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T/A Polymorphism of the FTO Gene and Adiposity in Young Mongolian Men

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Objectives: The purpose of the paper was to determine the association between T/A polymorphism of the FTO gene and fat accumulation and localization in young urban ethnic Mongolian males. **Methods**: The anthropogenetic study was conducted 247 ethnic Mongolian males in Ulaanbaatar, Mongolia from 18 to 24 years of age, whose parents were both of Mongolian origin. A large number of anthropometric characteristics (about 50) were taken on each individual using a standardized technique. The group surveyed was divided into groups according to the BMI values recommended by WHO for Asia. General anthropometric characteristics and obesity-related indexes were compared between the overweight/obesity group and the control group. The genotyping for the polymorphic system of the fat mass and obesity-associated genes (T/A, *rs9939609*) was performed. The correlation between different genotypes and obesity-related anthropometric traits was analyzed. **Results:** Body mass, body mass index, waist circumference, hip circumference, waist-hip ratio, body fat percentage were higher in the overweight and obesity groups compared with controls. The frequencies of AA genotype and A allele in the obesity group were higher than those in the control group. The body weight, BMI, waist circumference, hip circumference, and waist-to-hip ratio in individuals with *rs9939609* AA and AT genotypes were significantly higher than in those with TT genotype. **Conclusion:** Young men in Ulaanbaatar, Mongolia carrying the A allele accumulate more fat with the same BMI, mainly in the abdominal region, which indicates increased risks of developing diseases associated with central obesity.

Keywords: Waist-Hip Ratio, Obesity, Abdominal, Genotype, Mongolia

Introduction

Chronic non-communicable diseases such as cardiometabolic and oncological diseases, cause morbidity and mortality in a significant proportion of the population in developed and developing countries. Their contribution to total mortality is projected to further rise to 69% by 2030[1]. Such diseases are mainly caused by overweight and obesity, which in turn are controlled by endogenous (genetic, ethnic, sex and age) and exogenous (socio-economic, environmental, lifestyle, and

nutritional) factors. Changes in body composition associated with increased fat mass and accumulated visceral fat, as well as abdominal fat deposition, cause persistent pathological changes in lipid and glucose metabolism[2,3]. Studies conducted in Mongolia over the past decades confirm the global trend of the increasing proportion of overweight and obese people. In Mongolia, the percentage of men whose body mass index (BMI) that satisfies the obesity criteria (BMI ≥ 30 kg/m^2) nearly doubled from 10.8% to 17.6% between 2005 and 2013[4-6]. The risk of developing comorbid diseases associated with abdominal fat deposition has also doubled over this period to 17.7% for men. The Mongolian population showed an increase in waist circumference, regardless of the rise in BMI, which indicates a growing trend in the development of central obesity[7]. The anthropometric changes described above, which were previously characteristic of middle and old age, are now found among adolescents and young adults of working age. These changes adversely affect the health of the rising generation[7].

The global obesity epidemic affects both developed and developing countries and results from the obesogenic environment interacting with an individual's genetic background[8]. In view of the increasing risks of developing various chronic non-communicable diseases against the background of being overweight, or having abdominal and visceral fat deposition, it is necessary to study the factors that allow us to reasonably predict an individual's predisposition to accumulate fat, as well as to assess the inclination of the population to gain weight at the population level. The most promising factors for such prediction include genetic markers since genetic characteristics remain unchanged throughout human life and set the limits of the variability of all traits in response to environmental factors. The FTO (fat mass and obesity-associated) gene is a reliable predictor of susceptibility to obesity. Single-nucleotide substitutions in the first intron of the FTO gene have been widely investigated, and associations of mutant alleles with the increased risk of obesity, metabolic syndrome, and type 2 diabetes have been confirmed[9,10]. Associations of the FTO A allele (T/A, *rs9939609*) with increased fat accumulation have been shown for a large number of populations and ethnic groups[11]. However, such data are not available for the Mongolian population to date.

The purpose of the paper was to determine the association between T/A polymorphism of the FTO gene and fat accumulation and localization in young ethnic Mongolian males.

Materials and Methods

Study population

Our anthropogenetic study surveyed 247 ethnic Mongolian males ranging in age from 18 to 24 years of age living in Ulaanbaatar, Mongolia. The survey materials were collected from 2012 to 2018 on the premises of the National Institute of Physical Culture of Mongolia and the Mongolian National University of Medical Sciences in Ulaanbaatar. The survey involved ethnic Mongolian males, whose both parents were of Mongolian origin. Information was collected on the amount of physical activity, climatic and geographical living conditions, and socio-economic status of those surveyed. The volunteers did not have any diagnosed chronic metabolic or cardiovascular diseases at the time of the survey. The study group was divided into categories according to the BMI values recommended by WHO for Asia[12]: normal weight (18.5-22.9 kg/m^2); overweight (23.0-27.4 kg/m); obese (≥27.5 kg/m2).

