemical variables were evaluated. The exclusion criteria were as follows: chronic diseases such as diabetes, dyslipidemia, or hypertension; alcoholism or drug dependence; a restrictive diet during the 3 months prior to study; or a recent weight change of >3 kg in the previous 3 months. The volunteers were categorized into three experimental groups: Gln27Gln, Gln27Glu and Glu27Glu.

Ethical Approval

The volunteers were informed about the objectives and methodology of the study before all of them signed an informed consent form, which had been previously approved by the Research Ethics Committee of the UNAV [protocol 24(2)/2004].

Experimental Design

The experimental design is presented in Fig. 1. The study included short- and long-term nutritional interventions. At baseline, the habitual dietary intake was evaluated using a weighed food record, including 2 weekdays and 1 weekend day [21]. Also the level of physical activity was assessed by a questionnaire using the METs (metabolic equivalent index) [22] considering the frequency and type of activity.

Women came to the metabolic unit after 12 h of fasting (8:00 a.m.), and their standing height, body weight and body composition were measured. Fasting blood extraction was performed for biochemical and molecular analysis. After resting for 30 min, oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were measured over a 30-min period using open-circuit indirect calorimetry in order to calculate the basal energy expenditure (BEE) and non-protein respiratory quotient (NPRQ) with validated equations [18, 23]. A standard test meal (high fat and SFA) was provided and consumed within a 20-min period by every volunteer. After the test meal, the postprandial VO_2 and VCO_2 were recorded during a 3-h period to estimate the postprandial energy expenditure (PPEE).

To evaluate the dietary effects in the long term, the volunteers were given a hypocaloric diet (−30 % estimated EE) for 10 weeks and were monitored every 15 days. After this period (70 days), this dietary intervention was evaluated by means of food records as well as anthropometrics, body composition measurements and BEE.

Dietary Intervention

A standard test meal contained 50 % of the individual's BEE and 90 % SFA. A high-fat and SFA meal had 95 % fat—Fraîche nata (Champion Hendave, France).

A hypocaloric diet was prescribed individually with a 30 % energy restriction (500–1000 kcal) after calculating the resting EE values according to the WHO standards [24] and applying an individualized physical activity factor [25]. The diet comprised a normal distribution of carbohydrates, proteins and fats. Caloric restriction was corroborated with the basal measurement of EE carried out on the intervention day. Dietary compliance was monitored by biweekly dietary recalls.

Laboratory Analysis

Blood samples were used for insulin, leptin and triglyceride serum levels analyses. Insulin was determined by radioimmunoassay technique [26], while leptin was evaluated by immunoradiometric (IRMA) assay (Diagnostic Systems Laboratories, Inc.) [27]. Triglycerides were evaluated using a colorimetric enzymatic reaction [26].

Anthropometric Analysis

The women were weighed using a microdigital electronic balance (Seca model 700; lorca Medica, Pamplona, Spain) with 150-kg capacity and 100-g precision. Height was determined using a 0.5-cm scale vertical anthropometer [28]. BMI was calculated and classified according to the WHO standards [29], and the relationship between the WC and hip circumference (W/H) was determined [30, 31]. The WC was also evaluated independently because of its relation with comorbidity risks [30]. The bioelectrical

