Краткие сообщения

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PHYSICAL ACTIVITY ATTENUATES THE EFFECT OF THE FTO T/A POLYMORPHISM ON OBESITY-RELATED PHENOTYPES IN ADULT RUSSIAN MALES

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Introduction. Although the effect of the fat mass and obesity-associated (FTO) gene on adiposity is well established, there is a lack of evidence whether physical activity (PA) modifies the effect of FTO variants on obesity in Russians. Therefore, the purpose of this study was to examine PA influences and interactive effects between FTO variants and PA on measures of adiposity in Russians. **Materials and methods.** 110 Russian males aged 22–52 years old were examined. Anthropometry: height and weight, waist and hip circumferences were taken. The whole-body impedance was measured on the right-hand side of the body using the bio-impedance meter ABC-01 'Medas' (SRC Medas, Russia) according to a conventional tetrapolar scheme at a frequency of 50 kHz. For each subject participating in the study, the genotype was determined by the polymorphic systems of the T/A (rs9939609) polymorphism of the FTO gene (Lytekh, Moscow). **Results.** Participants who did not engage in regular PA exhibited higher BMI, fat mass, HC, and WC with statistical significance ($P \leq 0.01$). Although significant associations between the three FTO genotypes and adiposity measures were found in the sedentary group. There were no significant associations between FTO genotypes and obesity-related phenotypes in the PA group. **Conclusion.** Comparison of morphological parameters in carriers of alternative genotypes in two subgroups with different lifestyles makes it possible to conclude that the A allele determines a greater tendency to accumulate fat in cases where there is no regular physical activity.

Keywords: *physical activity, FTO, obesity, fat mass, BMI, Russians.*

Introduction. The spread of obesity in the modern world has reached the scale of a pandemic [4]. Overweight and obesity lead to a multitude of serious illnesses that result in disability or death of patients [4, 7]. The individual predisposition to weight gain and the speed of this process are influenced by the interaction of endogenous (genetic) and exogenous (environmental) factors [1, 3, 6]. Among a large number of molecular genetic markers associated with obesity, the FTO (fat mass and obesity-associated) gene is one of the most widely studied. The associations of the A allele in the first FTO intron (T/A, rs9939609) with a predisposition to fat accumulation and the risk of developing obesity and type 2 diabetes have been convincingly proven [1, 3]. Despite the ongoing study of FTO associations with a tendency to obesity in the context of lifestyle and diet peculiarities, age, sex, ethnicity, and other factors, the effect of the T/A substitution on fat accumulation and fat topography in the Russian population remains poorly studied. The purpose of the paper was to study the associations of the FTO T/A polymorphism with fat accumulation and fat topography in the group of Russian males depending on lifestyle specifics.

Materials and methods. 110 Russian males aged 22–52 years old were examined. Anthropometry: height and weight, waist and hip circumferences were taken. Standing height was measured using a Model 101 – Anthropometer (GPM manufacturers, Switzerland, http://www.seritex.com/gpm), and weight was measured on a digital scale. Both circumferences were measured using a measuring tape. Body mass index (BMI) was calculated as body mass (BM) divided by standing height (Ht) squared; waist/hip ratio was calculated as waist circumference divided by hip circumference. The whole-body impedance was measured on the right-hand side of the body using the bioimpedance meter ABC-01 'Medas' (SRC Medas, Russia) according to a conventional tetrapolar scheme at a frequency of 50 kHz. Body composition variables, such as fat-free mass, fat mass, skeletal muscle mass, active cell mass, were determined using appropriate equations provided by the manufacturer. Hand grip strength for right and left hands was measured with the dynamometer – DK 50.

Samples of buccal epithelium were used as the biological material for isolation of DNA genomic. The biological material was collected using sterile urogenital probes (Type A Universal, Jiangsu Suyun Medical Materials, China). For each subject participating in the study, the genotype was determined by the polymorphic systems of the T/A (rs9939609) polymorphism of the FTO gene (Lytekh, Moscow). Statistical processing of the data was carried out using the Statistica 8.0 software package (StatSoft, United States). To assess the significance of differences in the distribution of genotypes, the nonparametric $\chi 2$ test was used. To verify the normal distribution of the traits studied, the Shapiro–Wilk test was used. For the analysis of differences between the experimental and control groups in the mean values of indicators that did not follow the normal distribution, as well as for pairwise comparison of indicators between carriers of alternative genotypes, the Mann–Whitney test was used. To analyze the differences in the mean values of indicators that do not have a normal distribution, the Kruskal–Wallis test was used in groups of subjects with different FTO genotypes. To control the type I error in multiple pairwise comparisons of indicators that characterize obesity associated morphological traits, the Bonferroni correction was used; differences at $p < 0{,}017$ were considered significant. All subjects were informed of the research objectives and gave their informed consent.

