



Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/clnu>

Original article

Influence of *IL1B*, *IL6* and *IL10* gene variants and plasma fatty acid interaction on metabolic syndrome risk in a cross-sectional population-based study

Marina Maintinguer Norde, Erica Oki, Antonio Augusto Ferreira Carioca, Nágila Raquel Teixeira Damasceno, Regina Mara Fisberg, Dirce Maria Lobo Marchioni, Marcelo Macedo Rogero*

Department of Nutrition, School of Public Health, University of Sao Paulo, Dr. Arnaldo Avenue 715, São Paulo 01246-904, Brazil

ARTICLE INFO

Article history:

Received 3 October 2016

Accepted 9 February 2017

Keywords:

Metabolic syndrome

Interleukin

Polymorphism

Gene

Fatty-acid

SUMMARY

Background & aims: Metabolic syndrome (MetS) is a cluster of interrelated risk factors for type 2 diabetes mellitus, and cardiovascular disease, with underlying inflammatory pathophysiology. Genetic variations and diet are well-known risk factor for MetS, but the interaction between these two factors is less explored. The aim of the study was to evaluate the influence of interaction between SNP of inflammatory genes (encoding interleukin (IL)-6, IL-1 β and IL-10) and plasma fatty acids on the odds of MetS, in a population-based cross-sectional study.

Methods: Among participants of the Health Survey – São Paulo, 301 adults (19–59 y) from whom a blood sample was collected were included. Individuals with and without MetS were compared according to their plasma inflammatory biomarkers, fatty acid profile, and genotype frequency of the *IL1B* (rs16944, rs1143623, rs1143627, rs1143634 and rs1143643), *IL6* (rs1800795, rs1800796 and rs1800797) and *IL10* (rs1554286, rs1800871, rs1800872, rs1800890 and rs3024490) genes SNP. The influence of gene–fatty acids interaction on MetS risk was investigated.

Results: *IL6* gene SNP rs1800795 G allele was associated with higher odds for MetS (OR = 1.88; $p = 0.017$). Gene–fatty acid interaction was found between the *IL1B* gene SNP rs116944 and stearic acid (p inter = 0.043), and between rs1143634 and EPA (p inter = 0.017). For the *IL10* gene SNP rs1800896, an interaction was found for arachidonic acid (p inter = 0.007) and estimated D5D activity (p inter = 0.019).

Conclusion: The *IL6* gene SNP rs1800795 G allele is associated with increased odds for MetS. Plasma fatty acid profile interacts with the *IL1B* and *IL10* gene variants to modulate the odds for MetS. This and other interactions of risk factors can account for the unexplained heritability of MetS, and their elucidation can lead to new strategies for genome-customized prevention of MetS.

© 2017 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

1. Introduction

Metabolic syndrome (MetS) is a cluster of interrelated risk factors, which increase the risk of type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and cancer [1]. Each individual trait of MetS has an underlying inflammatory pathophysiology, which makes low-grade chronic inflammation the main target of lifestyle interventions [2,3].

Environmental factors, such as diet, can modulate MetS risk as well as inflammation status [4]. In this sense, dietary fatty acids (FA)

stand out for their inflammatory modulation properties [5,6]. Plasma FA profiles reflect dietary FA intake and FA endogenous synthesis and degradation, and have been used in a number of studies to investigate the association of FA subtypes and FA desaturase activity levels with inflammation or risk of MetS [7–9]. In this context, elevated plasma saturated FA – especially myristic acid (C14:0) and palmitic acid (C16:0) – palmitoleic acid (16:1 n-7) and estimated stearoyl-CoA desaturase (SCD) and delta-6-desaturase (D6D), as well as lower plasma linoleic acid (C18:2 n-6) and estimated delta-5-desaturase activity (D5D), are associated with MetS [7,8,10].

Besides environmental factors, genetic factors can also contribute to MetS risk. Genome Wide Association Studies (GWAS) have found a statistically significant association between single nucleotide polymorphisms (SNP) and MetS, predominantly located

* Corresponding author. Fax: +55 11 30617705.

E-mail address: mmrogero@usp.br (M.M. Rogero).

Abbreviations

AA	arachidonic acid
CI	confidence interval
CRP	C-reactive protein
CVD	cardiovascular disease
D5D	delta-5 desaturase
D6D	delta-6 desaturase
DHA	docosahexaenoic acid
EPA	eicosapentaenoic acid
FA	fatty acid
GWAS	Genome-wide association studies

HS-SP	Health Survey – São Paulo
IL	interleukin
MetS	metabolic syndrome
n-3	omega-3 fatty acids
n-6	omega-6 fatty acids
NFκB	Nuclear Factor κB
OR	odds ratio
SCD	stearoyl CoA desaturase
SNP	single nucleotide polymorphism
T2DM	type 2 diabetes mellitus
TLR	Toll-like receptor
TNF	tumor necrosis factor

in genes encoding proteins that regulate central nervous system hunger-satiety control and apolipoprotein synthesis [11]. However, although effective for screening for SNP-MetS risk, GWAS fail to detect gene–environment interactions, which can be a major determinant of risk variability [12].