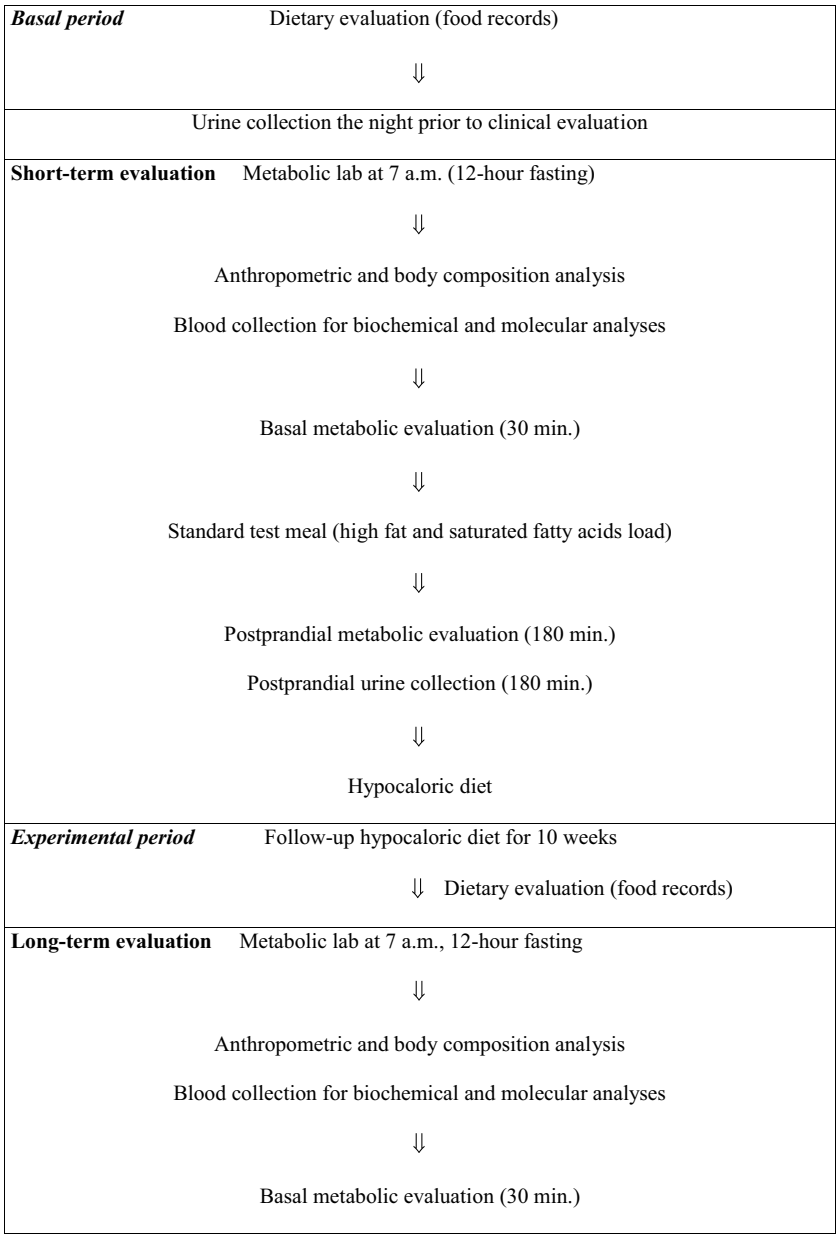

Fig. 1 Experimental design

impedance (Biodynamics model 310; Biodynamics Corp., Seattle, WA, USA) method was used to evaluate total body fat (TBF) contents [26, 32].

Energy Expenditure Analysis

The values concerning VO_2 and VCO_2 were measured at baseline and postprandially by open circuit indirect calorimetry with a canopy system (Deltatrac II, Datex, Finland). Before each test, O_2 and CO_2 sensors were calibrated using gas mixtures of precisely known O_2 and CO_2 concentrations. BEE, NPRQ and macronutrient oxidation were calculated using measurements of O_2 consumption, CO_2 production (ml/min) and urinary nitrogen excretion [18, 24]. After the test meal intake, the thermogenic effect of food (TEF) was measured during a 180-min period using the same indirect calorimetry system; it was calculated as PPEE and expressed in kilocalories. PPEE was calculated based on postprandial O_2 consumption, CO_2 production (ml/min) and nitrogen excretion. The substrate oxidation rate was calculated based on VO_2, nitrogen excretion and NPRQ in the basal (NPBRQ) and postprandial (NPPPRQ) periods to determine basal fat (BFATOX) and carbohydrate oxidation (BCHOX) as well as postprandial fat (PPFATOX) and carbohydrate oxidation (PPCHOX), respectively [23].

The urinary urea values used for assessing EE were obtained from urine collected during 12-h fasting and during the test meal to evaluate fasting and postprandial

urinary nitrogen, respectively. The urea concentration for urinary nitrogen analyses was determined using the enzymatic method with urease and desydrogenase glutamate, which was automated using COBAS MIRA equipment (Roche, Switzerland).

