Anthropometric and Metabolic Responses in *FTO* rs9939609 Gene Polymorphism after a Multidisciplinary Lifestyle Intervention in Overweight and Obese Adolescents

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J Pediatr Genet

Abstract

Few studies show the potential changing effect of fat-mass and obesity-associated (*FTO*) rs9939609 gene on cardiometabolic risk after a lifestyle intervention. This study aims to evaluate whether overweight and obese adolescents, carriers of the risk genotypes for obesity of the *FTO* rs9939609 gene polymorphism, have different anthropometric and biochemical responses to an interdisciplinary intervention program. The quasi-experimental study involved 34 adolescents aged 10 to 15 years. Schoolchildren with AA/AT genotype decreased glucose, total cholesterol, low-density lipoprotein cholesterol, and increased high-density lipoprotein cholesterol. However, there were no differences between the genotypes, suggesting that the "A" allele did not modify the subject's response to the intervention program.

Keywords
- clinical trial
- obesity
- genetic polymorphism

Introduction

The prevalence of childhood overweight and obesity has increased in both developed and developing countries.[1,2] The etiology of accumulating fat mass is likely to be a result of imbalances between energy intake and energy expenditure. However, nutritional behavior and physical inactivity are not the only determinants of obesity.[3,4] The environmental and genetic aspects linked to obesity are being increasingly investigated. The fat-mass and obesity-associated (*FTO*) gene has been associated with body mass index (BMI) of children and adolescents.[5,6] For *FTO* rs9939609 specifically, one of the most studied polymorphisms in this gene, the A allele is associated with obesity.[7,8] This gene has an effect on the hypothalamus indicating a possible influence in energetic homeostasis control, possibly on regulation of body fat accumulation.[9,10]

Children and adolescents carriers of the A allele of rs9939609 FTO polymorphism eat more frequently, ingest more food, and prefer foods with a higher fat content,[11] presenting a higher total energy intake.[12] Yang et al[8] also

received
February 28, 2019
accepted after revision
September 25, 2019

DOI https://doi.org/10.1055/s-0039-3399511.
ISSN 2146-4596.

highlighted differences in food preferences in different FTO genotypes, such as the preference of AA genotype carriers for meat-based diets. In addition, physical inactivity accentuates the rs9939609 polymorphism effect on body fat accumulation,[13] suggesting that lifestyle may attenuate the impact of FTO genotype on obesity. However, a potential modifier effect of *FTO* gene on body weight changes and parameters related to obesity reached by lifestyle intervention is limited: current studies are heterogeneous and with imprecise results.

This study aims to investigate whether adolescents with overweight and obesity, carriers of the risk genotypes for obesity (AA and AT) of the *FTO* rs9939609 gene polymorphism, have different anthropometric and biochemical responses to an interdisciplinary intervention program when compared with TT genotype.

Materials and Methods

Subject Selection

Overweight and obese adolescents aged 10 to 15 years from the municipality of Santa Cruz do Sul, State of Rio Grande do Sul, Brazil, participated in this quasi-experimental study. Subjects were divided into a control group (CG) and experimental group (EG). Subjects classified as overweight or obese from our previous cross-sectional study were invited to participate in this study. The intervention program was highlighted on local radio and newspapers, social networks, and in schools.

Subjects in the EG participated in an interdisciplinary intervention program based on physical exercises as well as nutritional and psychological counseling. Subjects allocated to the CG did not receive any kind of intervention. EG and CG were matched by age, gender, anthropometric variables such as BMI, waist circumference (WC), and body fat percentage (BF%).

Inclusion criteria to participate in this study were age between 10 and 17 years; present the consent form signed by parents or guardians and the assent term signed by the schoolchildren; current BMI percentile ≥ 85 associated with a WC classified as elevated or to a high BF% (classified as moderately high, high, or very high). Exclusion criteria were carrier of any disease, abnormality or health problem that precludes the participation in the intervention program, and evaluations of pre- and postinterventions; a frequency of participation less than 70% in all intervention sessions; and a long-term advice against practicing any physical activity during the intervention.