Interleukin (IL)-6 and IL-1β are pro-inflammatory cytokines, and SNP in their genes have been shown to interact with dietary [13–16], plasma [17] and erythrocyte [18,19] FA to influence MetS traits, such as body mass index (BMI) [15,16,19], plasma high-density lipoprotein cholesterol (HDL-c) and triglycerides [14,18], plasma glucose [17] and blood pressure [13] in representative samples of the United States of America [13,14], Europe [15,17,19], South Africa [16] and China [18] populations. In turn, IL-10 is an anti-inflammatory cytokine [20], and *IL10* gene variants have been associated with CVD [21,22] and T2DM risk [23], but interactions between *IL10* gene polymorphisms and plasma fatty acids have not been investigated yet. Taking into account the need for replication studies of the interactions between *IL6* and *IL1B* gene polymorphisms and plasma fatty acids in a Brazilian population and the novelty of investigating gene–FA interactions for the *IL10* polymorphisms, the present study aimed to evaluate the influence of gene–FA interaction between SNP of *IL6*, *IL1B* and *IL10* genes and plasma FA on risk of MetS, using a candidate gene approach, in a subsample from a population based cross-sectional study involving the Health Survey – São Paulo (HS-SP).

2. Methods

2.1. Subject population

Data was derived from the population-based study HS-SP, a cross-sectional study, of health and living conditions among a representative sample of individuals living in São Paulo, south-eastern Brazil, which data collection took place between 2008 and 2011 and has been described in details elsewhere [24].

For the present study, all individuals from whom a blood sample was collected and who aged >19 y and <60 y (n = 301) at the time of blood collection were included. Minimum sample size of 300 was calculated based on a prevalence of 0.5 with a standard error of 0.07 at a 5% significance level and a design effect of 1.5.

The study protocol (protocol number 2001) was reviewed and approved by the Research Ethics Committee of the School of Public Health, University of São Paulo. All participants signed the informed consent form.

2.2. Data collection and processing

Information on food intake, demographics and socio-economic status was obtained using 24 h recall and structured

questionnaires, carried out between 2008 and 2009, during the first home visit by trained fieldworkers under standardized procedure. There were additional questions on smoking habits, classifying respondents as a current smoker or non-smoker. The International Physical Activity Questionnaire long form was applied to collect data on physical activity [25].

Body weight, height and waist circumference, along with systolic and diastolic blood pressures, were measured on the second home visit, carried out between 2010 and 2011, by trained research assistants, following standardized procedures, as described elsewhere [26]. BMI was calculated as weight (kg)/height² (m²). Blood pressure was determined as the mean of 2 consecutive measurements, on the right arm, taken with an automatic device (Omron model HEM-712C, Omron Health Care, Hoofddrop, Netherlands).

2.3. Biochemical measurements

Blood samples were obtained by venipuncture after 12 h of overnight fasting and immediately centrifuged, aliquoted and stored in a freezer at –80 °C until analysis. Plasma high sensitivity C-reactive protein (CRP) concentration was measured by kinetic turbidimetry, using the IMMAGE[®] immunochemistry system kit (Beckman Coulter Inc., Brea, CA, USA). Plasma IL-1β, IL-6, tumoral necrosis factor (TNF)-α and adiponectin were measured using a Multiplex immunoassay (Milliplex, Merck Millipore, Darmstadt, Germany). Plasma triglyceride, total cholesterol, HDL-c and low density lipoprotein cholesterol (LDL-c) concentration were measured on the Roche Modular Auto Analyzer using an enzymatic colorimetric assay (Roche Diagnostics GmbH, Mannheim, Germany). Plasma glucose was measured by GOD-trinder method, using the Glicose Liquiform[®] kit and the auto analyzer Labmax 240[®] (Labtest Diagnostica SA, MG, Brazil). Plasma insulin was measured using insulin AccuBind[®] ELISA kit (Monobind Inc, Lake Forest, CA, USA). Homeostasis model assessment for insulin resistance (HOMA-IR) was calculated [27].

2.4. Plasma fatty acid profile determination

Total plasma lipids were analyzed by gas chromatography, and the methodology has already been published by our group elsewhere [26]. Individual peaks were quantified as the area under the peak and results expressed as percentages of the total area of all FA peaks.

A total of 12 FA were identified and desaturase activities were also estimated using product: precursor ratios of individual plasma FAs according to the following: SCD activity index: SCD-16, palmitoleic acid (C16:1 n-7)/C16:0 or SCD-18, oleic acid (C18:1 n-9)/stearic acid (C18:0); D5D, arachidonic acid/dihomo-gamma-linoleic

Download English Version:

<https://daneshyari.com/en/article/8586892>

Download Persian Version:

<https://daneshyari.com/article/8586892>

[Daneshyari.com](https://daneshyari.com)