Molecular Analysis

Genomic DNA was isolated from white cells in blood samples by organic extraction (phenol/chloroform) based on a density gradient centrifugation [18]. The samples were quantified in a Nanodrop ND-1000 spectrophotometer (Fisher Scientific, Madrid, Spain) at 260, 270, 280 and 310 nm and kept at −20 °C at a concentration of 100 ng/μl.

The differentiation of genotypes Gln27Gln, Gln27Glu and Glu27Glu in the ADRβ_2 gene was carried out by means of a polymerase-catalyzed chain reaction (PCR) [33], available in the DNA GenBank Y00106 (2003) [34]. The primers used were 5′ CCGCCGTGGGTCCGCC 3′ and 5′ CCATGACCAGATCAGCAGCAC 3′. The cycling conditions were as follows: a curling temperature of 65 °C, a denaturation temperature/time of 94 °C/5 min and an extension temperature/time of 72 °C/30 s, totaling 35 cycles. The generated fragment was 310 base pairs (bp). After enzymatic digestion of the sample (37 °C/180 min) using the restriction enzyme *Ita* I, the following fragments were generated: 171, 84 and 55 bp (Gln27Gln); 226, 171, 84 and 55 bp (Gln27Glu); 226 and 84 bp (Glu27Glu).

Statistical Analysis

Data are presented as means ± standard deviation (SD). The comparison between groups and analyses of the effects of the intervention in the long term were evaluated by ANOVA and paired tests, respectively, at probabilities of 5 %. The Pearson correlation coefficient was used to evaluate the relationship among anthropometrical, dietary and metabolic variables. The Statistical Package for Social Sciences 17.0 software (SPSS; SPSS Inc., Chicago, IL, USA) was used for the statistical analyses.

Results

The prevalence of genotypes Gln27Gln, Gln27Glu and Glu27Glu was 36.67 % ($n = 22$), 40.00 % ($n = 24$) and 23.33 % ($n = 14$), respectively.

At baseline, no differences ($p > 0.05$) were found between groups regarding the usual energy intake, fat, carbohydrates, proteins, MUFA and SFA, but all groups had high fat, SFA and MUFA levels. Only the PUFA intake was higher in Gln27Glu compared with Gln27Gln (data not shown). Therefore, the dietary pattern at baseline did not differ between genotypes. After the intervention, there was a reduction in fat, SFA and MUFA intake (Figs. 2, 3), while the carbohydrate intake increased in the three groups (Fig. 2). The energy, carbohydrate, protein, fat, SFA, MUFA and PUFA intake did not differ between groups ($p > 0.05$).

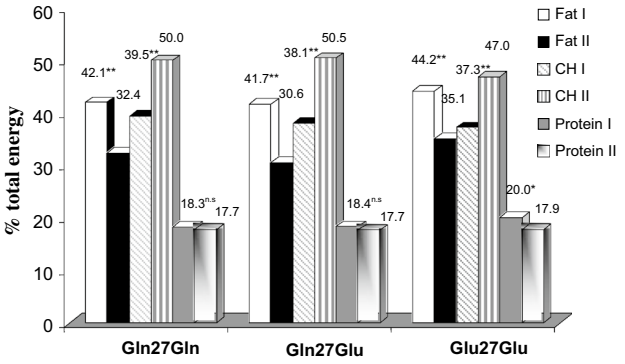

Fig. 2 Differences between the means of the dietary variables (fat, carbohydrate and protein) before (I) and after (II) the intervention in women with Gln27Gln, Gln27Glu and Glu27Glu genotypes in the ADRβ_2 gene. *CH* carbohydrate; *n.s.* not significant; *asterisk* significant at a 5 % probability; *double asterisk* significant at a 1 % probability as indicated by paired *t* test

