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Lack of relationship between 174G_C promoter polymorphism of the *IL-6* gene and indices of metabolic syndrome in non-obese healthy subjects

Brak związku między polimorfizmem 174G_C genu *IL-6* a wskaźnikami zespołu metabolicznego u osób zdrowych z należną masą ciała

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Abstract

Introduction: Homozygosity for interleukin-6 (IL-6) 174G_C promoter polymorphism has recently been associated with indices of metabolic syndrome; however, this problem has not been investigated in non-obese subjects.
The aim of this study was to explore the relation between abdominal fat distribution and some inflammatory risk factors of atheromatosis and IL-6 174G_C gene polymorphism in non-obese healthy subjects.
Material and methods: Relationships were investigated between anthropometric variables, i.e. weight, height, BMI, waist circumference (WC), waist-to-hip ratio (WHR), body fat distribution (DXA), serum CRP and IL-6, insulin sensitivity/resistance indices, and IL-6 174G_C gene polymorphism, in healthy non-obese Polish subjects: 232 women (age 31.4 ± 5.5 years) and 199 men (age 30.3 ± 6.0 years).
Results: The genetic study revealed that the CC genotype was observed in 15.56% of subjects, the CG genotype in 52.74%, and the GG genotype in 31.7%. IL-6 and CRP concentration did not differ among the genotypes. There were also no differences regarding BMI and WHR. The only differences among genotypes, observed only in men, were those concerning total fat (CC had higher fat content than CG and GG); the difference being statistically significant between CC and GG ($p < 0.05$), and gynoidal fat deposit (CC had higher gynoidal fat deposit than CG and GG); the difference being statistically significant between CC and GG ($p < 0.025$) and between CC and CG ($p < 0.05$). Biochemical parameters and insulin sensitivity did not differ among the genotypes.
Conclusions: These data show that IL-6 174G_C polymorphism is not associated with features describing metabolic syndrome in non-obese healthy subjects. **(Pol J Endocrinol 2009; 60 (3): 172–179)**

Key words: *IL-6 174G_C promoter polymorphism, metabolic syndrome, fat distribution, insulin resistance, insulin sensitivity*

Streszczenie

Wstęp: W ostatnim czasie pojawiły się doniesienia na temat związku polimorfizmu 174G_C genu interleukiny 6 (IL-6) z wskaźnikami zespołu metabolicznego. Jednak problem ten nie był badany u osób z należną masą ciała.
Celem opisanych badań było znalezienie związku między zawartością tkanki tłuszczowej brzusznej a wybranymi zapalnymi czynnikami ryzyka rozwoju miażdżycy i polimorfizmem 174G_C genu *IL-6* u zdrowych osób z należną masą ciała.
Materiał i metody: Badano związek między cechami antropometrycznymi, takimi jak: masa ciała, wzrost, wskaźnik masy ciała (BMI, *body mass index*), obwód talii, stosunek obwodu talii do obwodu bioder (WHR, *waist-to-hip index*), dystrybucja tkanki tłuszczowej (DXA), stężeniem białka C-reaktywnego (CRP, *C-reactive protein*) i IL-6 oraz wskaźnikami insulinowrażliwości/oporności a polimorfizmem 174G_C IL-6. Grupę badaną stanowiło 232 zdrowe nieotyłe kobiety (wiek 31,4 ± 5,5 lat) oraz 199 mężczyzn (wiek 30,3 ± 6,0 lat).
Wyniki: Autorzy stwierdzili, że genotyp CC występował u 15,56%, CG u 52,74%, a GG u 31,7% badanych. Stężenia IL-6 i CRP nie różniły się pomiędzy genotypami. Nie było także różnic odnośnie BMI i WHR. Jedyne różnice pomiędzy genotypami, widoczne tylko w grupie mężczyzn dotyczyły całkowitej zawartości tkanki tłuszczowej (genotyp CC wykazywał większą zawartość tłuszczu niż CG i GG), różnica ta była istotna statystycznie między CC a GG ($p < 0,05$), oraz depozytu gynoidalnego (wyższe wartości u genotypu CC niż u CG i GG), różnica ta była istotna statystycznie między CC a GG ($p < 0,025$) oraz między CC i CG ($p < 0,05$). Parametry biochemiczne i wrażliwość na insulinę nie różniły się pomiędzy genotypami.
Wnioski: Uzyskane wyniki wskazują na brak związku między polimorfizmem 174G_C IL-6 a zaburzeniami metabolicznymi u osób zdrowych z należną masą ciała. **(Endokrynol Pol 2009; 60 (3): 172–179)**

