Rocz Panstw Zakl Hig 2017;68(1):5-13

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REVIEW ARTICLE

THE ROLE OF MACRONUTRIENT INTAKE IN REDUCING THE RISK OF OBESITY AND OVERWEIGHT AMONG CARRIERS OF DIFFERENT POLYMORPHISMS OF FTO GENE. A REVIEW

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ABSTRACT

Obesity is a growing problem worldwide. The risk of the excessive body weight occurrence is a multifactorial issue. Environmental factors, lifestyle habits, diet, physical activity level, as well as genetic predisposition can increase obesity risk. One of the genes studied – the FTO gene - plays a crucial role in obesity occurrence. Individuals who carry risk alleles of specific single nucleotide polymorphisms (SNP) have a greater risk of being overweight. Recent studies revealed that specific macronutrient diet composition can influence differently on the FTO expression. The aim of this article is to review the recent literature on the topic of the FTO gene, its influence on overweight and obesity prevalence and the role of diet in modifying its impact on the risk of the excessive body weight occurrence. There are not many studies focusing on the dietary intervention influence on the FTO gene expression. As far as it has been researched it seems that the proper dietary habits can modify the FTO gene risk allele influence on obesity susceptibility.

Key words: *FTO gene, human, obesity, overweight, diet, diet therapy*

STRESZCZENIE

Otyłość jest rosnącym problemem na całym świecie. Ryzyko występowania nadmiernej masy ciała stanowi problem wieloczynnikowy. Czynniki środowiskowe, styl życia, dieta, poziom aktywności fizycznej, a także predyspozycje genetyczne mogą zwiększać ryzyko otyłości. Jeden z badanych genów - gen FTO - odgrywa kluczową rolę w występowaniu otyłości. Osoby, które są nosicielami alleli ryzyka specyficznych polimorfizmów pojedynczych nukleotydów (ang. SNP - *Single Nucleotide Polymorphism*) tego genu charakteryzują się większym ryzykiem wystąpienia nadwagi. Najnowsze badania wykazały, że specyficzny udział makroskładników diety może wpływać w różny sposób na ekspresję FTO. Celem niniejszego artykułu jest przegląd najnowszej literatury na temat genu FTO, jego wpływ na częstość występowania nadwagi i otyłości oraz roli diety w modyfikacji jego wpływu na ryzyko wystąpienia nadmiernej masy ciała. Niewiele jest badań dotyczących wpływu interwencji dietetycznych na ekspresję genu FTO. Tak dalece jak to zostało zbadane wydaje się, że odpowiednie nawyki żywieniowe mogą modyfikować wpływ alleli genu FTO na ryzyko wystąpienia otyłości.

Słowa kluczowe: *białko FTO, człowiek, otyłość, nadwaga, terapia dietą*

INTRODUCTION

Nutrigenetics is defined as a science that focuses on genetic differences among ethnic groups and individuals in population, which can influence the metabolism of diet components, therefore influence one's phenotype [29].

The aim of this science is to identify polymorphisms that occur in a single gene (SNP, Single Nucleotide Polymorphism), as well as the alleles responsible for the different organism's response to nutrients and bioactive substances. Exploring the individual genetic characteristics enables us to recommend the best, personalized nutrition, taking into account the individual allele status [29].

Polymorphism is the effect of point mutation occurrence in which this one nucleotide becomes substituted by another in the DNA sequence. Because of that substitution, different particles of informational RNA are created. The sequence of amino acids in the protein chain is changed too, what leads to functional and structural modification of the protein that is the product of gene expression [1].

In order not to qualify it as a mutation, the change must occur in at least 1% of the population [15]. Human genome includes approximately 10 million SNP, and it occurs on average in one in three hundred nucleotides [29]. Modification of DNA sequence can affect dually: positively in specific conditions and environment,

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however negatively in others. Changes in the genotype caused by the polymorphisms that lead to changes in protein activity and function, can increase the risk of metabolic diseases [15]. One of the possible gene variants, which differs in DNA sequence and influences single product, is called the allele [27]. If the genes' configuration, with the changed nucleotide, increase the possibility of disease occurrence, it is called a „risk allele". The disease possibility can be even bigger, if that individual has two specific polymorphism alleles, so called homozygote variant. Specific alleles of different polymorphism activity effect can sum up and increase the risk of disease occurrence [27].

It is established that fat tissue distribution and body weight are regulated with many genes such as: LEP, PPARɤ, ADRB3, CNR1 and FTO. FTO (Fat mass and obesity-associated gene) is the least known of these mentioned [28].