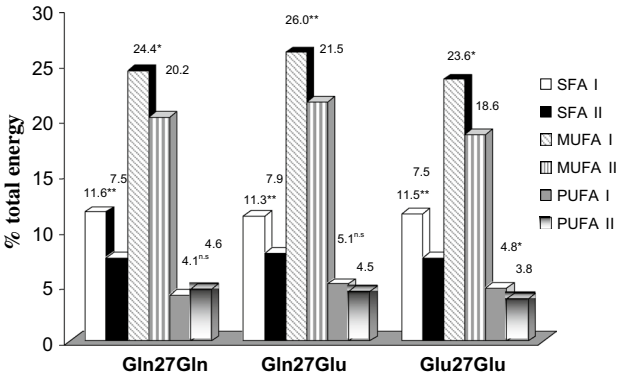

Fig. 3 Differences between the means of the dietary variables (SFA, MUFA and PUFA) before (I) and after (II) intervention in women with Gln27Gln, Gln27Glu and Glu27Glu genotypes in the ADRβ_2 gene; *n.s.* not significant; *asterisk* significant at a 5 % probability; *double asterisk* significant at a 1 % probability as indicated by paired *t* test

At baseline, age, anthropometrical variables (BMI, W/H, WC, TBF), insulin, leptin, triglycerides and EE did not differ between groups ($p > 0.05$) (Table 1). Also, the PPEE, NPPPRQ, TEF, PPFATOX and PPCHOX did not differ between groups (Table 2).

After dietary intervention, there was no difference in anthropometric variables and EE ($p > 0.05$) (Table 3). Comparing the baseline and after the intervention by group, there was a reduction in BMI, TBF, WC, W/H and BEE

Table 1 Descriptive characteristic of the women (mean ± SD) with the Gln27Gln, Gln27Glu and Glu27Glu genotypes

	Gln27Gln ($n = 22$)	Gln27Glu ($n = 24$)	Glu27Glu ($n = 14$)	p value
BMI (kg/m^2)	38.1 ± 6.7	36.9 ± 5.5	37.7 ± 6.6	0.79
W/H	0.82 ± 0.06	0.84 ± 0.07	0.86 ± 0.05	0.21
WC (cm)	102.3 ± 19.5	102.0 ± 12.8	104.9 ± 20.6	0.83
TBF (%)	47.1 ± 5.7	46.5 ± 4.9	46.7 ± 5.2	0.94
Insulin (μIU/ml)	11.1 ± 7.2	12.4 ± 9.6	12.1 ± 5.7	0.85
Leptin (ng/ml)	82.4 ± 25.5	73.8 ± 24.0	76.9 ± 25.4	0.51
Triglycerides (mg/dl)	97.1 ± 43.1	82.4 ± 31.8	92.0 ± 33.7	0.41
Weight loss (kg)	6.8 ± 3.0	8.1 ± 2.4	5.7 ± 4.1	0.07
BEE (kcal/min)	1.20 ± 0.21	1.20 ± 0.17	1.21 ± 0.14	0.94
BNPRQ (VCO_2/VO_2)	0.81 ± 0.05	0.79 ± 0.06	0.82 ± 0.06	0.43
BFATOX (g/min)	0.07 ± 0.02	0.07 ± 0.03	0.06 ± 0.02	0.49
BCHOX (g/min)	0.08 ± 0.04	0.08 ± 0.05	0.10 ± 0.05	0.46

Values were significantly different at a 5 % probability by ANOVA test

BMI body mass index, *W/H* waist-hip ratio, *WC* waist circumference, *TBF* total body fat, *BEE* basal energy expenditure, *BNPRQ* basal non-protein respiratory quotient, *BFATOX* basal fat oxidation, *BCHOX* basal carbohydrate oxidation

Table 2 Postprandial metabolic variables (mean ± SD) of Gln27Gln, Gln27Glu and Glu27Glu genotypes after high-fat and saturated fatty acid meals

Variables/groups	Gln27Gln ($n = 22$)	Gln27Glu ($n = 24$)	Glu27Glu ($n = 14$)	p value
PPEE (%)	27.6 ± 2.1	28.5 ± 2.8	28.4 ± 2.3	0.49
NPPPRQ (VCO_2/VO_2)	0.77 ± 0.04	0.75 ± 0.07	0.77 ± 0.04	0.21
TEF (kcal)	20.3 ± 11.6	22.6 ± 10.5	18.9 ± 9.8	0.56
PPFATOX (kcal)	14.6 ± 4.4	15.7 ± 5.5	14.1 ± 4.6	0.57
PPCHOX (kcal)	12.4 ± 7.1	9.2 ± 8.9	12.9 ± 8.1	0.37