In this study, adolescence was defined according to the World Health Organization,[14] beginning at 10 and finishing at completion of 19 years of age. Sample size calculation was performed using the software G*Power by de Faul et al,[15] based on estimates of Hulley et al.[16] For a test power of 0.8, an effect of 0.9 and an experimental significance level of 95% calculate the need of at least 17 subjects in each group (CG and EG) (►**Fig. 1**).

Intervention Program

This intervention study is part of a wider research project entitled "Obesity in schoolchildren from basic education: an interdisciplinary intervention study" approved by the research ethics committee of the University of Santa Cruz do Sul under number 357.403. This study is also registered on ClinicalTrials.gov (54985316.0.0000.5343).

Interdisciplinary intervention program sessions took place three times per week (Mondays, Wednesdays, and Fridays) in campus and lasted for 2 hours, beginning on May and ending on November, totalizing 6 months of intervention. The intervention was based on exercise sessions. On Mondays, warm up, walking, stretching, and sports (soccer, basketball, and handball) were held. On Wednesdays, aquatic activities including water aerobics, recreational activities, and swimming were held. On Fridays, walking, resisted and aerobic exercises, circuit and respiratory exercises were basically held. Heart rate (HR) during exercises was monitored through HR monitors (Polar FT1), maintaining the frequency between 50 and 70% of maximum HR. The values were previously defined using the calculation of Karvonen (maximum HR = 220 – age).

Schoolchildren also received group nutritional and psychological counseling. Nutritional intervention sessions took place on Wednesday with 1-hour duration, focusing on food re-education through conversation circles, interactive games, movies, lectures, and workshops for making healthy recipes. Group psychological intervention was performed once a week during 1 hour (Monday), comprising cognitive orientation and training in groups, using directed techniques in the handling of thoughts related to obesity.

Anthropometric, Biochemical, Blood Pressure, and Genetic Polymorphism Evaluations

All these evaluations were performed on two separate occasions, pre- and postinterventions, except for genetic polymorphism, that was performed only preintervention. BMI was calculated by the formulae: BMI = weight/height^2 (kg/m^2) using calibrated anthropometric scale with coupled stadiometer and the results were classified according to the World Health Organization[17] percentile curves. Waist and hip circumference (HC) were performed using an inflexible tape measure. For groups pairing, WC was classified according to Fernández et al's[18] protocols and HC according to the established criteria of Picon et al.[19] Waist–hip ratio (WHR) was obtained through the equation: WHR = waist (cm)/hip (cm). BF% was determined by measuring triceps and subscapular skinfolds using a skinfold compass model Lange. For calculations, we use Slaughter et al's[20] equation and later, for pairing, the classification according to Lohman.[21]

For biochemical tests, peripheral venous blood was collected from each subject following a 12-hour (overnight) fast. Total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), and glucose were determined using Miura 200 (I.S.E., Rome, Italy) automated system and commercial kits Kovalent/DiaSys (DiaSys Diagnostic Systems, Germany). Insulin was determined by chemiluminescence on ARCHITECT *i*2000SR (Abbott Park, Illinois, United States). HOMA-IR (Homeostatic Model Assessment) was calculated through the formulae: fasting glucose (mmol/L) $\times$ insulin (μU/L)/22.5.[22]