Słowa kluczowe: *polimorfizm IL-6 174G_C, zespół metaboliczny, dystrybucja tkanki tłuszczowej, insulinooporność, insulinowrażliwość*

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Introduction

Obesity is a well-known risk factor of cardiovascular diseases, type 2 diabetes, and some neoplasms. Excessive fat accumulation, especially in the abdominal region, is accompanied by metabolic disturbances such as insulin resistance, dyslipidemia, increased levels of inflammatory markers, and higher blood pressure. All these disturbances significantly increase the risk of developing atherosclerosis and cardiovascular diseases.

It is known that insulin resistance and hyperinsulinaemia play important roles in the pathogenesis of obesity-related consequences. Interleukin 6 (IL-6) is one of the cytokines that can modulate insulin sensitivity and energy balance [1]. Some studies have described a link between IL-6 174G_C promoter polymorphism and BMI [2, 3]. Berthier et al. [4] reported that the *174CC* variant was associated with indices of obesity, while Kubaszek et al. [1] observed an association of increased BMI and the *–174C* allele, which, however, was non-significant. In humans, the effect of 174G_C promoter polymorphism of the IL-6 gene on fat distribution has not been studied. Therefore, we investigated the effect of this polymorphism not only on BMI and insulin sensitivity, but also on anthropometric features characterizing fat distribution in 431 healthy, non-obese young subjects.

Material and methods

The study was performed in 232 healthy, non-obese (BMI [body mass index] < 30 kg/m^2) women and 199 men aged 20–40 years, who were randomly selected from among Wroclaw's citizens. This group was part of an ongoing epidemiological study. Exclusion criteria were chronic diseases requiring special diet or treatment with anti-diabetic or lipid lowering drugs, neoplasmatic diseases, and, in women, use of oral contraceptives or a period shorter than three months after withdrawal from oral contraceptives. Subjects with infections were excluded at the physical examination stage.

The study protocol was approved by the Ethics Committee of Wroclaw Medical University, and all the subjects gave their informed consent in writing.

All the subjects were interviewed and a physical examination was carried out, which included arterial blood pressure and anthropometrical measurements such as body mass, body height, and waist circumference. The BMI was calculated from the equation: BMI = body mass [kg]/height-squared [m^2]. The waist-to-hip ratio was defined as waist circumference divided by hip circumference. Body mass and height were measured without top clothing and shoes; waist circumference was measured halfway between the costal angle and the iliac crests. The percentage of body fat and visceral fat deposit were assessed using the dual-energy X-ray absorptiometry method (DXA) using a "DPX (+) Lunar" device (USA). The percentage of abdominal fat (android fat deposit) was calculated using a computerized method after measuring fat tissue volume in the area from the upper edge of the L2 to the lower edge of the L4 vertebrae. Gynoid fat deposit was calculated after measuring fat volume in the area between the trochanter major of the femur and the knees.

Peripheral venous blood samples were collected between 7:00 and 9:00 a.m. after overnight fasting, and the plasma was stored immediately after centrifugation at — 80°C until assay.

IL-6 was measured by ultra-sensitive enzyme-linked immunosorbent assay – ELISA (BioSource). Intra-Assay precision was 4.71% CV and Inter-Assay precision was 6.7% CV.