Values were significantly different at a 5 % probability by ANOVA test

PPEE Postprandial energy expenditure, *RQ* non-protein postprandial respiratory quotient, *TEF* thermic effect of food, *PPFATOX* postprandial fat oxidation, *PPCHOX* postprandial carbohydrate oxidation

Table 3 Differences between anthropometric and metabolic variables (mean) in baseline and long-term evaluations of Gln27Gln, Gln27Glu and Glu27Glu genotypes

Variables/groups	Gln27Gln ($n = 22$)			Gln27Glu ($n = 24$)			Glu27Glu ($n = 14$)			p value*
	Δ	95 % IC	p value	Δ	95 % IC	p value	Δ	95 % IC	p value	
BMI (kg m^{-2})	−2.65	−2.14 to −3.16	<0.001	−3.17	−2.76 to −3.58	<0.001	−2.23	−1.33 to −3.14	<0.001	0.06
TBF (%)	−2.58	−1.92 to −3.24	<0.001	−3.58	−2.89 to −4.27	<0.001	−2.51	−1.54 to −3.47	<0.001	0.06
WC (cm)	−5.61	−2.97 to −8.25	<0.001	−7.71	−6.03 to −9.39	<0.001	−5.43	−2.84 to −8.02	0.001	0.25
W/H (cm/cm)	−0.01	−0.002 to −0.03	0.03	−0.02	−0.003 to −0.03	0.02	−0.03	−0.02 to −0.05	<0.001	0.29
BEE (kcal min^{-1})	−0.09	−0.04 to −0.14	0.001	−0.11	−0.06 to −0.17	<0.001	−0.07	−0.007 to −0.14	0.03	0.60
NPRQ (VCO_2/VO_2)	+0.02	+0.10 to −0.07	0.71	−0.02	+0.008 to −0.05	0.14	−0.01	+0.02 to −0.04	0.31	0.62
BFATOX (g min^{-1})	+0.001	+0.01 to −0.01	0.88	+0.001	+0.009 to −0.009	0.97	+0.001	+0.01 to −0.007	0.49	0.96
BCHOX (g min^{-1})	−0.021	−0.0006 to −0.05	0.04	−0.02	+0.003 to −0.048	0.09	−0.014	+0.01 to −0.04	0.30	0.80

Δ values were significantly different at a 5 % probability by paired test

BMI body mass index, *TBF* total body fat, *WC* waist circumference, *W/H* waist/height ratio, *BEE* basal energy expenditure, *BNPRQ* basal non-protein respiratory quotient, *BFATOX* basal fat oxidation, *BCHOX* basal carbohydrate oxidation, *CI* confidence intervals, *Δ* variable differences

* Comparison between groups was performed by ANOVA

in the three groups. BCHOX decreased only in Gln27Gln (Table 3).

There was no difference among groups in EE with physical activity ($p > 0.05$). Physical activity EE was positively correlated with BMI ($r = 0.55$, $p < 0.05$) and BFATOX in Glu27Glu ($r = 0.56$, $p < 0.05$).

Discussion

Gene-environment interactions play an important role in obesity, a multifactorial disease [35]. In the future, dietary changes based on the subject's genotype will be an alternative in the prevention and treatment of the disease. Genes involved in the regulation of catecholamine function may be important in the control of obesity [6].

In this study, we did not observe an influence of the Gln27Glu polymorphism on the anthropometric and biochemistry variables and EE. We also did not observe the influence of gene-diet interaction on anthropometric variables and EE, although woman who had no polymorphism demonstrated decreased carbohydrate oxidation. On the other hand, the Glu27Glu genotype showed a relation between EE and physical activity and fat oxidation.