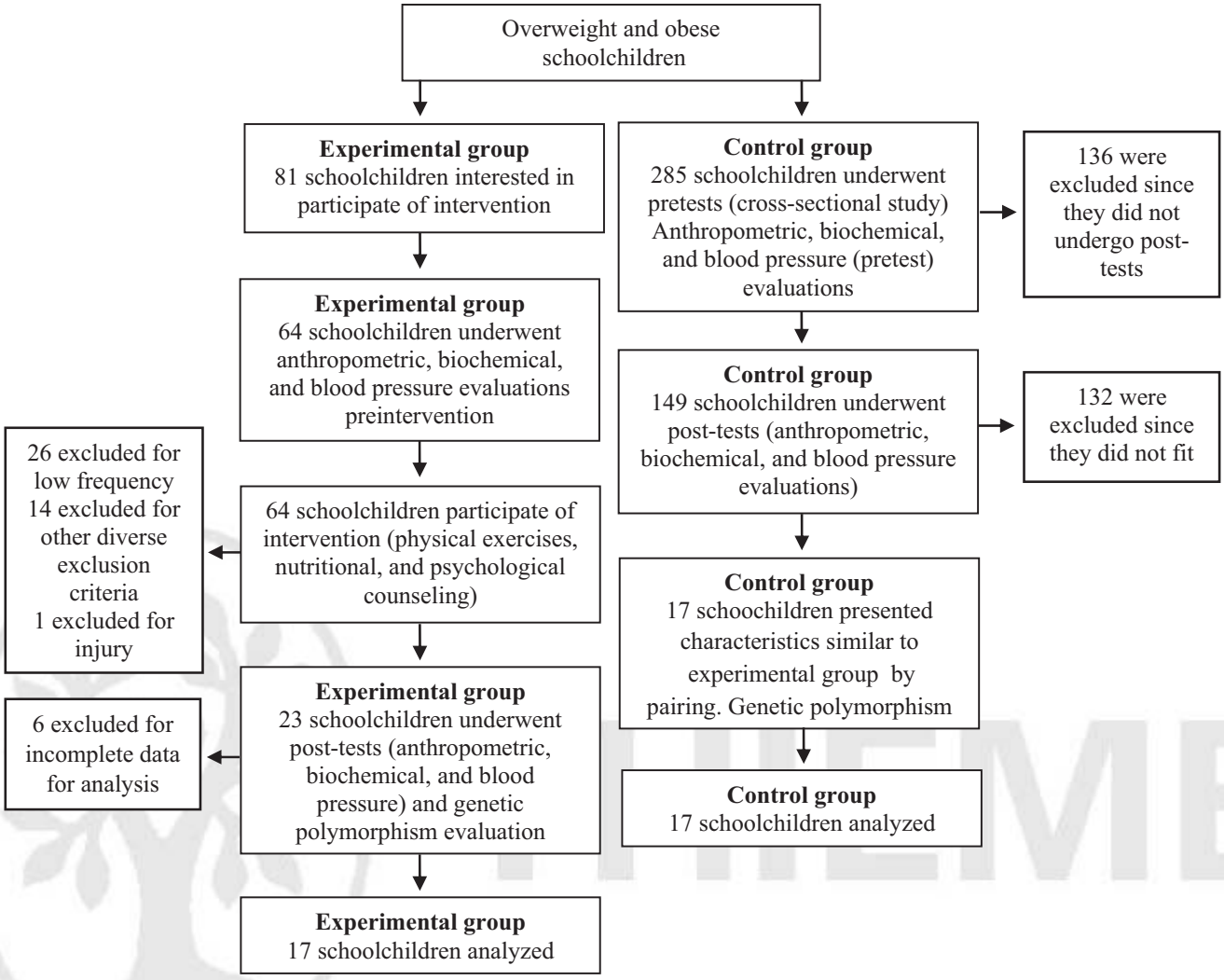

Fig. 1 Distribution flowchart of subjects.

Genetic polymorphism determination of carriers of risk genotypes for obesity (AA or AT) and of TT genotype of *FTO* rs9939609 gene was performed through DNA extraction, quantification, and genotyping. DNA extraction was performed using whole blood samples through the salting out method described by Miller et al.[23] DNA quantification was performed using NanoDrop 2000c Spectrophotometer (Thermo Scientific, Wilmington, United States), and later the samples were diluted with ultrapure water to the concentration of 10 mg/dL. Genotyping was performed through allele discrimination assays using quantitative polymerase chain reaction with TaqMan probes (Applied Biosystems, Foster City, California, United States) on StepOnePlus (Applied Biosystems).