Glucose level, total cholesterol, HDL cholesterol, and triglycerides were measured using commercially available kits, and LDL levels were calculated using the Friedewald formula [5]. Fasting insulin was measured using an immunoenzymatic method (Abbott Diagnostics, USA). The insulin sensitivity index (QUICKI) and the insulin resistance indices (HOMA and FIRI) were calculated from the fasting glucose (G_0) and fasting insulin (I_0) levels:

$$QUICKI = \frac{1}{[\log I_0\ (\mu\ \text{IU/ml}) + \log G_0(\text{mg/dl})]} \quad [6]$$

$$HOMA = \frac{[I_0\ (\mu\text{IU/ml}) \times G_0\ (\text{mg/dl})]}{405} \quad [7]$$

$$FIRI = \frac{[I_0\ (\mu\text{IU/ml}) \times G_0\ (\text{mg/dl})]}{450} \quad [8]$$

All the study participants were genotyped for IL-6 174G/C promoter polymorphism. Genomic DNA was extracted from human blood leukocytes using a Blood Mini Kit (A&A, Biotechnology) according to the manufacturer's recommendation.

Genotyping of promoter –174G/C (rs1800795) polymorphism of the *IL-6* gene was carried out by polymerase chain reaction - restriction fragment length polymorphism (PCR-RFLP) analysis as described previously (9) with our own modification. A 198-bp fragment of the *IL-6* gene was amplified. The forward and reverse primer sequences were IL-6-174F: 5′-TGA CTT CAG CTT TAC TCT TTG-3′ and IL-6-174R: 5′-CTG ATT GGA AAC CTT ATT AAG-3′ (Proligo), respectively. The reaction was carried out in a final volume of 10 μL containing 2 μL of Q-Solution (Qiagen), 2.25 μL of sterile double distilled water, 2 μL of PCR Buffer (containing 15 mM $MgCl_2$, Qiagen), 0.25 μL of each dNTP (Fermentas), 0.8 μL of each primer, 5 U/μL *Taq* DNA poly-

Table I. *Baseline characteristics (mean, SD) of the study participants*

Tabela I. *Wyjściowa charakterystyka (średnia, SD) uczestników badania*

	Whole group (431)	Women (232)	Men (199)
Age (years)	30.93 (5.72)	31.4 (5.47)	30.34 (5.98)
Weight [kg]	67.93 (13.57)	58.7 (7.85)	79.4 (9.93)
Height [cm]	171.8 (9.36)	165.23 (5.62)	179.88 (6.16)
BMI [kg/m^2]	22.88 (3.1)	21.48 (2.54)	24.61 (2.85)
Waist circumference [cm]	79.39 (11.19)	71.84 (6.64)	89.06 (7.92)
Hip circumference [cm]	99.99 (6.62)	97.87 (5.94)	102.93 (6.41)
WHR	0.79 (0.09)	0.73 (0.05)	0.87 (0.07)
Systolic BP [mm Hg]	110.31 (14.46)	107 (13.46)	114.49 (14.64)
Diastolic BP	72.5 (10.37)	69.52 (9.56)	76.25 (10.16)

BMI — body mass index; WHR — waist-to-hip ratio

Table II. *Lipid profile, glucose, insulin, and indices of insulin sensitivity/resistance in the study group*

Tabela II. *Profil lipidowy, stężenie glukozy, insuliny i wskaźniki wrażliwości/oporności na insulinę w badanej grupie*