The frequency of the genotype ADRβ_2 gene was similar to those found in the literature. Meirhaeghe *et al*. [36] found that the frequency of the ADRβ_2 gene polymorphism is equivalent to three isoforms, with 33.1, 51.0 and 15.9 % for Gln27Gln, Gln27Glu and Glu27Glu, respectively, with similar values in males and females.

Rossum *et al*. [37] evaluated the frequency of the ADRβ_2 gene polymorphism in different values and BMI in both sexes. Considering obese males, it was found that 30.7, 53.0 and 16.3 % presented genotypes Gln27Gln, Glu-27Glu and Gln27Glu, respectively, while normal-weight males showed values of 26.7, 55.8 and 17.5 % for the same isoforms. Obese women had a frequency of 34.4, 45.7 and 19.9 % for genotypes Gln27Gln, Gln27Glu and Glu27Glu, respectively. In normal-weight women, the frequency of these genotypes was 31.5, 49.1 and 19.4 %. No difference was observed among genotypes between males and females.

Large *et al*. [8] verified that the frequency of obese women who had the Glu27 variant was higher (48 %) compared with that of normal-weight women (30 %). The opposite occurred with the Gln27 allele, which was more frequent in normal-weight women. In our study, the frequency of Glu27 was higher (63.33 %), but was similar to the result in Meirhaeghe *et al*. [36].

It is important to note that the usual diet of the groups was high fat, low carbohydrate, and high SFA and MUFA. After the intervention, the diets of these groups were adequate in fats, carbohydrates, SFA and MUFA [24, 38].

In this study, anthropometrics, biochemistry and metabolic variables did not differ among groups. According to Hellström *et al*. [12], the WC did not differ among genotypes. Bouchard *et al*. [39] reported that gluteal-femoral fat cells have a lower lipolytic response to catecholamines compared with abdominal cells, which have a higher density of beta adrenergic receptors. Due to the presence of the allele variant in ADRβ_2 gene, the lipolytic effect exerted by pancreatic beta cells could be reduced; the density and number of these cells are reduced in the gluteal-femoral region compared with the abdominal. Macho-Azcarate [40] also found no differences between groups in anthropometrics variables and leptin.

Only Glu27Glu showed a positive relationship between EE in physical activity and fat oxidation.

Studies are still controversial regarding the interaction of BMI with physical activity. Arner [14] verified that the interaction between the ADRβ_2 gene polymorphism and BMI was observed in sedentary individuals, but not in those who performed physical activity. In this case, the presence of the Glu variant did not alter the effectiveness of exercise. Moreover, Gungor *et al*. [15] observed that during physical exercise, individuals with the Glu variant in ADRβ_2 have a lower maximum volume of oxygen, suggesting a reduction of lipolysis and increase in RQ.

Macho-Azcarate *et al*. [40] compared the fat metabolism during exercise between eight obese women with the Glu27Glu genotype and seven obese women with the Gln27Gln genotype, and they found that the fat oxidation was significantly lower the Glu27Glu group during recovery compared to those with Gln27Gln. These data suggest that both lipolysis and fat oxidation promoted by an acute submaximal exercise intervention could be blunted in the polymorphic ADRβ_2 Glu27Glu group of our female obese population.

Moore *et al*. [41] found that in Glu27Glu the O_2 consumption was lower and the increase in body fat was associated with a reduction of the maximal O_2 compared with other genotypes, but Meihaeghe *et al*. [36] verified that physical activity can counteract the effect of genetic predisposition to gain weight and that individuals with ADRβ_2 polymorphism can benefit from physical activity to reduce body weight.

However, Saitoh *et al*. [42] studied polymorphisms of genes associated with obesity, including ADRβ_2, and suggest that obesity and diabetes mellitus are not the result of the presence of an obesity-related gene polymorphism but rather the absence of daily physical activity.

Environmental factors and the ADRβ_2 gene polymorphism did not influence the anthropometrics, biochemistry variables and EE; however, physical activity seems to promote the fat oxidation in obese women with genotype Glu-27Glu. We suggest conducting further studies to evaluate

interactions of environmental factors with several candidate genes; however, it is important to encourage physical exercise considering the high frequency of this polymorphism in obese subjects.

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Conflict of interest The authors declared no competing interests exist.

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