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined according to Brazilian guidelines (SBC, 2010).[24] Puberty was determined using the adapted staging method of Tanner,[25] which consists in a self-assessment test with pictures representing the stages of developing pubic hairiness. Socioeconomic status was evaluated according to the self-reported questionnaire of the Brazilian Market Research Association, which divides the socioeconomic classes in A–B (high), C (middle), and D–E (low).[26] Skin color was determined according to self-reported questionnaire, being posteriorly regrouped in white and nonwhite.

Data Analysis

Statistical analysis was performed using SPSS (IBM, Armonk, New York, United States) version 23.0. Normality of sample was tested using the Shapiro–Wilk's test. Normal distribution data were analyzed using *t*-test for independent samples and paired *t*-test. For data without normal distribution, we use Mann–Whitney and Wilcoxon's tests. The effect size calculation considering the Cohen's *d* test was performed according to Sullivan and Feinn.[27] Statistical significance was considered for $p < 0.05$. Hardy–Weinberg's equilibrium was tested for the rs9939609 polymorphism using the same statistical software ($p = 0.356$). Moraes et al[28] described the genotype distribution and allele frequency of the rs9939609 polymorphism in EG and CG.

Results

General characteristics of subjects participating in this study regarding age, gender, BMI, pubertal stage, skin color,

Table 1 General characteristics of all subjects' participants of this study

Variables	Experimental group	Control group	Total
	n	*n*	*N*
Sex			
Male	4	5	9
Female	13	12	25
Age (y)			
10–12	12	10	22
13–15	5	7	12
BMI			
Overweight	1	1	2
Obesity	16	16	32
Maturational stage			
Prepubertal	8	6	14
Continuous maturation	8	9	17
Matured	1	2	3
Skin color			
White	11	10	21
Nonwhite	6	7	13
Socioeconomic level			
AB	4	3	7
C	11	12	23
DE	2	2	4
rs9939609 FTO genotype			
AA/AT	11	8	19
TT	6	9	15

Abbreviations: BMI, body mass index; FTO, fat-mass and obesity-associated.

socioeconomic level, and rs9939609 FTO genotype are shown in ►**Table 1**. No differences were found in the comparison of the odds ratio (OR) values of the genotypic frequencies for the experimental and control groups (OR: 2.06; confidence interval: 0.52–8.17; $p = 0.303$; data are not shown in the table).

Anthropometric, biochemical, and blood pressure variables pre- and postinterventions according to genotype AA/AT and TT are shown in ►**Table 2**. The levels of HDL cholesterol and glucose were significantly different between the CG and EG after the intervention in the TT and AA/AT genotypes, respectively. Insulin and HOMA-IR levels, which were statistically different between the CG and EG groups before intervention in the AA/AT genotype carriers, did not differ after the intervention.

►**Table 3** shows the mean difference of anthropometric, biochemical, and blood pressure variables pre- and post-interventions for EG and CG according to rs9939609 FTO genotype. Schoolchildren from EG with the risk allele A had a significant decrease in glucose ($p = 0.014$), TC ($p = 0.004$), LDL cholesterol ($p = 0.003$), and an increase of HDL cholesterol ($p = 0.033$). Among schoolchildren of EG (genotype TT) there was significant increase for HDL cholesterol ($p = 0.028$) only. However, the differences between AA/AT and TT genotypes were not significant.

Discussion and Conclusion

This study verified that after the intervention, schoolchildren from EG and carriers of A allele had significant decrease in glucose, TC and LDL cholesterol, and increase in HDL cholesterol. Among schoolchildren from EG with TT genotype, there was a significant increase of HDL cholesterol, showing the effectiveness of an intervention program on these biochemical parameters in overweight and obese adolescents. However, when comparing the AA/AT with the TT genotypes after the intervention, there were no significant differences, showing that both groups had a similar response to the intervention program.

