



## 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, insulinoporność, 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<sup>2</sup>) women and 199 men aged 20–40 years, who were randomly selected from among Wrocław'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, neoplastic 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 Wrocław 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<sup>2</sup>]. 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<sub>0</sub>) and fasting insulin (I<sub>0</sub>) 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' (Prologo), 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<sub>2</sub>, 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 <sup>2</sup> ]	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 [ $\mu$ U/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  $\mu$ L 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  $\mu$ L of 198 bp PCR products were digested with 10 U/ $\mu$ L *LweI* (*Sfa*NI, Fermentas) restriction enzyme in a total volume of 20  $\mu$ L (2  $\mu$ L of Buffer Tango with BSA, Fermentas and 7.7  $\mu$ L of sterile double distilled water) at 37°C overnight, incubated with 4  $\mu$ L of SYBERGreen 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 homozygotes, and the presence of all three bands represented GC heterozygotes. 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<sup>2</sup>), 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  $\geq 30$  kg/m<sup>2</sup>) 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 $\pm$ SD)		
	CC	GG	CG
Women	16.4889 $\pm$ 4.62	18.2986 $\pm$ 9.1734	17.0897 $\pm$ 6.1134
Men	15.9458 $\pm$ 5.5083	4.74228 $\pm$ 4.7422	16.3543 $\pm$ 6.5774
	$p > 0.1$	$p > 0.1$	$p > 0.1$
	CRP concentration [pg/ml] (mean $\pm$ SD)		
	CC	GG	CG
Women	2.4119 $\pm$ 3.0378	4.4482 $\pm$ 13.297	2.1041 $\pm$ 2.8881
Men	3.0357 $\pm$ 2.6944	2.5543 $\pm$ 2.7115	4.5707 $\pm$ 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/m <sup>2</sup> ] (mean ± SD)			
		CC	GG	CC	CG
Women		21.2213 ± 2.887	21.6614 ± 2.4708	21.2213 ± 2.887	21.4388 ± 2.4455
		p > 0.1		p > 0.1	21.4388 ± 2.4455
Men		25.4959 ± 3.3534	24.3563 ± 2.7937	25.4959 ± 3.3534	24.5105 ± 2.7209
		p > 0.1		p > 0.1	24.5105 ± 2.7209
		WHR (mean ± SD)			
		CC	GG	CC	CG
Women		0.7312 ± 0.0470	0.7408 ± 0.0575	0.7312 ± 0.0470	0.7298 ± 0.0490
		p > 0.1		p > 0.1	0.7298 ± 0.0490
Men		0.8736 ± 0.0572	0.8697 ± 0.0930	0.8736 ± 0.0572	0.8648 ± 0.0418
		p > 0.1		p > 0.1	0.8648 ± 0.0418
		Total fat [g] (mean ± SD)			
		CC	GG	CC	CG
Women		16 785.53 ± 5404.162	17 194.74 ± 4807.575	16 785.53 ± 5404.162	16 951.10 ± 4551.274
		p > 0.1		p > 0.1	16 951.10 ± 4551.274
Men		18 142.50 ± 7084.946	15 679.13 ± 5248.462	18 142.50 ± 7084.946	17 301.21 ± 6371.521
		p < 0.05		p > 0.1	17 301.21 ± 6371.521
		Androidal deposit [g] (mean ± SD)			
		CC	GG	CC	CG
Women		1044.11 ± 517.339	1161.49 ± 563.475	1044.11 ± 517.339	1109.56 ± 507.258
		p > 0.1		p > 0.1	1109.56 ± 507.258
Men		1811.41 ± 939.992	1533.75 ± 730.021	1811.41 ± 939.992	1657.29 ± 778.970
		p > 0.1		p > 0.1	1657.29 ± 778.970
		Gynoidal deposit [g] (mean ± SD)			
		CC	GG	CC	CG
Women		5546.98 ± 1970.655	5372.06 ± 1381.852	5546.98 ± 1970.655	5373.29 ± 1366.971
		p > 0.1		p > 0.1	5373.29 ± 1366.971
Men		4461.09 ± 1708.746	4013.06 ± 1311.770	4461.09 ± 1708.746	4178.91 ± 1323.939
		p < 0.025		p < 0.05	4178.91 ± 1323.939

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	GG
Women		192.5405 ± 35.6811	188.4384 ± 32.4007	192.5405 ± 35.6811	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
		p > 0.1		p > 0.1	p > 0.1
		Triglycerides [mg/dl] (mean ± SD)			
		CC	GG	CC	GG
Women		69.1892 ± 53.5100	64.6575 ± 32.9562	69.1892 ± 53.5100	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
		p > 0.1		p > 0.1	p > 0.1
		HDL-C [mg/dl] (mean ± SD)			
		CC	GG	CC	GG
Women		74.6757 ± 17.2208	71.3288 ± 14.5430	74.6757 ± 17.2208	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
		p > 0.1		p > 0.1	p > 0.1
		LDL-C [mg/dl] (mean ± SD)			
		CC	GG	CC	GG
Women		106.3429 ± 32.0587	104.1918 ± 28.7748	106.3429 ± 32.0587	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
		p > 0.1		p > 0.1	p > 0.1
		Glucose [mg/dl] (mean ± SD)			
		CC	GG	CC	GG
Women		79.3514 ± 8.5284	78.9589 ± 7.1461	79.3514 ± 8.5284	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
		p > 0.1		p > 0.1	p > 0.1

Table V. Continuation

Tabela V. Ciąg dalszy

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

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 banding (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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