The FTO gene was first identified in 1999, with the study led on mutated mice. In 2007 the results of GWAS (Genome-wide Association Study) and the study by Frayling et al. [16] concerning the FTO gene discovery in the human genome and its influence on obesity occurrence in population were published [28, 40]. The meaning of FTO in obesity predisposition was confirmed with studies in several populations. What is more, this gene is said to be the strongest factor that increases probability of obesity known by now [20, 50]. The FTO gene can even contribute to 22% obesity cases in the population [13]. The prevalence of FTO gene polymorphism as well as the influence of its risk alleles vary between populations and ethnic groups. It has been assessed that the greatest role of FTO SNP in obesity susceptibility increase occurs in white Europeans and North Americans. In east and south Asia population, the occurrence of the FTO polymorphism risk alleles is lower, respectively 20% and 30%. In this group a weaker association between BMI and FTO polymorphisms variation is seen. However the researchers point out that there is a difference between BMI cut-off points defining overweight and obesity in European and Asian population [30].

It is suggested that the FTO gene influence on increased body weight is the least significant among black population. However several studies confirmed the association between FTO polymorphism and BMI in Afro-Americans [23]. It can be a clue, that environmental factors, such as lifestyle and dietary habits have a significant role in regulating SNP risk alleles influence level on obesity prevalence.

FTO gene is located on the long arm of chromosome 16 on position 12.2 and it consists of 9 exons. It occupies the area of more than 400 kb [6]. All FTO polymorphisms, discovered so far, are situated on its first and the biggest intron, the noncoding part of the gene [6]. The main FTO substrate is N(6) methyladenosine (m6a) RNA that is the most frequent modification of matrix RNA which occurs in eukaryotes. M6a methylation plays an important role in gene expression regulation, influencing the splicing process mainly by activating exons [55]. The FTO gene is highly expressed in fetus as well as in adult human. The highest level of its expression was identified to appear in the central nervous system. What is more, the FTO gene plays a role in regulation of growth and translation processes, causing retardation and organ malformations when deleted [20].

It is suggested that it has an important role in shaping food preferences, what explains the differences between macronutrient intake among different SNP alleles carriers [20]. What is more, *Brunwall* et al. [4] revealed that diet of rs9939609 polymorphism A risk allele carriers was richer in fatty meat, cheese, ice cream and cookies, compared to homozygous variant TT carriers.

Especially high levels of FTO gene expression occurs in hypothalamus, more precisely in the part that is responsible for appetite regulation, thereby the amount of energy received with food [38, 39]. High expression of FTO mRNA in adipocytes was demonstrated too [54]. Research review revealed that in mice FTO gene overexpression results in food caloric intake increase, that contributes to body weight and fat mass increase [20].

FTO gene mRNA amount is nutritionally modified [6]. Researchers demonstrated that FTO gene expression decreases after a 48-hour fast but on the other hand it increases on a high-fat diet. *Thung* et al. [53] study results analysis showed that 2.5-fold overexpression of FTO gene in Arcuate nucleus causes a 14% decrease in food calorie intake. A 40% expression decrease leads to a 16% larger calorie intake.

It is supposed that the FTO expression level depends on essential amino acid availability, which means their presence in diet too [5]. Limiting protein supply leads to mTORC1 enzyme activity reduction. This enzyme takes part in translation processes and cell growth, its high level inhibits cell autophagy processes. Autophagy processes target skeletal muscle proteins, that are the biggest protein store in the organism. That leads to lean body weight decrease, without affecting adipose tissue stores [58].

There are 19 polymorphisms of the FTO gene claimed to be associated with obesity susceptibility. Among these genes those that show the strongest association with the BMI and fat tissue level are: SNP rs1121980, rs9939973, rs7193144, rs9940128, rs8050136 and rs9939609, rs9939506 [40,x59].

According to World Health Organization data in 2014, 1.9 billion people over the age of eighteen were overweight. 600 million of them could be diagnosed as obese, based on the BMI value more than 30 kg/m^2 [37].

BMI of 30 kg/m^2 or higher increases risk of diseases such as hypertension, hyperlipidemia, type II diabetes and coronary heart disease. What is more, obesity is one of the risk factors of cancer of breast, uterus, esophagus and kidney [40].

According to WHO, the obesity is defined as an excessive body weight caused by fatty tissue accumulation. The obesity became one of the main health problems worldwide and it affects every ethnic and age group. Overweight and obesity are a rising issue all over the world [37].