A 4-month intervention study from southern Brazil with 36 schoolchildren aged 8 to 16 years observed that after the intervention with physical exercises and nutritional and oral health counseling, there was an absolute improvement of WC, HC, and C-reactive protein in subjects with the presence of A allele and of HC and uric acid for the TT genotype. However, there was no difference in other biochemical parameters (glucose, insulin, and lipid profile) and blood pressure (SBP and DBP), disagreeing of our study, which presented improvement in biochemical profile, but not in anthropometric parameters. Similar to our study, they also did not find statistical significance when comparing the AA/AT and TT genotypes after the intervention.[28]

A study with 136 overweight/obese children and adolescents and 172 normal weight subjects observed that after a 12-week program of physical exercises (aerobic, high-intensity interval training, combined training, and walking in water), *FTO* rs9939609 gene alleles did not show interaction with changes in anthropometric parameters.[29]

As well as in our study, a study with a subset of 207 overweight and obese individuals (94 males, mean age 10.79 ± 2.52 years) performed in Germany reported that after an intervention program based on physical exercises and nutritional education and behavioral therapy (individual psychological care of the child/adolescent and his or her family), there was no association of the *FTO* rs9939609 gene alleles with weight loss, fasting glucose, TG, and LDL and HDL cholesterol.[30] Likewise, Lappalainen et al,[31] in a study with 502 adult subjects with overweight and impaired glucose tolerance from Finland, performed an intervention of lifestyle that recommends and follows the increase in physical activities practice and proposed a personalized diet, and did not observe differences between the FTO rs9939609 markers regarding the weight reduction after the intervention. Both studies suggest that subjects with genetic predisposition to obesity may also benefit from lifestyle changes.

The same conclusion of the above paragraph was reported in a systematic review that evaluated interventions aiming weight loss on overweight adults; differences between FTO

Table 2 Biochemical, anthropometric, and blood pressure variables pre- and postinterventions with subjects divided according to genotype AA/AT and TT

rs9939609 FTO genotype	Preintervention			Postintervention		
	Control	Experimental	*p*-Value	Control	Experimental	*p*-Value
TT	***n* = 9**	***n* = 6**		***n* = 9**	***n* = 6**	
BMI (kg/m^2)	30.21 (4.51)	29.81 (4.76)	0.556	29.91 (3.87)	29.20 (5.03)	0.637
WC (cm)	86.67 (7.60)	84.33 (5.91)	0.409	86.90 (7.44)	83.68 (5.94)	0.346
Waist–hip ratio	0.83 (0.05)	0.80 (0.03)	0.259	0.84 (0.04)	0.79 (0.04)	0.124
Fat percentage (%)	41.83 (6.14)	41.04 (1.68)	0.814	34.60 (7.96)	42.10 (6.83)	0.077
Glucose (mg/dL)	92.44 (5.87)	94.83 (7.75)	0.636	86.22 (8.10)	93.00 (8.07)	0.098
Insulin (ng/mL)	15.02 (8.64)	16.45 (8.29)	0.637	13.28 (8.08)	15.68 (6.33)	0.289
HOMA-IR	3.45 (2.06)	3.88 (2.07)	0.637	2.88 (1.94)	3.60 (1.47)	0.289
Total cholesterol (mg/dL)	161.00 (37.09)	170.16 (20.96)	0.345	149.55 (50.08)	162.16 (19.03)	0.126
HDL cholesterol (mg/dL)	45.98 (7.00)	51.19 (9.31)	0.239	46.65 (9.85)	58.78 (8.33)	0.045
LDL cholesterol (mg/dL)	97.57 (33.01)	100.81 (22.86)	0.556	74.83 (38.97)	86.22 (22.36)	0.239
Triglycerides (mg/dL)	90.88 (33.26)	90.03 (33.11)	0.906	82.57 (35.57)	85.81 (31.44)	0.556
SBP (mm Hg)	119.11 (16.52)	110.33 (11.34)	0.203	122.44 (13.37)	113.67 (11.69)	0.246
DBP (mm Hg)	80.67 (14.45)	71.17 (10.59)	0.227	81.11 (11.66)	71.67 (11.69)	0.145
AT/AA	***n* = 8**	***n* = 11**		***n* = 8**	***n* = 11**	
BMI (kg/m^2)	28.08 (6.23)	30.32 (5.87)	0.283	27.23 (6.73)	29.69 (6.48)	0.364
WC (cm)	82.62 (10.23)	89.07 (11.97)	0.186	79.96 (12.67)	87.48 (13.24)	0.126
Waist–hip ratio	0.84 (0.04)	0.86 (0.07)	0.707	0.82 (0.03)	0.84 (0.07)	0.901
Fat percentage (%)	40.43 (6.92)	38.30 (5.76)	0.649	38.88 (11.30)	38.36 (9.75)	0.804
Glucose (mg/dL)	90.62 (6.02)	97.72 (7.12)	0.035	86.37 (7.68)	93.18 (5.13)	0.038
Insulin (ng/mL)	11.26 (5.31)	19.69 (6.13)	0.009	10.95 (5.69)	17.44 (8.99)	0.099
HOMA-IR	2.51 (1.20)	4.72 (1.38)	0.004	2.38 (1.36)	3.99 (2.03)	0.069
Total cholesterol (mg/dL)	143.25 (26.59)	161.72 (38.62)	0.076	143.37 (38.16)	145.27 (28.38)	0.967
HDL cholesterol (mg/dL)	46.24 (8.49)	45.47 (7.34)	0.620	48.33 (12.68)	50.38 (10.24)	0.364
LDL cholesterol (mg/dL)	82.36 (23.12)	95.18 (30.92)	0.322	81.24 (27.69)	77.46 (23.55)	0.804
Triglycerides (mg/dL)	73.22 (25.01)	99.64 (41.85)	0.186	68.97 (26.11)	86.98 (27.46)	0.099
SBP (mm Hg)	111.25 (15.81)	110.45 (12.93)	0.934	106.25 (13.91)	111.55 (16.56)	0.530
DBP (mm Hg)	69.38 (14.25)	74.18 (11.24)	0.357	67.50 (24.23)	70.18 (17.33)	0.895