Results. The frequencies of genotype occurrence in the total sample studied were FTO*TT 14%, FTO*AT 52,6%, FTO*AA 33,4%, which corresponds to the Hardy-Weinberg distribution ($\chi^2_{HW} = 1{,}65$ $p = 0{,}19$). The allele frequencies were 40% and 60% for FTO*T and FTO*A, respectively. For European populations, the A allele frequency ranges from 40 to 70% [4]. Distribution of genotypes of the FTO gene in the subgroups of the studied sample according to the level of physical activity of the subjects is displayed in table 1.

Table 1

Genotype distribution frequencies in the studied subgroups

Genotype	PA, n (%)	Sedentary, n (%)	P-value
FTO*TT	16 (28,2)	23 (42,1)	$\chi^2 = 13{,}3$ p = 0,0013
FTO*AT	35 (64,1)	20 (36,8)	
FTO*AA	4 (7,7)	12 (21,1)	

The analysis of associations of the FTO T/A polymorphism with anthropometric traits characterizing adiposity in general in the studied group revealed a connection between the A allele and the increased fat accumulation in the extremities. Many studies indicate a relationship between the A allele and high values of BMI and the ratio of waist circumference to hip circumference, indicators commonly used in medical screenings to assess the risk of metabolic syndrome, obesity, and type 2 diabetes [5, 7]. When reaching adulthood, exogenous factors come to the fore, such as the level of physical activity, diet peculiarities, and changes in socioeconomic status, which have the greatest impact on fat mass accumulation and can significantly mask individual genetic characteristics [2, 6].

The analysis of morphofunctional traits in two subgroups of males (22–52 years) with different lifestyles revealed significant differences in almost all traits characterizing fat content and fat topography (table 2).

The control group differs from the athletes in terms of higher values of fat mass (19,9 ± 5,5 vs 15,7 ± 5,6 kg, respectively. U = 578,0 p < 0,0001), body weight (88,3 ± 10,4 vs 81,1 ± 9,8 kg, re-

Table 2

Descriptive characteristics of participants by groups

Phenotype	PA Median ± IQR	Sedentary Median ± IQR	P-value
BMI (kg/m^2)	25,7 (22,6÷27,1)	28,1 (27,6÷30,1)	≤ 0,01
Fat mass (kg)	15,7 (10,6÷21,1)	19,9 (14,4÷24,5)	≤ 0,01
WHR	0,85 (0,81÷0,89)	0,89 (0,80÷0,96)	≤ 0,01
Fat free mass (kg)	65,4 (59,9÷71,2)	68,4 (63,1÷72,1)	0,05
Dynamometry	48,5 (41,0÷55,1)	47,3 (40,0÷54,2)	0,84

Note. IQR – interquartile range.

spectively. U = 618,5 $p < 0,0001$), BMI (28,1 ± 3,2 vs 25,7 ± 3,1 kg/m^2, respectively, U = 550,0 $p < 0,0001$), all skinfold thicknesses, and the ratio of waist circumference to hip circumference (0,89 ± 0,09 vs 0,85 ± 0,04, respectively. U = 409,0 $p < 0,0001$), which indicates a predominantly abdominal topography of fat deposition in the control group together with its excess, compared with the subgroup of athletes. Thus, representatives of the control group have the highest risks of multifactorial diseases associated with abdominal/visceral obesity [7]. Regular physical activity of medium and high intensity in adulthood is reflected in a significant decrease in the level of adiposity according to the results of caliperometry and bioimpedancemetry. However, it does not lead to significant differences in the amount of muscle (34,7 ± 3,1 and 35,8 ± 3,3 kg, U = 418,5 Z = 1,1 p = 0,25) and lean body weight (68,4 ± 5,9 and 65,4 ± 5,8 kg U = 358,5 Z = 1,9 p = 0,05), or strength indicators according to the results of hand dynamometry (47,3 ± 7,2 and 48,5 ± 7,1 kg, U = 445.5 Z = –0,2 p = 0,84) between the control and athlete subgroups. The obtained result is confirmed by several other studies on the effect of physical activity on obesity and metabolic syndrome [2, 5].