The most frequently used anthropometric measure to diagnose obesity is BMI (Body Mass Index). Other indicators used are: WHR, waist circumference, body fatty tissue evaluation [17]. More than 25% of body fatty tissue implies obesity in men, 30% of fatty tissue in women [57]. The 57 studies meta-analysis Prospective Studies Collaboration showed that each 5 kg/m^2 BMI increase above the optimum range associates with 30% overall mortality increase, and a 60-120% increase of death resulting from diabetes or renal and hepatic diseases. Median life expectancy among people with 30-35 kg/m^2 BMI value is reduced by 2-4 years, and when it reaches 40-45 kg/m^2 median survival is even 10 years shorter compared to individuals with an optimum BMI level [41].

Obesity appears as an effect of excessive caloric diet intake in combination with insufficient physical activity, what leads to abnormal energy balance [15]. Body weight gain can be influenced by environmental, cultural and endocrinal factors as well as genetic predisposition [15].

Even 99.9% of genetic sequence is identical among individuals in population. The remaining 0.1% of the genome determines hair and eye color, height and other appearance properties, but also nutrient metabolism differences that can contribute to disease prevalence increase [46].

FTO GENE POLYMORPHISM INFLUENCE ON OVERWEIGHT AND OBESITY PREVALENCE

Within the FTO gene, rs9939609 SNP is the most weight gain influential polymorphism. Especially in European population, where allelic frequency of A risk allele is close to 60% and double A allele variant is associated with 3 kg higher body weight on average [6]. Carriers of G risk allele rs9930506 adjacent to rs9939609 are characterized by 1.3-fold higher BMI value. Among double G rs1781449 carriers obesity risk is 1.7-fold higher, and among TT rs1121980 polymorphism variant obesity susceptibility can be even 2.76-fold higher compared to double C carriers of this SNP. Being a carrier of each additional C allele of this polymorphism is associated with 0.22 kg/m^2 higher BMI value [47].

C*alussnitzer* et al. [48] examined FTO gene influence on adipocyte differentiation. The research showed that this gene can regulate the expression of two other genes: IRX3 and IRX5, that have a role in white and brown adipose tissue differentiation in fetal period. Low expression level of these two genes is associated with developing less white adipose tissue and more brown adipose tissue, which triggers thermogenesis. Correspondingly, increased expression level associates with greater white adipose tissue differentiation. Samples of subcutaneus adipose tissue obtained from 100 hundred healthy Europeans were examined. The analysis revealed, that among rs1421085 risk allele carriers IRX3 and IRX5 expression was increased what led to great amount of beige adipose tissue differentiation and, as a consequence, higher body weight. This mechanism can explain why double C allele carriers of this SNP have a 1.7-fold higher obesity risk compared to homozygous TT variant [48].

Studies involving adult population

In *Sonestedt* et al. [50] study, 4839 subjects in the population-based Malmo Diet and Cancer Study participants were examined. Participants were identified with FTO gene rs9939609 polymorphism variant. The researchers gathered anthropometric measurements, a detailed weeks' menu and a 168-item dietary questionnaire covering the previous year. Participants were also asked to fill the leisure-time physical activity assessment questionnaire. The data analysis showed that double A carriers of polymorphism examined were characterized by 1.7 kg higher body weight and they rarely undertook physical activity. Dietary interview of this group had significantly lower energetic value, and their diet was higher in total fat, and total carbohydrate intake was significantly lower compared to homozygotous TT variant carriers. It was also showed that AA variant carriers compared to TT carriers of FTO gene had higher obesity susceptibility, when consuming more fat and less carbohydrates. BMI value of AA carriers, whose diet was high-fat and low-carbohydrate was statistically higher compared to TT variant carriers being on the same diet. What is more, among AA carriers that had low physical activity level, BMI value was 0.8 kg/m^2 higher compared to TT carriers having the same physical activity level. Authors drew a conclusion, that limiting total fat intake could reduce obesity risk among SNP rs9939609 A risk allele carriers [50].

Similar conclusions were drawn by *Corel* et al. [8] Researchers examined the GOLDN and BPRHS populations focusing on association between diet components and BMI value with rs9939609 and rs1121980 polymorphisms. Analysis showed that individuals on high-fat diet who carry homozygotous

variant of T rs1121980 risk allele and A rs9939609 risk allele had higher BMI value. There was a positive association between saturated fatty acids intake and BMI. AA and TT variants carriers of polymorphism examined characterized by higher body weight.