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FTO, fat-mass and obesity-associated; HDL, high-density lipoprotein; HOMA-IR, Homeostatic Model Assessment; LDL, low-density lipoprotein; SBP, systolic blood pressure; WC, waist circumference.
Note: Statistic, data are mean (standard deviation). *t*-test for independent samples or Mann–Whitney's test.

genotypes regarding BMI, body weight, and WC after intervention with dietary, physical activity, or drug-based weight loss were not observed.[32]

However, a study on 138 Chinese adolescents aged 10 to 18 years from Shanghai and submitted to a dietary (individual and supplied according to the basal metabolic rate) and physical exercises intervention (such as ball games, swimming, and aerobics) for 4 weeks concluded that the subjects with genotype AA or AT decreased significantly the levels of total and LDL cholesterol when compared with the TT genotype ($p < 0.05$).[33]

In this sense, there is contradictory evidence about the association of the genetic variability of *FTO* gene with weight loss and cardiometabolic improvements following increased physical activity. Future research is required to understand the role of FITT principles (frequency, intensity, time, and type) in obese children with different genetic profiles and susceptibility to premature disease.

In 2009, Rendo et al[34] reported that few studies investigated the influence of *FTO* gene variables through intervention studies with physical exercise and that it was not elucidated if the increment of the physical exercise modifies the interaction of the risk allele A in the excess fat of the body. Recently, Leońska-Duniec et al[35] reinforced that this fact is not solved yet and there is few knowledge on the genetic variability and its interaction with physical activity.

Analysis of the studies so far shows that they are heterogeneous regarding the evaluated populations, intervention