	Whole group (431)	Women (232)	Men (199)
Total cholesterol [mg/dl]	193.62 (35.8)	188.79 (31.19)	199.53 (40.04)
Triglycerides [mg/dl]	79.64 (51.9)	64.46 (34.33)	98.33 (62.76)
HDL-C [mg/dl]	64.87 (16.59)	70.77 (15.62)	57.64 (14.83)
LDL-C [mg/dl]	112.72 (34.08)	105.1 (29.02)	122.37 (37.48)
Glucose [mg/dl]	82.09 (8.68)	79.72 (7.77)	85.03 (8.88)
Insulin [μIU/ml]	6.811 (3.76)	5.95 (3.65)	7.892 (3.63)
HOMA	1.393 (0.8)	1.17 (0.73)	1.669 (0.81)
QUICKI	0.376 (0.04)	0.39 (0.04)	0.363 (0.03)
FIRI	1.254 (0.72)	1.06 (0.66)	1.502 (0.73)

merase (Qiagen), and 1 μL of genomic DNA. DNA was denatured for 2 minutes at 95°C and then subjected to 40 amplification cycles. Each PCR cycle consisted of denaturation for 30 seconds at 95°C, annealing for 30 seconds at 60°C, and extension for 30 seconds at 72°C; followed by a final extension at 72°C for 5 minutes. Hold step at 4°C forever. 10 μL of 198 bp PCR products were digested with 10 U/μL *Lwe*I (S*fa*NI, Fermentas) restriction enzyme in a total volume of 20 μL (2 μL of Buffer Tango with BSA, Fermentas and 7.7 μL of sterile double distilled water) at 37°C overnight, incubated with 4 μL of *SYBER*Green for 15 minutes, and then separated by electrophoresis on 2% agarose gel. The presence of a single 198 — bp band corresponded to CC homozygotes, bands at 140 bp and 58 bp were related to GG homozygots, and the presence of all three bands represented GC heterozygots. Genotypes were confirmed separately by two experienced technicians assigned to the study.

Statistical analysis

Data are presented as means and standard deviations (SD). A nonparametric Mann-Whitney *U* test and Kolmogorov-Smirnov test were used to compare groups of genotypes. The minimal level of significance was fixed at $p < 0.05$ for all procedures. Results of borderline significance ($0.05 < p < 0.1$) were also taken into consideration. The statistical analysis was performed using Statistica 6.0 software.

Results

Table I presents the baseline characteristics of the study group. We observed that 25.87% of the whole group were overweight (BMI > 25 kg/m^2), the percentage of overweight women being 8.66%, and men 45.96%. Higher values of waist circumference, above the recommended 80 cm for women and 94 cm for men,

were observed in 10.82% of the women and 17.68% of the men. Although we excluded obese subjects (with BMI ≥ 30 kg/m^2) from the study, we found visceral obesity (according to the IDF criteria) in 0.43% of the women and 3.53% of the men.

Table II summarizes the data on lipid profile, glucose, insulin, and insulin sensitivity/resistance indices in the study group. Impaired fasting glucose was observed in 1.69% of the subjects, with 0.873% of the women and 2.717% of the men.

The genetic study revealed that the CC genotype was observed in 15.56%, the CG genotype in 52.74%, and the GG genotype in 31.7% in the subjects of our study group. The G and C allele frequencies were 58% and 42%, respectively.

IL-6 and CRP concentrations did not differ among the genotypes (Table III). There were also no differences regarding BMI and WHR (Table IV). The only differences among genotypes, observed only in men, were those concerning total fat (CC had higher fat content than CG and GG carriers), the difference being statistically significant between CC and GG ($p < 0.05$), and gynoidal fat deposit (CC had higher gynoidal fat deposit than CG and GG), the difference being statistically significant between CC and GG ($p < 0.025$), and between CC and CG ($p < 0.05$). These results are shown in Table IV. There were no differences in lipid concentrations, glucose levels, or insulin sensitivity/resistance indices among genotypes. These results are summarized in Table V.

Discussion

All the study participants were genotyped for IL-6 174G_C promoter polymorphism, with 15.56% having the CC, 31.7% the GG, and 52.74% the CG genotypes. The G and C allele frequencies were 58% and 42%, respectively. The allele frequencies are similar to those reported in previous studies for European whites [2–4, 10, 11].

