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Original Research

Physical activity, but not dietary intake, attenuates the effect of the FTO rs9939609 polymorphism on obesity and metabolic syndrome in Lithuanian adult population

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ABSTRACT

Objectives: This study aimed to examine the associations between the fat mass and obesity associated (*FTO*) gene rs9939609 variant with obesity and metabolic syndrome and interactions between *FTO* alleles, dietary intake and physical activity in Lithuanian adult population.

Study design: Cross-sectional study.

Methods: A health survey was carried out in randomly selected municipalities of Lithuania. The random sample was obtained from the lists of 25–64 year-old inhabitants. The data from 1020 individuals were analyzed. The single-nucleotide polymorphism, rs9939609, in the *FTO* gene was assessed using a real-time polymerase chain reaction. 24-hour recall was used for evaluation of dietary habits. Information on physical activity at work, traveling to and from work and at leisure time was gathered by a standard questionnaire.

Results: The carriers of the AA genotype had the highest mean values of body mass index (BMI) and waist circumference (WC). They had 1.72 time higher odds of obesity ($P = 0.009$) and 1.67 time higher odds of increased WC ($P = 0.013$) than those with the TT genotype. Carriers of the T allele had lower prevalence of metabolic syndrome compared to carriers of the AA genotype (33.8% and 42.5% respectively; $P = 0.018$). No interaction between the rs9939609 variant and energy or dietary intakes on weight status was found. Significant effect of the interactions 'genotype × age' and 'genotype × physical activity' on BMI was demonstrated. The *FTO* rs9939609 polymorphism was associated with anthropometric

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parameters and metabolic syndrome in the younger age group (25–44 years) and in individuals having low level of physical activity.

Conclusions: Age and physical activity modulated the effect of the *FTO* polymorphism on weight status and metabolic syndrome in Lithuanian adult population.

Introduction

The increasing prevalence of obesity and related comorbidities is a major public health problem worldwide.[1,2] Abdominal obesity is the main component of metabolic syndrome which is highly associated with type 2 diabetes.[3] Obesity is a consequence of unhealthy lifestyle and genetic susceptibility. In recent years, many common genetic variations in the human genome associated with BMI were identified.[4,5] Among those genes, the *FTO* gene on chromosome 16 explained the largest variation of BMI. Single nucleotide polymorphism (SNP), rs9939609, in the *FTO* gene was significantly associated with BMI and the risk of obesity in numerous independent populations.[6–8] This association was found in both children and adults.[9,10] However, some studies demonstrated that an effect of the *FTO* rs9939609 genotype on BMI was lower in elderly populations.[11,12] In addition, a positive association was determined between the *FTO* rs9939609 variant and risk of metabolic syndrome.[13–15]

The fact that not all individuals with the *FTO* gene obesity-risk allele are overweight indicates the importance of possible interactions with other genetic and/or environmental factors for weight gain. Previous studies reported that high physical activity could attenuate the effect of the *FTO* gene on body weight.[16–18] However, data on association of the *FTO* polymorphism with energy expenditure are controversial.[19,20] Most evidence suggests that the main reasons for the increase in body weight are an increased energy intake, decreased satiety and increased food responsiveness in the subjects with risk allele.[21–24] An understanding of the effects of interactions between lifestyle and genes on obesity has important public health implications for prevention and control of obesity and obesity-related metabolic complications.

Epidemiological studies have demonstrated that overweight and obesity are very prevalent in Lithuania. In 2014, almost every fifth adult (19% of men and 17% of women) was obese and every third was overweight.[25] Metabolic syndrome was found in 34% of the middle-aged population.[26] In Lithuania, obesity-related lifestyle factors have been investigated in many studies; however, there is a lack of data regarding the role of genetic factors and gene-environmental interactions for the risk of obesity and metabolic syndrome. The aim of this study was to examine the associations between the *FTO* rs9939609 variant with obesity and metabolic syndrome and interactions between *FTO* alleles, dietary intake and physical activity in Lithuanian adult population.

Methods

A cross-sectional health survey was carried out in five randomly selected municipalities of Lithuania, with populations ranging from 20,000 to 45,000. The random sample was obtained from the lists of 25–64 year-old inhabitants. Health examination including FTO genotyping was conducted for 1020 individuals (420 men and 600 women, response rate 58%).

The study protocol was approved by the Lithuanian Bioethics Committee. Written informed consent for participation in the study was obtained from all participants.

Anthropometric measurements were obtained by trained examiners according to a standardized protocol. The height of participants, without shoes, was measured to the nearest centimetre with a stadiometer. The body weight of participants, wearing light indoor clothing and no shoes, was measured to the nearest 0.1 kg with standardized medical scales. BMI was calculated as weight divided by height squared (kg/m^2). Overweight was defined as BMI of 25–29.9 kg/m^2, and obesity as BMI equal to or higher than 30 kg/m^2. WC was measured at the mid-point between the lower margin of the last palpable rib and the top of the iliac crest using a stretch-resistant tape, to the nearest 0.5 cm. Increased WC was defined using criteria of International Diabetes Federation ($\geq$94 cm for men and $\geq$80 cm for women).[3] In logistic regression analysis, the National Cholesterol Education Program Adult Treatment Panel III criteria of central obesity (WC $\geq$ 102 cm for men and WC $\geq$ 88 cm for women) were also used.[27]

Blood samples for lipid and glucose measurements were taken in the morning after fasting at least 12 h. Lipid and glucose levels were determined by an automatic analyzer using conventional enzymatic methods. All laboratory analyses were made in the same certified laboratory.

Metabolic syndrome was determined according to criteria of the International Diabetes Federation: central obesity defined as WC $\geq$ 94 cm for men and $\geq$80 cm for women plus any two of the following four factors: raised triglyceride level ($\geq$1.7 mmol/L); reduced level of high-density lipoprotein cholesterol (for men <1.03 mmol/L and for women <1.29 mmol/L); raised blood pressure (BP) (systolic BP $\geq$ 130 mm Hg or diastolic BP $\geq$ 85 mm Hg, or treatment of previously diagnosed hypertension); raised fasting plasma glucose ($\geq$5.6 mmol/L or previously diagnosed type 2 diabetes).[3]

A 24-h dietary recall was used for the assessment of dietary intake. The data were collected by trained dietary