Table 3 Mean difference of pre- and postintervention variables

Experimental group	TT			AT/AA			p^b
	Δ (SD)	Δ (%)	p^a	Δ (SD)	Δ (%)	p^a	
BMI (kg/m^2)	−0.61 (0.93)	−2.04	0.249	−0.62 (2.82)	−2.07	0.477	0.763
WC (cm)	−0.65 (2.89)	−0.77	0.500	−1.59 (4.74)	−1.78	0.213	0.651
Waist–hip ratio	−0.008 (0.03)	−1.25	0.588	−0.02 (0.03)	−2.32	0.087	0.448
Fat percentage (%)	1.05 (6.97)	2.58	0.600	0.06 (11.95)	0.15	0.722	1.000
Glucose (mg/dL)	−1.83 (7.08)	−1.92	0.500	−4.54 (4.92)	−4.64	0.014	0.267
Insulin (ng/mL)	−0.76 (10.64)	−4.68	0.917	−2.24 (6.19)	−11.42	0.197	0.840
HOMA-IR	−0.28 (2.62)	−7.21	0.753	−0.72 (1.53)	−15.46	0.131	0.841
Total cholesterol (mg/dL)	−8.00 (22.56)	−4.70	0.463	−16.45 (14.19)	−10.17	0.004	0.614
HDL cholesterol (mg/dL)	7.58 (4.93)	14.82	0.028	4.91 (5.83)	10.79	0.033	0.482
LDL cholesterol (mg/dL)	−14.59 (16.73)	−14.47	0.116	−17.71 (10.12)	−18.61	0.003	0.763
Triglycerides (mg/dL)	−4.21 (29.80)	−4.68	0.600	−12.66 (36.85)	−12.70	0.424	0.841
SBP (mm Hg)	3.33 (13.42)	3.02	0.416	1.09 (10.63)	0.99	0.591	0.649
Control group	**TT**			**AT/AA**			p^b
	Δ (SD)	Δ (%)	p^a	Δ (SD)	Δ (%)	p^a	
BMI (kg/m^2)	−0.29 (1.26)	−0.99	0.953	−0.84 (0.83)	−3.02	0.012	0.068
WC (cm)	0.22 (0.78)	0.26	0.482	−2.66 (3.38)	−3.21	0.063	0.060
Waist–hip ratio	0.003 (0.02)	1.20	0.394	−0.02 (0.04)	−2.38	0.175	0.133
Fat percentage (%)	−7.23 (10.67)	−17.28	0.066	−1.55 (7.19)	−3.83	0.674	0.178
Glucose (mg/dL)	−6.22 (5.06)	−6.72	0.011	−4.25 (8.56)	−4.68	0.340	0.122
Insulin (ng/mL)	−1.73 (3.31)	−11.58	0.173	−0.31 (4.09)	−2.75	1.000	0.630
HOMA-IR	−0.56 (0.74)	−16.52	0.086	−0.12 (0.94)	−5.17	0.779	0.336
Total cholesterol (mg/dL)	−11.44 (17.43)	−7.11	0.086	0.12 (18.82)	0.08	0.441	0.123
HDL cholesterol (mg/dL)	0.67 (9.35)	1.45	0.441	2.09 (12.12)	4.51	1.000	0.773
LDL cholesterol (mg/dL)	−22.73 (38.41)	−23.30	0.021	−1.12 (8.85)	−1.38	0.674	0.773
Triglycerides (mg/dL)	−8.31 (35.77)	−9.14	0.441	−4.25 (34.19)	−5.80	0.889	0.630
SBP (mm Hg)	3.33 (13.85)	2.79	0.438	−5.00 (13.00)	−4.49	0.223	0.207
DBP (mm Hg)	0.44 (10.08)	0.54	1.000	−1.87 (6.51)	−2.70	0.450	0.617

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HOMA-IR, Homeostatic Model Assessment; LDL, low-density lipoprotein; SBP, systolic blood pressure; SD, standard deviation; WC, waist circumference.
Note: Statistic, data are mean (standard deviation).
[a]Paired *t*-test or Wilcoxon.
[b]Paired *t*-test for independent samples or Mann–Whitney.

period, intervention methods, and sample size. Few studies indicate the type, intensity, and frequency of proposed exercises. This is also observed in the systematic review of Xiang et al[36] that evaluated the relationship between FTO genotypes and the response to the obesity treatment; the studies included had differences regarding intervention type, study period (3 months–4 years), sample size, and breed/ethnicity, indicating the need of other studies that consider these characteristics. Livingstone et al[32] showed that the relationship was influenced by the kind of study (diet, physical exercise, or drugs), study period (8 weeks–3 years), breed/ethnicity, gender, or BMI; however, the study did not evaluate the kind of diet or physical exercises proposed and these can be a possible contributing factor for answering in the intervention programs.