In the late nineties a study by Fishman et al. on the biological relevance of IL-6 174G_C promoter polymorphism indicated that the C allele resulted in a lower *IL-6* gene expression than the G allele [9], suggesting that average IL-6 concentrations might be lower in subjects with the homozygous (CC) genotype. In addition, in a study by Terry et al., CC genotype was shown to be a weaker inducer of IL-6 gene expression than the G allele [12]. However, later studies in humans gave contradictory results [3, 13, 14]. In our study, IL-6 and CRP plasma levels were not significantly different among the genotypes of the IL-6 174G_C promoter polymorphism (Table 3), which is in accordance with the observations of Klipstein-Grobusch et al. [3] and Yang et al. [15].

Table III. *IL-6 and CRP concentrations according to the genotypes of the IL-6 174G_C promoter polymorphism in subgroups of women and men*

Tabela III. *Stężenie IL-6 i CRP w zależności od genotypu polimorfizmu genu* **IL-6 174G_C** *w podgrupach mężczyzn i kobiet*

	Il-6 concentration [pg/ml] (mean ± SD)					
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	16.4889 ± 4.62	18.2986 ± 9.1734	16.4889 ± 4.62	17.0897 ± 6.1134	18.2986 ± 9.1734	17.0897 ± 6.1134
	p > 0.1		p > 0.1		p > 0.1	
Men	15.9458 ± 5.5083	4.74228 ± 4.7422	15.9458 ± 5.5083	16.3543 ± 6.5774	4.74228 ± 4.7422	16.3543 ± 6.5774
	p > 0.1		p > 0.1		p > 0.1	
	CRP concentration [pg/ml] (mean ± SD)					
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	2.4119 ± 3.0378	4.4482 ± 13.297	2.4119 ± 3.0378	2.1041 ± 2.8881	4.4482 ± 13.297	2.1041 ± 2.8881
	p > 0.1		p > 0.1		p > 0.1	
Men	3.0357 ± 2.6944	2.5543 ± 2.7115	3.0357 ± 2.6944	4.5707 ± 9.9185	2.5543 ± 2.7115	4.5707 ± 9.9185
	p > 0.1		p > 0.1		p > 0.1	

Table IV. *Anthropometric features according to the genotypes of the* **IL-6 174G_C** *promoter polymorphism in subgroups of women and men*

Tabela IV. *Cechy antropometryczne w zależności od polimorfizmu genu* **IL-6 174G_C** *w podgrupach kobiet i mężczyzn*

			BMI [kg/m²] (mean ± SD)			
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	21.2213 ± 2.887	21.6614 ± 2.4708	21.2213 ± 2.887	21.4388 ± 2.4455	21.6614 ± 2.4708	21.4388 ± 2.4455
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	25.4959 ± 3.3534	24.3563 ± 2.7937	25.4959 ± 3.3534	24.5105 ± 2.7209	24.3563 ± 2.7937	24.5105 ± 2.7209
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
			WHR (mean ± SD)			
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	0.7312 ± 0.0470	0.7408 ± 0.0575	0.7312 ± 0.0470	0.7298 ± 0.0490	0.7408 ± 0.0575	0.7298 ± 0.0490
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	0.8736 ± 0.0572	0.8697 ± 0.0930	0.8736 ± 0.0572	0.8648 ± 0.0418	0.8697 ± 0.0930	0.8648 ± 0.0418
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
			Total fat [g] (mean ± SD)			
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	16 785.53 ± 5404.162	17 194.74 ± 4807.575	16 785.53 ± 5404.162	16951.10 ± 4551.274	17 194.74 ± 4807.575	16 951.10 ± 4551.274
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	18 142.50 ± 7084.946	15 679.13 ± 5248.462	18 142.50 ± 7084.946	17301.21 ± 6371.521	15 679.13 ± 5248.462	17 301.21 ± 6371.521
	$p < 0.05$		$p > 0.1$		$p > 0.1$	
			Androidal deposit [g] (mean ± SD)			
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	1044.11 ± 517.339	1161.49 ± 563.475	1044.11 ± 517.339	1109.56 ± 507.258	1161.49 ± 563.475	1109.56 ± 507.258
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	1811.41 ± 939.992	1533.75 ± 730.021	1811.41 ± 939.992	1657.29 ± 778.970	1533.75 ± 730.021	1657.29 ± 778.970
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
			Gynoidal deposit [g] (mean ± SD)			
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	5546.98 ± 1970.655	5372.06 ± 1381.852	5546.98 ± 1970.655	5373.29 ± 1366.971	5372.06 ± 1381.852	5373.29 ± 1366.971
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	4461.09 ± 1708.746	4013.06 ± 1311.770	4461.09 ± 1708.746	4178.91 ± 1323.939	4013.06 ± 1311.770	4178.91 ± 1323.939
	$p < 0.025$		$p < 0.05$		$p > 0.1$	