Survey method

All anthropometric measurements were measured with the participant bare-foot, in their underwear. A large number of anthropometric characteristics (about 50) were taken on each individual using a standardized technique[13]. Each participant's standing height was measured using an anthropometer (Model 101 – GPM manufacturers, Switzerland, http://www.seritex.com/gpm), and their weight was measured on a digital scale. Circumferences (chest, waist, hips, arm, forearm, thigh, lower leg) were measured using a measuring tape; skinfold thicknesses (subscapular, over triceps, over biceps, abdominal, suprailiac) were measured with Harpenden skinfold caliper. The whole-body impedance was measured on the right side of the body using the bioimpedance meter (ABC-01 'Medas', SRC Medas, Russia) using a conventional tetrapolar method 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[14].

The body mass index (BMI) was calculated from the measurements: BMI= W/L2, where W – weight in kilos, and L – height in meters.

The waist-to-height ratio or index for central obesity was calculated by dividing the waist circumference by height, both measured in centimeters.

Waist-to-hip ratio was calculated by dividing the waist circumference by hip circumference, both measured in centimeters.

The body adiposity index hip was the hip circumference divided by height$^{1.5}$ minus 18.

A hand dynamometer (DK-140, Russia) was used for handgrip strength testing. The strength of both the left and right hands was measured thrice each in a standing position (with the elbow in complete extension without touching any part of the body with the dynamometer), and the best score for each hand (kg_f) was used in the analysis. Samples of buccal epithelium were used as the biological material for isolation of genomic DNA. The biological material was collected using sterile urogenital probes (Type A Universal, Jingsu Suyun Medical Materials, China). For all subjects participating in the study who agreed to genotyping (n=169) buccal smears were collected, and the genotype was determined by the polymorphic system of the FTO (T/A, *rs9939609*). The genotyping was carried out at the Laboratory Lytech (Moscow, Russia).

Statistical analysis

Statistical processing of the data was carried out using the Statistica 12.0 software package (StatSoft, United States). To assess the significance of differences in the distribution of genotypes and alleles, the nonparametric Chi square test was used. To verify the normal distribution of the traits studied, the Shapiro–Wilk test was used. To analyze the differences in the mean values of indicators that did not have a normal distribution, the Kruskal–Wallis test was used in groups of subjects with different FTO genotypes (FTO genotypes grouping factor and anthropometric features as dependent variables) and for BMI groups (BMI levels as grouping factor and anthropometric features as dependent variables) comparison. For pairwise comparison of indicators between carriers of alternative genotypes and BMI groups, the Mann–Whitney test was used. A Bonferroni correction was used to control for the type I error in multiple pairwise comparisons with $p < .0167$, $p < .00033$, and $p < .000033$ considered statistically significant for results that would have been accepted as significant at the $p < .05$, $p < .001$, and $p < .0001$ respectively without the correction.

Ethical statements

The survey was conducted following the principles of bioethics. Institutional review board approval was received from the local Bioethics Committee of the Mongolian National Institute of Physical Education (No. 153 of March 16, 2011, and No. 262 of February 05, 2018) and from the local Bioethics Committee at the Faculty of Biology of the Lomonosov Moscow State University (No. 79-d of April 12, 2016 and No. 91-o of May 24, 2018), for the studies in 2011-2016 and 2017-2018, respectively. All volunteers who participated in the survey were informed of the survey objectives and methods and gave their written informed consent. Genetic samples were encoded, and all data were analyzed anonymously.

Results

General description of sample

The anthropometric characteristics and age of the study participants are presented in Table 1.

Table 1. Characteristics of the surveyed sample

Anthropometric features	Median (IQR)
Height, cm	169.4 (165.4-173.9)
Weight, kg	69.9 (63.0-80.7)
Fat mass, kg	10.5 (8.1-14.2)
Chest circumference, cm	92.2 (87.1-97.2)
Waist circumference, cm	77.2 (74.0-80.5)
Hip circumference, cm	96.1 (90.6-102.1)
Arm circumference, cm	30.0 (28.5-32.4)
Subscapular skinfold, mm	9.4 (8.2-12.0)
Triceps skinfold, mm	8.0 (5.6-11.0)
Biceps skinfold, mm	3.2 (2.4-5.0)
Abdominal skinfold, mm	11.2 (7.6-18.0)
Suprailiac skinfold, mm	7.9 (6.4-10.8)
Waist-to-hip ratio	0.83 (0.81-0.85)
Waist-to-height ratio	0.46 (0.44-0.48)
Body mass index, kg/m^2	24.6 (22.7-26.9)
Body adiposity index	25.6 (24.1-27.8)
Age, yrs	20.0 (18.9-23.0)