KoGES research results carried out by *Baik* et al. [3] showed significant influence of SNP rs9939609 on hypertension risk among A risk allele carriers, who characterized by higher than 29 kg/m^2 BMI value.

Ahmad et al. [2] examined grup of 21675 women over 45 years old, Women's Genome Health Study participants. Participants had anthropometric measures made, physical activity level was assessed based on questionnaire and energy intake was evaluated based on past year food frequency questionnaire. The analysis revealed that allele A SNP rs8050136 carriers were characterized by increased obesity susceptibility compared to CC variant. A allele carriers who had hypercaloric diet and showed low physical activity level had 39% higher excessive body weight risk. Allele A carriers who undertaken physical activity and led hypocaloric diet still had a 13% higher obesity risk comparing to CC variant carriers. Each carried A allele increased the BMI by 0.57 kg/m^2.

Q*i* et al. [43] led meta-analysis of 40 studies focusing on the impact of FTO gene's different variants and macronutrients diet intake on BMI. Meta-analysis included data of 177,330 adults. Authors revealed that SNP rs9939609 A risk allele was associated with lower percentage of carbohydrate energy intake and higher protein intake. The authors also confirmed the previous reports concerning the diet energy underreporting by overweight individuals. A allele carriage was associated with lower caloric intake. There was no association with percentage of total fat intake in diet. These results were confirmed in meta-analysis extended to another 16 studies by *Livingstone* et al. [32]. Their results revealed that among carriers of risk alleles the percentage of total fat and protein in diet was higher.

More than that, *Sobczyk-Kopciol* et al. [49] and *Corella* et al. [9] revealed that polymorphism rs9939609 A risk allele carriers were characterized by significantly lower alcohol beverage intake compared to FTO gene TT variant carriers.

Studies involving children and adolescent population

Similar observations about significant rs9939609 A allele influence on BMI and fatty tissue content among children and adolescents were made by *Johnson* at al. [25], *Liu* et al. [31], *Wardle* et al. [56], and *Tonofsky-Kraff* et al. [51]. In Polish children population the influence of FTO gene on overweight and obesity was confirmed by *Tercjak-Recko* et al. [42], *Pyrzak* et al. and *Luszczynski* et al. [33].

In research led by *Johnson* et al. [25] the group of 2275 children, participants of ALSPAC study, were examined. The study was conducted in 10-year-old children, and then the data was collected again after 3 years. The anthropometric measurements were made, the FTO gene rs9939609 polymorphism variant was identified and the 3-day unweight diet diaries were collected. The results showed that FTO gene A allele carriers were characterized by higher energy intake and carrying each next A allele was associated with 0.35 kg fat mass increase in 13-year olds.

Another study conducted in children and adolescent population, participants of LACHY and ASPEX study was led by *Liu* et al.[31] and it showed significant association between double A allele carriage, BMI value, body weight and waist circumference. Each next copy of A allele was associated with 0.4 kg/m^2 higher BMI value, 1.3 kg higher body weight and 0.8 cm larger waist circumference.

T*onofsky-Kraff* et al. [51] led the study focusing on rs9939609 A allele carriage among children and adolescents aged between 9 and 16 years and its influence on loss of control (LOC) over eating. The anthropometric measurements were collected, Eating Disorder Examination questionnaire was administered to all participants to determine the LOC episodes presence. Then the experiment examine binge-eating behaviours was conducted. After an overnight fast the participants were provided with a breakfast and after a 6-hour break each participant was presented with a multiple-item test meal buffet. Children were invited to eat ad libitum. The analysis showed that among A allele carriers in 34.7% LOC episodes occurred, whereas among TT variant carriers there was 18.2% LOC episodes. During the experimental buffet meal participants with at least one A allele consumed a significantly greater percentage of fat compared to the TT subjects. Carrying at least one copy of A allele was associated with significantly higher BMI, BMI z scores and fat mass.

Luszczynski et al. [33] carried out a study on 968 Polish children aged 9-14 years, participants of FTO-DIAB study. In this study different rs9939609 polymorphism variants influence on body weight and metabolic indicators were researched. Data analysis showed significant positive association between double A allele carrying with BMI, body weight, waist and arm circumferences. In addition to this, AA variant carriers were characterized by higher blood pressure, triglycerides, fasting insulin level and HOMA index.

FTO gene polymorphism can also have influence on lower birth weight among newborns, which is a risk factor for excessive body weight in adults. In the study of *Descamps* et al. [12] SNP rs9939609 and rs990506 influence on birth body weight among 494 children-mother pairs. In both cases, the risk allele

occurrence in children was negatively associated with birth body weight. Each one risk allele of rs9939609 polymorphism was associated with 79 g lower body weight on average, whereas carrying rs9930506 risk allele - 83 g lower.