However, within these subgroups, which differ significantly in body composition, there are carriers of all three FTO genotypes. In our opinion, the studied sample makes it possible to evaluate the effect of regular physical activity on adiposity and associated risks of multifactorial diseases for carriers of alternative FTO alleles. The function of FTO is to regulate food intake and energy homeostasis [1]. It is shown that A allele carriers consume more food and prefer higher calorie food items [4], which leads to more intensive fat accumulation. In the subgroup of men who engage in regular sports activities at either the amateur or professional level, no significant differences were found between carriers of alternative genotypes. One of the most significant results of the effect of physical exercise on the traits studied is, in our opinion, a decrease in the amount of abdominal fat, which occurs in all men surveyed in this subgroup, regardless of the FTO genotype. The average value of BMI in the subgroup of athletes was 25,7 ± 3,1 kg/m^2, which, according to WHO standards, corresponds to overweight. However, bioimpedance study of the body composition of this group makes it possible to conclude that the increase in BMI is due to good development of muscle mass, not body fat. High BMI values are common in athletes and people involved in regular sports activities, while not accompanied by adverse changes in blood biochemical parameters that are typical for metabolic changes resulting from weight disorders [8]. In the control group, which is characterized by the highest body fat mass, a number of significant differences in somatic characteristics between carriers of different FTO genotypes were found. A allele carriers have a larger waist circumference and a higher value of the waist-to-hip ratio, which indicates the abdominal topography of adiposity. The absence of significant differences in the thickness of skin-fat folds on the abdomen against the background of differences in the above parameters suggests the development of visceral adiposity in A allele carriers (FTO*AA and FTO*TA) in the control group.

Conclusion. Comparison of morphological parameters in carriers of alternative genotypes in two subgroups with different lifestyles makes it possible to conclude that the A allele determines a greater tendency to accumulate fat in cases where there is no regular physical activity. In general, the results obtained for a group of adult Russian males confirm the associations of the FTO A allele with a predisposition to weight gain and obesity. In the absence of dietary restrictions and regular exercise, truncal (abdominal) adiposity develops in male A allele carriers, which is also accompanied by accumulation of visceral fat. The most effective way to reduce the risk of fat accumulation caused by the FTO A allele is a regular exercise, which ensures not only a low content of adipose tissue in the body but also sufficient development of muscle mass. Thus, our study highlights the possibility that genetic susceptibility to obesity may be modified by engaging in regular physical activity.

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РЕГУЛЯРНАЯ ФИЗИЧЕСКАЯ НАГРУЗКА СНИЖАЕТ ВЛИЯНИЕ А-АЛЛЕЛЯ ГЕНА FTO НА ПРЕДРАСПОЛОЖЕННОСТЬ К ОЖИРЕНИЮ В ГРУППЕ РУССКИХ МУЖЧИН

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Цель. Несмотря на то, что влияние жировой массы и связанного с ожирением гена FTO на набор веса хорошо изучено, по-прежнему недостаточно данных о том, меняет ли физическая активность воздействие вариантов гена FTO на избыточный вес у россиян. Таким образом, цель данного исследования – изучить влияние физической активности, а также воздействие вариантов гена FTO и физической активности на показатели ожирения у россиян. **Материалы и методы.** В исследовании приняли участие 110 мужчин из России в возрасте от 22 до 52 лет. Были получены следующие антропометрические данные: длина и масса тела, объем талии и бедер. Импеданс тела был измерен с правой стороны с использованием биоимпедансметра АВС-01 МЕДАСС (ООО НТЦ Медасс, Россия) на частоте 50 кГц в соответствии с традиционной тетраполярной схемой. У каждого участника исследования генотип определялся по полиморфным системам Т/А (rs9939609) полиморфизма гена FTO (лаборатория Литех, Москва). **Результаты.** Участники исследования, не практиковавшие регулярную физическую нагрузку, продемонстрировали более высокие статистически значимые показатели ИМТ, жировой массы, объема талии и бедер ($P \leq 0{,}01$). При этом в группе лиц, ведущих малоподвижный образ жизни, были установлены значительные корреляции между тремя генотипами гена FTO и показателями ожирения. Участники, практикующие регулярную физическую нагрузку, не продемонстрировали статистически значимых связей между генотипами гена FTO и связанными с ожирением фенотипами. **Заключение.** Сравнение морфологических параметров у носителей альтернативных генотипов из двух подгрупп, ведущих разный образ жизни, позволяет сделать вывод, что А-аллель определяет большую предрасположенность к накоплению жировой массы в отсутствие регулярной физической нагрузки.

Ключевые слова: *физическая активность, ген FTO, ожирение, жировая масса, ИМТ, население России.*

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