Abbreviation: IQR, interquartile range

These characteristics were stratified into three categories according to the BMI values for Asian populations (Table 2). As expected, the categories were statistically significantly different in almost all attributes that reflect fat accumulation and localization. No significant differences were found between the results of the right and left handgrip test ($p = .063$ and $p = .305$, respectively). Comparison of the normal and overweight

groups demonstrated that the subcutaneous fat thickness for triceps and biceps skinfolds not differ from each other (U = 892.0, Z= .100, p = .920 and U = 876.5, Z = -.229, p = .817, respectively). Likewise, no significant differences were found between these categories in the parameters that characterize truncal fat localization: abdominal skinfold (U = 779.0, Z = -1.044, p = .296), suprailiac skinfold (U = 814.0, Z = -1.357, p = .174), waist-to-hip ratio (U = 3302.5, Z = -0.998, p = .317), subscapular skinfold (U = 621.0, Z = -2.364, p = .018) and fat mass calculated from body adiposity index data (U = 791.0, Z = -1.906, p = .057). This lack of differences existed despite the high values of these attributes in the overweight group. The overweight and obese groups showed statistically significant differences in all parameters, except for the skeletal muscle mass calculated from body adiposity index data (U = 78.0, Z = -1.403, p = .160). Thus the increase in weight and other attributes was due to excess fat. Normal weight and obese groups differed in all parameters with a high degree of confidence (p<.0001), except for handgrip test results (U = 57.5, Z = -0.955, p = .339 and U = 74.5, Z = -0.053, p = .957) for the right and left hands, respectively. Thus, the anthropometric characteristics stratified by BMI categories differed mainly in the parameters

Table 2. Anthropometric characteristics of the study population stratified according to BMI categories for Asian populations.

Anthropometric features	Body Mass Index Category, Median (IQR)		
	Normal weight	Overweight	Obesity
Body mass index, kg/m^2***	21.6 (20.6-26.9)	24.9 (23.9-25.8)	29.8 (29.0-31.8)
Waist-to-height ratio***	0.44 (0.42-0.45)	0.46 (0.45-0.48)	0.52 (0.51-0.57)
Body adiposity index***	23.4 (21.7-22.4)	25.6 (24.6-26.9)	29.3 (28.2-31.2)
Waist-to-hip ratio*	0.82 (0.81-0.84)	0.83 (0.81-0.85)	0.87 (0.85-0.92)
Height, cm**	166.9 (162.8-171.4)	169.7 (165.9-174.5)	172.1 (168.4-175.6)
Weight, kg***	60.0 (56.8-63.3)	71.1 (66.8-77.3)	88.5 (83.6-97.9)
Chest circumference, cm***	85.6 (83.4-88.4)	92.8 (90.0-95.8)	102.8 (99.9-105.6)
Waist circumference, cm***	73.0 (70.0-75.1)	78.0 (75.8-80.2)	87.6 (85.1-94.5)
Hip circumference, cm***	89.3 (86.0-92.1)	96.6 (93.0-101.0)	106.5 (103.0-110.5)
Arm circumference, cm***	27.0 (25.0-28.8)	30.5 (29.2-32.2)	35.5 (33.2-36.6)
Subscapular skinfold, mm***	8.6 (7.6-10.4)	9.2 (8.2-11.4)	14.8 (12.2-27.0)
Triceps skinfold, mm**	7.8 (5.8-9.0)	7.0 (5.4-11.0)	14.0 (10.6-17.2)
Biceps skinfold, mm*	3.0 (2.4-3.6)	3.0 (2.4-5.0)	4.0 (3.2-7.2)
Abdominal skinfold, mm***	10.4 (6.8-13.0)	10.0 (7.4-17.0)	23.0 (12.2-36.0)
Fat mass, kg***	8.2 (5.9-10.3)	10.3 (8.1-13.2)	19.1 (18.6-23.3)
Fat free mass, kg**	52.7 (48.7-56.9)	59.4 (57.0-63.6)	66.5 (62.1-70.9)
Skeletal muscle mass, kg	30.0 (27.6-31.9)	33.1 (31.2-35.2)	35.6 (33.4-36.0)
Handgrip strength (right), kg$_f$	32.0 (30.0-38.0)	38.5 (33.0-46.0)	35.0 (33.0-46.0)
Handgrip strength (left), kg$_f$	35.0 (30.0-38.0)	38.0 (32.0-40.5)	33.0 (29.0-44.0)

* p-value calculated between BMI groups using the Mann-Whitney test with Bonferroni correction. * p < .0167, ** p < .00033, *** p < .000033

Table 3. P-values for the pairwise comparisons of anthropometric measurements between the three categories of BMI values for Asian populations.