Studies involving elderly population

Jackobsson et al. [24] have analyzed anthropometric measurements, genetic tests and 7-day food record of 985 participants of Swede PIVUS study. The aim of the study was to examine the SNP rs9939609 and other FTO gene polymorphisms influence on excessive body weight occurrence in group of 70-year olds. The data analysis showed no association between variants investigated and BMI, waist circumference and fat mass among elderly. Authors have drawn a conclusion that the effect of FTO gene and its polymorphisms risk alleles decreases with age.

DIETARY INTERVENTION AND PHISICAL ACTIVITY INFLUENCE ON FTO GENE SNP EFFECT

So far, few studies have focused on identifying the most effective dietary intervention among different variants of the FTO gene polymorphisms carriers.

Life interventions in adult population

R*azquin* et al. [44] conducted the study, which aimed to examine the influence of 3-year dietary intervention including Mediterranean-style diet (MD) supplemented with nuts or virgin olive oil on different variant of the FTO gene rs9939609 polymorphism carriers. 776 individuals, participants of PERIMED study were enrolled in the study. The results obtained showed that, after 3 years of intervention with both Mediterranean-style diets, including nuts end olive oil as well, the A allele copy carriers had lower body weight compared to wild type subjects (TT). Among A allele carriers, individuals from the MD group were characterized by greater body weight loss compared to the low-fat control group. The study also showed the "protective effect" of Mediterranean diet on body weight change in AA homozygotes. In this group the lowest body weight gain during the study was observed.

A study led by *de Luis* et al. [11] investigated the influence of diet rich in mono- and polyunsaturated fatty acids on body weight loss, insulin resistance and cholesterol level. Dietary intervention was introduced in group of 233 overweight patients for two-month period. The result analysis showed that among A allele carriers of rs9939609 polymorphism a more positive effect of body weight loss was observed among individuals from the polyunsaturated fatty acid diet group. Another study [10] by this researcher revealed that dietary intervention among different variants of rs9939609 polymorphisms carriers including a 3-month hypocaloric low-fat or low-carbohydrate diet led to body weight decrease in both group independently of allele T or A carriage. In both groups BMI index, waist circumference and fat mass decrease was observed, and total cholesterol, LDL and fasting glucose level decreased as well. Leptin level decrease was recorded in both groups too. However the greatest decrease was observed in homozygous AA allele group following the low-fat diet.

In the study by *Zhang* et al. [59] a 2-year dietary intervention among The POUNDS LOST trial participants was introduced. 742 subjects, different variants of FTO gene rs558902, were enrolled in the study. The participants were assigned to one of the four diets differing in macronutrient composition. The percentage distribution of fat, protein and carbohydrates in the diets was as follows: 20, 15, 65%; 20, 25, 55%; 40, 15, 45%; and 40, 25, 35%. The results showed that a high-protein diet introduced among A allele carriers was associated with 1.38 kg higher body weight loss compared to low-protein diet. The greatest visceral fat and fat tissue loss was observed in the group where 25% of energy was derived from protein. In the study of *Grau* et al. [19] it was observed that among A allele of rs9939609 polymorphism carriers the drop-out percentage was lower for those randomized for low-fat diet compared to high-fat diet. In TT subjects the drop-out percentage was lower while they were on a high-fat diet, but the metabolic results were greater on a low-fat diet - HOMA-IR, HOMA-B indices decrease was greater and resting energy expenditure decrease was smaller compared to high-fat diet.

Dlouhá et al. [14] conducted a study which aimed to assess an association between different variants of rs17818902 and rs17817449 polymorphisms and body weight loss among women participating in 4-week program including dietary intervention and physical activity. The analysis results revealed that none of the polymorphisms studied had an influence on BMI change during the study.

No influence of FTO gene polymorphism on body weight loss during the dietary intervention in adult population was also showed in studies conducted by *Haupt* et al. [22] and *Matsuo* et al. [34].

The study concerning the role of the diet in 16 genes risk alleles influence on body weight change was conducted by *Goni* et al. [18] Based on the number of risk alleles they had, the participants were divided into two groups. First „low genetic risk group" included subjects with 7 or less risk alleles, while the second „high genetic risk group" included individuals with more than 7 risk alleles of genes studied. The results showed that in the „low genetic risk group"

higher intake of vegetables, vegetable protein and fiber lowered body fat mass. In the second group, higher animal protein intake was associated with greater body fat mass. High total fat, carbohydrates and protein intake were also positively correlated with body fat mass in this group. Authors also reported that total fat and monounsaturated fatty acids in diet have an important role in the influence of rs9939609 polymorphism on body fat mass.