Since there are few intervention studies verifying the *FTO* gene variability and its response to physical exercise, we look other nonexperimental studies and notice that the presence of physical activity can attenuate the effects of *FTO* gene. Celis-Morales et al,[37] in a cross-sectional study with 1,280 European adults, reported that the effect size of the FTO associations on BMI and WC for active subjects were lower than for inactive subjects, indicating that the genetic susceptibility to overweight can be diminished with the implementation of physical exercises. By the same way, in the Lithuanian adult population, Petkeviciene et al[38] observed that the physical activity could weaken the effect of FTO polymorphism on the body weight and metabolic syndrome. The same was found in Nigeria, where a case-control

pilot study conducted in young adults with a mean age of 22.6 years (103 subjects with obesity and 98 controls), verified that environmental factors such as physical inactivity mediated the relationship between polymorphism and obesity.[39]

The earlier association is also observed in the adult–juvenile population. In a cross-sectional study with 752 European adolescents, Ruiz et al[40] reported that the effect of *FTO* gene polymorphism on body fat parameters (BMI, WC, and BF%) is attenuated when the daily recommendations of physical activity are fulfilled (>60 minutes of moderate to vigorous physical activity). Xi et al,[41] in a population study with 3,503 children and adolescents aged 6 to 18 years from Pequin (China), reported interaction between the rs9939609 FTO genotype and physical activity, in which the effect of the A allele on BMI was reduced as increased physical activity intensity (low, moderate, and severe). However, a meta-analysis with 218,166 adults and 19,268 children and adolescents verified that, in adults, the physical activity attenuated the risk effect of the A allele for obesity; however, this was not found in children and adolescents.[42]

Thus, although association studies shows that physical exercise practice can attenuate the effect of *FTO* gene on obesity, experimental studies are yet few and contradictory. Knowing the relationship of *FTO* rs9939609 gene polymorphism with obesity, we need more studies like this, which aims to identify whether subjects with genetic predisposition to obesity also can benefit of intervention program focused on physical exercise practice, improving your overall health. In this way, future intervention programs can be designed according to the subject's genetic variability, offering more effective personalized intervention programs.

The strengths of this study are as follows: first, including genetic analysis in conducting a clinical trial and supplying the lack of intervention studies which evaluate genetic interference in weight loss programs focused on physical exercises; second, group pairing, in which the study subjects were paired by gender, age, and anthropometric variables (BMI, WC, and BF%). To decrease the natural differences among subjects, we organized pairs with features as similar as possible.

Among the limitations of this study are the analyses of only the rs9939609 genetic variant, since the subjects of this study can carry other different genetic alterations that predispose the body fat accumulation. However, we chose the *FTO* rs9939609 gene polymorphism because it was strongly related with the overweight presence in schoolchildren from the same city in a previous cross-sectional study.[43] The study also has few subjects. However, a sample size calculation was performed to make the inferences with a stipulated test power. The loss of subjects in the intervention program was a challenge for our study. However, it is known the difficulty of permanence of the subjects in intervention programs[44] as well as that biological and psychosocial factors might be associated with desistance of obese adolescents from intervention programs.[45]

In conclusion, we demonstrate that the interdisciplinary intervention program with physical exercises and nutritional and psychological counseling was effective for decreasing glucose, TC, and LDL cholesterol levels and increasing HDL cholesterol in overweight/obese adolescents with the A allele of *FTO* rs9939609 gene polymorphism, as well as the increasing of HDL cholesterol in TT genotype adolescents. However, adolescents with AA and AT genotype have the same answer to intervention when comparing with TT genotype adolescents, suggesting that the presence of the risk allele for obesity did not modify the subject's answer to anthropometric, biochemical, and blood pressure variables after an interdisciplinary intervention program. This indicates that subjects who had genetic predisposition to overweight also can be beneficiated for changes in lifestyle.

Conflict of Interest
None declared.

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