Anthropometric features	Normal weight - Overweight	Overweight - Obesity	Normal weight - Obesity
Body mass index, kg/m^2	.000	.000	.000
Waist-to-height ratio	.000	.000	.000
Body adiposity index	.000	.000	.000
Waist-to-hip ratio	.318	.002	.001
Height, cm	.004	.031	.000
Weight, kg	.000	.000	.000
Chest circumference, cm	.000	.000	.000
Waist circumference, cm	.000	.000	.000
Hip circumference, cm	.000	.000	.000
Arm circumference, cm	.000	.000	.000
Subscapular skinfold, mm	.018	.000	.000
Triceps skinfold, mm	.920	.000	.000
Biceps skinfold, mm	.818	.014	.000
Abdominal skinfold, mm	.174	.001	.000
Fat mass, kg	.056	.000	.000
Fat free mass, kg	.006	.019	.005
Skeleto-muscle mass, kg	.020	.160	.013
Hand grip strength (right), kg_f	.017	.697	.339
Hand grip strength (left), kg_f	.133	.457	.957

* p-value between BMI categories using the Mann-Whitney test.

Table 4. Genotype distribution of the normal and high BMI groups.

Genotype	Normal BMI, n	Elevated BMI, n	*p-value
FTO*TT	26	56	
FTO*TA	15	48	p = .148
FTO*AA	3	21	

* p-value between the normal (BMI≤22.9) and overweight and obese groups (BMI≥23.0) BMI using the chi-square test.

that characterize fat accumulation. The largest differences were found between normal BMI and obese groups, while normal and high BMI groups were very similar in anthropometric traits.

Population-based genetic study

The frequencies of genotypes in the sample surveyed were FTO*TT 48.5%, FTO*AT 37.3%, and FTO*AA 14.2%. The genotype frequencies in participants with normal BMI (≤ 22.9 kg/m) and elevated BMI (≥ 23.0 kg/m^2) categories (Table 3) were, respectively: FTO*TT 59.1%, FTO*AT 34.1%, and FTO*AA 6.8%, FTO*TT 44.8%, FTO*AT 38.4%, and FTO*AA 16.8% (Chi^2 =3.81, p = 0.148). The differences in allele frequencies between participants with normal BMI (FTO*T 76% and FTO*A 24%) and an elevated BMI (FTO*T 64% and FTO*A 36%) were on the border of statistical significance (Chi^2 = 3.81, p = .051). The allele frequencies in the study population stratified into BMI categories are in Table 4. The increase in the A allele frequency with the increasing BMI of those surveyed was statistically significant between the normal weight and overweight groups (Chi^2 = 3.99, p = .046). The allele frequencies in the overweight and obese groups were not significantly different (Chi^2 = .11, p = .742).

Analysis of Associations between T/A Polymorphism and Anthropometric Parameters

The anthropometric characteristics of participants who were carriers of alternative FTO genotypes in the study population

are presented in Table 5. In general, AA genotype carriers were characterized by the highest values of almost all studied traits characterizing fat content and fat topography; however, only some differences reach the level of statistical significance. With the numbers available, we conclude that those surveyed whose genome contains at least one risk allele (AT and AA genotypes) had no significant differences in the anthropometric traits and indices studied. The carriers of the two original alleles (TT*FTO) have thinner subscapular (U = 801.5, Z = -2.365, p = .016), biceps (U = 724.5, Z = -2.938, p = .003), and abdominal (U = 677.5, Z = -3.289, p = .0008) skinfolds compared with the heterozygous genotype carriers.

The anthropometric characteristics of carriers of stratified by alternative FTO genotypes are presented in Table 6. Pairwise comparisons revealed statistically significant differences in chest circumference (U = 80.0, Z = -3.086, p =.001) and biceps skinfold thickness (U = 28.0, Z = -2.463, p = .011) between carriers of TT and AT genotypes in terms in the normal BMI group. In the elevated BMI category, TT carriers differ from AT carriers only in their abdominal skinfold thickness (U = 356.5, Z = -2.996,

Table 5. FTO alleles frequencies of study participants (n = 169) stratified into BMI categories.