Life interventions in children and adolescent population

The significance of the FTO gene risk allele occurrence in the body weight loss process in the adolescent population was examined by *Moreles* et al. [35] The researchers examined group of 168 adolescents, the EVASYON study participants. Researchers assesed the association between different 9 polymorphisms of 6 different genes (i.a. rs9939609 and rs7204609) with the BMI and body fat mass. Also the impact of SNP studied on both obesity indicators was assessed. The results showed significant influence of the FTO gene SNP rs9939609 on BMI value decrease. Participants who had more than 9 risk alleles of polymorphisms studied were characterized by lower body weight loss during the dietary intervention.

Similar results were obtained by *Reinher* et al. [45] in the study assessing the role of FTO gene rs9929609 and INSIG2 gene rs7566605 on body weight loss process among children. Analysis showed that among carriers of two risk alleles body weight loss after two-year lifestyle intervention was significantly lower compared to those who had no obesity-susceptibility risk allele.

On the other hand, the study carried out by *Zlatohalavak* et al. [60], which aimed to assess the role of FTO gene rs17817449 and MC4R gene rs8882313 polymorphisms in body weight loss process among 357 Czech children revealed that intensive lifestyle intervention including hypocaloric diet and great amount of physical activity (5x/d) led to better effects among risk allele carriers compared to those who did not carry any risk allele of the studied genes.

No association between polymorphism rs9939609 occurrence and body weight loss was showed in *Muller* et al. [36] and *Hankanen* et al. [21] studies.

Physical activity role in FTO gene influence on obesity-susceptibility modification

*T*he meta-analysis of studies focusing on physical activity influence on obesity risk among gene FTO rs9939609 risk allele carriers, made by *Kilpeläinen* et al. [26] showed that among A allele carriers of SNP studied probability of obesity occurrence was 27% lower, and probability of overweight occurrence was 26% lower when they were physically active, compared to those who led sedentary lifestyle. Authors compared 45 studies results including adult population and 9 studies including children and adolescent. The FTO gene polymorphism influence on BMI among physically active subjects was 30% lower compared to inactive subjects. What's more, among physically active A allele carriers waist circumference and fat mass were lower 33% and 36% compared to inactive group. Such an effect was not observed in children and adolescent studies.

CONCLUSIONS

Almost half of the world population can carry at least one of the FTO gene obesity-susceptibility alleles [20]. Analyzing the results of available data we can draw a conclusion, that the influence of these alleles on obesity prevalence can be modified by environmental factors, including proper diet and physical activity. The change of dietary habits, focusing on minimising western dietary model and reducing caloric intake in risk allele carriers' diet could be effective during the weight-loss process. Among the FTO gene risk alleles carriers such as rs9939609 A allele, rs1121980 T allele, rs1421085 C allele, introduction of dietary weight-loss intervention can be less effective. Proper macronutrient intake can increase the effectiveness of dietary intervention. Change of total fat intake, especially dietary sources of saturated fatty acids (SFA) can decrease the FTO gene SNP influence on body fat mass, and consequently on BMI. The positive effect can be obtained by adding food rich in mono- and polyunsaturated fatty acids such as nuts, seeds and olive oil to diet. In studies that included Mediterranean diet rich in monounsaturated fatty acids successful body mass reduction was obtained. The diet also influenced positively their lipid profile and insulin resistance [10, 59]. In another study participants who had hipocaloric, low-fat diet had similar, weight-reducing effect to those on a low-carbohydrate diet [10].

Introducing high-fat diet in the risk allele carriers group can influence negatively the FTO gene expression. High total fat intake, especially SFA, in diet can increase the gene expression resulting in the body fat mass and BMI increase.

Although so far there is no unequivocal evidence of specific diet positive influence on reducing the overweight and obesity risk among the FTO gene SNP risk allele carriers, it seems that every dietary intervention including high-fat foods and products rich in saturated fatty acids reduction may lead to intended effects.

Particular attention should be paid to the diet of children and adolescents, because the FTO gene expression is the highest during the growth period and decreases with age [24]. Introducing the proper dietary habits in this population would be beneficial in reducing the risk of overweight and obesity.

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Received: 16.08.2016
Accepted: 18.11.2016