Table V. *Lipid profile, glucose, insulin, and indices of insulin sensitivity/resistance according to the genotypes of the* **IL-6 174G_C** *promoter polymorphism in subgroups of women and men*

Tabela V. *Profil lipidowy, stężenie glukozy, insuliny i wskaźniki wrażliwości /oporności na insulinę w zależności od polimorfizmu genu* **IL-6 174G_C** *w podgrupach kobiet i mężczyzn*

Total cholesterol [mg/dl] (mean ± SD)						
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	192.5405 ± 35.6811	188.4384 ± 32.4007	192.5405 ± 35.6811	188.0342 ± 29.0878	188.4384 ± 32.4007	188.0342 ± 29.0878
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	201.3750 ± 39.9367	204.3469 ± 45.0247	201.3750 ± 39.9367	198.2933 ± 40.5325	204.3469 ± 45.0247	198.2933 ± 40.5325
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Triglycerides [mg/dl] (mean ± SD)						
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	69.1892 ± 53.5100	64.6575 ± 32.9562	69.1892 ± 53.5100	62.9060 ± 27.2336	64.6575 ± 32.9562	62.9060 ± 27.2336
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	129.0833 ± 110.9477	95.8571 ± 51.7260	129.0833 ± 110.9477	93.0270 ± 56.6157	95.8571 ± 51.7260	93.0270 ± 56.6157
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
HDL-C [mg/dl] (mean ± SD)						
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	74.6757 ± 17.2208	71.3288 ± 14.5430	74.6757 ± 17.2208	69.2991 ± 15.7492	71.3288 ± 14.5430	69.2991 ± 15.7492
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	57.8696 ± 16.0378	55.6531 ± 12.3550	57.8696 ± 16.0378	56.7333 ± 11.9337	55.6531 ± 12.3550	56.7333 ± 11.9337
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
LDL-C [mg/dl] (mean ± SD)						
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	106.3429 ± 32.0587	104.1918 ± 28.7748	106.3429 ± 32.0587	106.1453 ± 27.5027	104.1918 ± 28.7748	106.1453 ± 27.5027
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	114.7895 ± 36.2853	130.0833 ± 40.5572	114.7895 ± 36.2853	122.2568 ± 38.5202	130.0833 ± 40.5572	122.2568 ± 38.5202
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Glucose [mg/dl] (mean ± SD)						
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	79.3514 ± 8.5284	78.9589 ± 7.1461	79.3514 ± 8.5284	80.3761 ± 7.9521	78.9589 ± 7.1461	80.3761 ± 7.9521
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	84.5455 ± 9.5405	86.2245 ± 7.6165	84.5455 ± 9.5405	86.2162 ± 8.6535	86.2245 ± 7.6165	86.2162 ± 8.6535
	$p > 0.1$		$p > 0.1$		$p > 0.1$	