Allele	Normal Weight, %	Overweight, %	Obese, %	p-value
FTO*T	76.0	63.1	66.2	p = .046
FTO*A	24.0	36.9	33.8	

* p-value comparing the frequency of FTO*T with FTO*A in the BMI categories for Asians using the chi-square test.

Table 6. Anthropometric characteristics of who are carriers of alternative FTO genotypes.

Anthropometric features	Genotype		
	FTO*TT	FTO*TA	FTO*AA
Number of subjects	82	63	24
Body mass index, kg/m^2	24.5 (22.4-27.3)	25.2 (23.1-26.9)	25.4 (24.1-28.8)
Waist-to-hip ratio	0.45 (0.44-0.48)	0.46 (0.44-0.48)	0.47 (0.45-0.49)
Height, cm	168.0 (163.4-172.2)	168.7 (163.8-176.3)	172.0 (166.9-175.5)
Weight, kg	68.1 (61.8-80.5)	71.5 (64.4-82.4)	76.9 (67.6-83.4)
Chest circumference, cm*	90.6 (86.0-96.7)	93.0 (88.5-98.6)	94.8 (91.3-100.2)
Waist circumference, cm	76.2 (73.7-79.1)	77.9 (74.1-81.6)	78.4 (73.0-86.5)
Hip circumference, cm	94.7 (89.0-102.5)	95.5 (92.0-101.0)	100.1 (95.2-103.6)
Thigh circumference, cm	54.4 (52.0-57.3)	54.3 (52.9-60.2)	52.0 (51.2-61.3)
Arm circumference, cm	29.3 (28.0-32.3)	30.5 (28.8-33.0)	32.2 (28.0-33.4)
Subscapular skinfold, mm*	9.00 (7.8-11.0)	10.2 (8.6-14.0)	10.0 (9.3-12.6)
Triceps skinfold, mm	6.9 (5.6-9.4)	9.0 (6.2-12.0)	9.0 (5.0-12.4)
Biceps skinfold, mm**	2.8 (2.4-3.5)	3.8 (2.8-7.2)	3.2 (2.4-5.2)
Abdominal skinfold, mm**	9.5 (7.1-12.9)	14.0 (9.0-20.0)	12.2 (9.0-22.0)
Waist-to-hip ratio	0.83 (0.81-0.85)	0.83 (0.81-0.85)	0.84 (0.45-0.49)
Fat mass, kg**	10.6 (8.1-14.2)	9.9 (8.1-13.4)	17.9 (16.7-19.1)

* p-value calculated between FTO genotype groups, Mann-Whitney test with Bonferroni correction * $p < .017$ ** $p < .0003$

Table 7. Anthropometric characteristics of carriers of alternative FTO genotypes in normal and high BMI groups

Anthropometric features	Normal BMI			p-value	Elevated BMI			p-value
	FTO*TT	FTO*TA	FTO*AA		FTO*TT	FTO*TA	FTO*AA	
Body mass index, kg/m^2	21.5 (20.6-26.9)	22.3 (21.9-22.5)	21.9 (21.4-22.5)	p =.07	25.8 (24.4-28.7)	25.6 (24.9-27.2)	25.8 (24.5-29.2)	p =.97
Waist-to-height ratio	0.43 (0.42-0.45)	0.44 (0.43-0.45)	0.45 (0.44-0.45)	p =.37	0.46 (0.45-0.49)	0.47 (0.45-0.49)	0.48 (0.47-0.49)	p =.69
Body adiposity index	23.1 (20.3-22.4)	24.4 (22.4-25.8)	24.4 (23.3-25.0)	p =.23	26.4 (24.7-29.0)	26.0 (24.6-27.9)	26.6 (25.1-28.5)	p =.53
Height, cm	166.5 (162.7-171.0)	165.2 (159.5-168.9)	170.5 (161.4-171.2)	p =.56	168.7 (164.0-172.5)	169.7 (165.0-177.8)	173.0 (167.7-176.4)	p =.17
Weight, kg	60.0 (57.4-62.7)	61.0 (56.8-64.4)	62.3 (57.0-66.6)	p =.66	73.9 (66.6-83.3)	75.4 (69.3-83.7)	79.7 (72.9-83.8)	p =.49
Chest circumference, cm	84.9 (82.0-86.4)	88.4 (86.3-89.9)	89.5 (84.1-94.2)	p =.004	94.9 (20.6-26.9)	94.4 (91.2-99.3)	96.0 (92.6-100.2)	p =.82
Waist circumference, cm	73.0 (68.2-75.5)	71.7 (71.3-75.0)	73.0 (71.9-75.9)	p = .98	77.4 (75.9-82.4)	80.0 (76.5-84.0)	81.8 (78.0-86.5)	p =.40
Hip circumference, cm	89.1 (85.0-91.9)	90.0 (86.6-93.5)	93.0 (87.0-95.8)	p =.46	98.0 (93.1-105.6)	97.5 (94.5-101.9)	101.5 (98.5-105.0)	p =.44
Subscapular skinfold, mm	8.0 (7.3-8.9)	8.8 (8.5-11.2)	11.0 (9.5-13.4)	p = .143	9.7 (8.1-11.7)	10.6 (9.0-16.0)	9.9 (9.3-12.6)	p =.29
Triceps skinfold, mm	6.5 (5.6-8.4)	8.4 (7.2-9.4)	9.0 (8.0-12.0)	p =.16	7.2 (5.5-10.7)	9.0 (5.6-13.0)	10.4 (5.0-12.4)	p =.56
Biceps skinfold, mm	2.6 (2.4-3.1)	3.6 (3.0-4.0)	4.0 (3.8-5.3)	p =.02	2.8 (2.3-4.0)	3.7 (2.6-7.2)	3.0 (2.4-5.2)	p =.10
Abdominal skinfold, mm	8.7 (6.5-12.3)	11.0 (7.8-15.8)	12.0 (8.2-16.0)	p =.52	9.0 (7.1-13.0)	14.6 (9.6-20.0)	15.8 (9.0-22.0)	p =.008
Waist-to-hip ratio	0.82 (0.81-0.84)	0.82 (0.81-0.83)	0.84 (0.83-0.85)	p = .64	0.83 (0.82-0.85)	0.83 (0.81-0.85)	0.86 (0.82-0.88)	p =.62
Fat mass, kg	8.8 (5.6-10.8)	7.6 (7.5-10.9)	9.0 (8.6-10.8)	p = .76	11.6 (8.2-15.3)	10.0 (8.7-13.9)	17.9 (16.7-19.1)	p = .16
Fat-free mass, kg	53.6 (49.0-57.0)	48.4 (48.0-50.0)	52.8 (49.6-55.0)	p = .83	59.4 (57.3-63.3)	60.2 (55.0-64.0)	65.2 (63.6-66.8)	p = .35
Hand grip strength (right), kg_f	32.0 (29.0-38.0)	33.5 (31.0-37.0)	38.0 (36.9-41.2)	p =.59	36.0 (32.0-51.0)	38.0 (32.0-46.0)	38.0 (35.0-38.0)	p =.99
Hand grip strength (left), kg_f	35.0 (28.0-36.0)	37.0 (33.5-39.0)	36.0 (32.6-38.6)	p =.18	37.5 (30.0-48.0)	38.0 (30.0-40.0)	40.0 (34.0-40.0)	p =.81

* p-value calculated between FTO genotype groups for the normal BMI (≤22.9) and high BMI (>23.0) groups separately. Mann-Whitney test with Bonferroni correction was used

p = .002). In both categories, the AT and AA genotype carriers did not have statistically significant anthropometric differences. Thus, we were unable to draw conclusions on the difference in the fat content or the particularities of fat localization.

The anthropometric characteristics of carriers of stratified both by alternative FTO genotypes and BMI level are presented in Table 7.

Discussion

The scale of obesity in today's world and the increasing levels of associated cardiometabolic and oncological diseases caused by obesity cause the scientific community to comprehensively study the causes of obesity. Information regarding the factors that increase the risk of obesity may make it possible to develop strategies to prevent obesity and effective treatment methods. These may decrease the disability and mortality from obesity-associated comorbid diseases. Almost every country in the world in recent decades has seen a steady increase in the proportion of overweight and obese people of all age and gender groups. Similar trends are observed in Mongolia's adult population[4-7]. Obesity in adolescents and youth negatively affect the physical

condition and health of the rising generation and the working population. Over the past decades, the proportion of the population over the age of 15 with overweight and central obesity has increased[15].