Table V. *Continuation*

Tabela V. *Ciąg dalszy*

	Insulin [μIU/ml] (mean ± SD)					
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	5.6189 ± 3.0853	5.7817 ± 2.2446	5.6189 ± 3.0853	5.8096 ± 3.0401	5.7817 ± 2.2446	5.8096 ± 3.0401
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	6.6739 ± 2.1600	8.1792 ± 4.38741	6.6739 ± 2.1600	8.4041 ± 3.47856	8.1792 ± 4.38741	8.4041 ± 3.47856
	$p > 0.1$		$p > 0.1$		$p < 0.05$	
	QUICKI (mean ± SD)					
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	0.3913 ± 0.0396	0.3835 ± 0.0296	0.3913 ± 0.0396	0.3870 ± 0.0386	0.3835 ± 0.0296	0.3870 ± 0.0386
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	0.3685 ± 0.0260	0.3595 ± 0.0296	0.3685 ± 0.0260	0.3578 ± 0.0296	0.3595 ± 0.0296	0.3578 ± 0.0296
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
	HOMA (mean ± SD)					
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	1.1019 ± 0.6317	1.1254 ± 0.4417	1.1019 ± 0.6317	1.1612 ± 0.6314	1.1254 ± 0.4417	1.1612 ± 0.6314
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	1.4114 ± 0.4978	1.7484 ± 0.9553	1.4114 ± 0.4978	1.7843 ± 0.7829	1.7484 ± 0.9553	1.7843 ± 0.7829
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
	FIRI (mean ± SD)					
	CC	**GG**	**CC**	**CG**	**GG**	**CG**
Women	0.9917 ± 0.5685	1.0128 ± 0.3975	0.9917 ± 0.5685	1.0451 ± 0.5683	1.0128 ± 0.3975	1.0451 ± 0.5683
	$p > 0.1$		$p > 0.1$		$p > 0.1$	
Men	1.2702 ± 0.4480	1.5736 ± 0.8597	1.2702 ± 0.4480	1.6059 ± 0.7046	1.5736 ± 0.8597	1.6059 ± 0.7046
	$p > 0.1$		$p > 0.1$		$p > 0.1$	

It has been shown that many tissues, including adipose tissue, secrete IL-6, and that the levels of IL-6 correlate with BMI [16, 17]. There are also some studies indicating a link between IL-6 174G_C promoter polymorphism and BMI or other obesity indices [2, 3], especially in men [4]. However, although we observed slightly higher values of BMI and WHR in male carriers of the C allele, we did not find significant differences regarding BMI or WHR among the genotypes. A similar observation was made by other authors [1, 15, 17, 18].

There are interesting data demonstrating that genetic factors, among them IL-6 174G_C promoter polymorphism, may account for differences in therapeutic response to laparoscopic adjustable gastric binding (LAGB). Sesti et al. investigated the impact of IL-6 174G_C promoter polymorphism on weight loss in morbidly obese subjects after LAGB and a hypocaloric diet, showing that carriers of the GG genotype lost more weight than those with the CG or CC genotype [19]. This study shows that IL-6 174G_C promoter polymorphism may play an important role in the regulation of body weight. What is more, 174G_C promoter polymorphism of the IL-6 gene influences energy expenditure: subjects with the CC genotype of the IL-6 gene had significantly lower energy expenditure than subjects with the CG or GG genotypes, both in fasting and during the euglycaemic hyperinsulinemic clamp [1].

The results of Cardellini et al. indicate that the GG genotype of the IL-6 gene may contribute to variations in insulin sensitivity, resulting in impaired insulin sensitivity [18].

Increasing evidence suggests that low-grade inflammation, which is observed in obesity [20, 21], could be one of the determinants in the pathogenesis of insulin resistance and type 2 diabetes [22, 23]. Although there is one study showing a relationship between insulin resistance and IL-6 concentrations in non-obese subjects [24], in most cases elevated plasma and adipose tissue levels of IL-6 have been associated with insulin resistance, but in an obese state [23, 25]. This may explain why in our study of healthy non-obese subjects we did not observe any relationship between IL-6 174G_C promoter polymorphism and insulin resistance.

Conclusions

In conclusion, our data show that IL-6 174G_C polymorphism is not associated with features describing metabolic syndrome in non-obese healthy subjects.

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