The median body fat percentage in our group of young Mongolian males was 15.6%, and their body adiposity index value was 25.6%. These results indicate increased risks of cardiovascular diseases and type 2 diabetes in general for young males living in Ulaanbaatar, Mongolia. A study of overweight risk factors in a similar group of ethnic male Mongolians living in Inner Mongolia, China, found that a total body fat percentage over 25% increased the risk of these diseases by 3.7[16]. The data obtained from screening surveys of Mongolia's adult population in 2005-2013 indicate a progressively rising risk for the illnesses comorbid with obesity in the light of increasing waist circumference in those surveyed[7]. In general, the volunteers surveyed in this study had normal values of the above traits and indices (Table 1) that characterize central (abdominal) obesity. This may be due to many of group participating in regularly (28.3%). However, the group had a heterogeneous BMI composition. Of the 247 volunteers, 57.2% were of normal weight, 34.8% were overweight, and 10.5% were obese, according to the WHO classification for Asian countries[12]. Two percent of those surveyed were underweight (BMI<18.5kg/m^2). The analysis of anthropometric traits associated with fat content and fat topography revealed numerous expected statistically significant differences (Table 2). These were caused by an increase in the values of the traits reflecting the endomorphic component of the body composition, between the normal weight and obese groups. Indices which indicate the development of abdominal obesity and visceral fat deposition increased significantly with increasing in BMI among those in our survey, portending increased risks of cardiometabolic diseases in participants with high BMI[3,17]. It is well known that waist circumference, waist-to-hip circumference ratio, waist-to-height ratio, used to assess central (abdominal) obesity, are closely associated with metabolic markers, which in turn indicate the development of cardiometabolic diseases based on general obesity estimated by BMI[18]. In particular, an increased risk of heart attack has been shown in Mongols living in Inner Mongolia who have central obesity[19]. Moreover, several studies show that it is the abdominal and visceral fat deposition constitute the main anthropometric characteristic of metabolic disorders and increased risks of cardiometabolic diseases, even in people with a normal BMI[20]. However, in our study, there was no difference in the waist-to-hip ratio between the normal weight and overweight categories. The overweight and obese categories differ significantly in all indicators except height, biceps, and triceps skinfold thicknesses, and skeletal muscle mass calculated from body adiposity index data. The right grip strength measurements were significantly higher between participants in the overweight group comparing with normal weight group, while the left grip strength is almost the same. Thus, the analysis of the anthropometric characteristics and body composition of those surveyed allows us to conclude that those with higher BMI values have more fat, predominantly abdominal, while lean body mass and physical fitness indicators remain approximately the same.

Sharp changes in lifestyle patterns that shape an obesogenic environment create the conditions for excess weight gain and obesity development for each individual, but those who have a genetic susceptibility to obesity are at highest risk in the obesogenic environment[21]. Earlier, associations of molecular genetic markers with waist circumference values and waist-to-hip ratio were shown[9,22], including for the FTO gene. For many populations, the frequency of obesity risk alleles determined by the FTO gene is already known, which actually makes it possible to assess the predisposition to obesity at the population level. However, data on the frequency of occurrence of FTO genotypes and the association of T/A-polymorphism with obesity in ethnic Mongolians living in Mongolia are virtually absent. Frequencies of FTO genotypes and alleles in the male sample surveyed stratified according to BMI value are presented in Tables 3-4. In general, ethnic Mongols have a relatively low frequency of AA genotype (14.2%) and A allele (31.3%), which are associated with an increased risk of obesity and cardiometabolic diseases. The result obtained corresponds with other studies that have shown that the A allele frequency is lower in Asian populations than in Europe and America[23].

Studies of associations of T/A-polymorphism with fat deposition parameters for the ethnic Mongolians living in Inner Mongolia showed that the A allele frequency in the obese group was higher in the obese group than in the normal BMI group (17.8% vs. 12.0%, $p = .013$)[11]. However, for the ethnically close group of Altaians living in Russia, a very high FTO A allele frequency was shown. However, the Kalmyks (another ethnic group related to Mongols) living in Russia had a low A allele

frequency[24]. Therefore, to assess the population risks of obesity, it is necessary to study frequencies of occurrence directly in each specific population, since related groups may have completely different patterns of distribution of obesity markers. Analysis of genotype and allele distributions between groups with different BMI revealed no significant differences or tendencies in genotype and allele frequencies (from 12.7% to 18.7%, $Chi^2 = 0.71$, $p = .77$) and the A allele (from 30% to 37.5%, $Chi^2 = 0.51$, $p = .47$). The analyzed associations of T/A-polymorphism of the FTO gene with a tendency to accumulate fat in young Mongolian men confirm the association of the A allele and AA genotype with increased fat accumulation in ethnic Mongols (Table 5). For a variety of anthropometric parameters characterizing fat mass and its topography, carriers of the risk allele (A*FTO) have more fat, as well as a tendency to localize it in the abdomen, indicating they are more prone to central obesity. The results are well consistent with those for populations of Europe, Asia, Africa, and America, as well as for Mongols living in Inner Mongolia[11,25-28]. It should be noted that against the background of the lack of reliable differences in BMI and body length between the carriers of different genotypes, there were differences in body composition of those we surveyed. AA genotype carriers had a fat mass almost twice as high as TT carriers, with an increase in body weight from TT to AA being on the border of significance (Table 5). This result confirms the criticism of using nothing but BMI to predict the risks of overweight- and obesity-related diseases[29]. The analysis of the body composition allows us to identify the risk group among the groups that do not differ in BMI. Inter-ethnic differences in body composition parameters corresponding to healthy and pathological conditions have been shown[29,30]. In particular, South Asian populations with BMI <25.0 kg/m^2 have a higher thickness of subcutaneous fat when compared to Caucasians[31]. The increase in subcutaneous fat thickness is associated with the development of metabolic syndrome in healthy individuals, regardless of total fat mass and visceral fat content[32].

Our data confirm the role of the FTO A allele in increased propensity towards corpulence for ethnic Mongolian males. As mentioned above, a tendency towards an increased A allele frequency was identified in overweight and obesity categories. Next, we analyzed the associations of anthropometric traits with the FTO T/A polymorphism in the BMI categories of the study participants with normal (BMI≤22.9 kg/m^2) and high BMI (≥23.0 kg/m^2) (Table 6). In males with a normal BMI the A allele of the FTO gene was also associated with increased fat deposition (Table 7). The chest circumference and biceps skinfold thickness were significantly higher in A allele carriers. The BMI, weight, and subscapular skinfold thickness are on the border of significance. Thus, even with normal BMI, weight-to-height ratio and body adiposity index values, FTO A allele carriers had higher levels of fat and a tendency for it to be located in the abdominal area, which indicates that development of central obesity already starts at a young age. The absence of significant differences in waist circumference between carriers of alternative FTO genotypes in the normal BMI group may indirectly indicate an insignificant accumulation of visceral fat in this group. In the overweight and obese groups (BMI≥23.0 kg/m^2), significant differences in the abdominal skinfold thickness were identified between carriers of alternative genotypes. At the same time, values of waist-to-hip ratio, BMI, and body fat mass calculated from body adiposity index data tended to be higher in AA genotype carriers, but not significantly so. Thus, for those with an elevated BMI and AA genotype, the abdominal and visceral fat deposition is more pronounced, which only exacerbates their risks for the diseases comorbid with general, central/visceral obesity.

Our results indicate that the presence of the FTO gene A allele in Mongolian males is associated with increased susceptibility to fat accumulation. The A allele carriers accumulate more fat with the same BMI, mainly in the abdominal region, which increases their risk of developing diseases associated with central obesity[33].

The complex nature of obesity requires a multifactorial approach to its study. The rapidly changing way of life associated with globalization and economic development of nations creates an obesogenic environment for modern human populations. Compared to exogenous factors that can change the direction of their impact on humans, genetic characteristics are fixed and can serve as a basis to predict the individual risk of obesity. Risk allele carriers may either maintain normal BMI values and a low percentage of body fat due to regular exercise and a low-calorie diet or follow the nutritional patterns traditional in the region[15]. At the same time, the TT genotype is not absolute protection against obesity. The obesogenic environment common to urban populations dramatically increases the risk of excess weight accumulation for all urban dwellers and further exacerbates the development of obesity in carriers of obesity susceptibility alleles[34]. In general, our study participants had a relatively low

frequency of the A allele, which creates favorable conditions for maintaining a healthy body weight for a large proportion of the population, provided that they are physically active and the observe the principles of proper nutrition.

This study had several limitations. We had a relatively small sample size compared with other similar studies[9,11]. This led to the possibility of type II statistical error with us incorrectly concluding that there was only a tendency to accumulate fat in young Mongolian men with the A allele and AA when in reality there were population-level differences but we could not detect them with the data available in our study. The survey only included male students, which are not representative of all young men in Mongolia and there may be differences in body composition between those who attend a university and those who do not. We used bio-electrical impedance and caliperometry to estimate body composition, and these methods have less sensitivity and specificity than a dual-energy X-ray absorptiometry. Also, several different types of FTO gene mutations at the first intron exist. We only identified T/A (*rs9939609*) in this study. Furthermore, since this study was based on data collected in a cross-sectional survey and no causal conclusions can be drawn. Several other environmental factors can be related to fat accumulation and were not assessed in this study, and should be assessed in future studies. Therefore, future association studies with larger numbers of participants from both genders and studies with direct fat estimation methods are needed to validate and expand our understanding of these results.

Conclusion

Fat accumulation and distribution are associated with A allele of the FTO gene in a group of urban-dwelling young Mongolian men.

Conflict of Interest

The authors state no conflict of interest.

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