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PHYSICAL ACTIVITY ATTENUATES THE EFFECT OF THE FTO GENOTYPE ON OBESITY TRAITS IN EUROPEAN ADULTS: THE FOOD4ME STUDY

AUTHOR NAMES


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KEYWORDS

FTO, genetic, genotype, obesity, physical activity

RUNNING TITLE

FTO and physical activity interaction

CORRESPONDING AUTHOR

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Human Nutrition Research Centre
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Conflict of interest

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Author responsibilities were as follows: YM, IT, CAD, ERG, LB, JAL, JAM, WHMS, HD, MG and JCM contributed to the research design. JCM was the Food4Me Proof of Principle study leader. CCM, CFMM, HF, CBO, CW, AM, RF, SNC, RSC, SK, LT, CPL, MG, AS, MCW, ERG, LB and JCM
contributed to the developing the Standardized Operating Procedures for the study. CCM, SNC, RSC, CW, CBO, HF, CFMM, AM, RF, SK, LT, CPL, MG, AS, MCW and JCM conducted the intervention. CCM, CFMM and WHMS contributed to physical activity measurements. CCM and CFMM wrote the paper and CCM performed the statistical analysis for the manuscript. CCM and CFMM are joint first authors. All authors contributed to a critical review of the manuscript during the writing process. All authors approved the final version to be published.
WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT?

• Most of the studies to date have been focused on the interplay between FTO gene and self-reported physical activity.

• However, measurement errors associated to a self-reported nature of questionnaires may have attenuated the true strength of the gene-physical activity interplay.

• Limited data is available on objective measured physical activity and its interaction with the FTO gene on obesity-related markers.

WHAT DOES YOUR STUDY ADD?

• Our findings emphasise that physical activity may be a particularly effective way of controlling body weight in individuals with a genetic predisposition towards obesity.

• The apparent effect of an active lifestyle on genetic predisposition to obesity (~4kg differences in the FTO-related effect size on body mass for inactive vs active individuals) is large enough to be clinically relevant.
ABSTRACT (words=198)

**Objective:** To examine whether the effect of FTO loci on obesity-related traits could be modified by physical activity (PA) levels in European adults.

**Methods:** Of 1,607 Food4Me participants randomised, 1,280 were genotyped for the FTO (rs9939609) and had available PA data. PA was measured objectively using accelerometers (TracmorD, Philips), whereas anthropometric measures (BMI, and waist circumference; WC) were self-reported via the internet.

**Results:** FTO genotype was associated with a higher body weight (β: 1.09 kg per risk allele, [95%CI: 0.14-2.04]; P=0.024), BMI (β: 0.54 kg.m\(^{-2}\), [0.23-0.83]; P<0.0001) and WC (β: 1.07 cm, [0.24-1.90]; P=0.011). Moderate-equivalent PA attenuated the effect of FTO on BMI (P\(_{\text{interaction}}\)=0.020). Among inactive individuals, FTO increased BMI by 1.06 kg.m\(^{-2}\) per allele (p=0.024) whereas the increase in BMI was substantially attenuated among active individuals (0.16 kg.m\(^{-2}\), p=0.388). We observed similar effects for WC (P\(_{\text{interaction}}\)=0.005): the FTO risk allele increased WC by 2.72 cm per allele among inactive individuals but by only 0.49 cm in active individuals.

**Conclusions:** PA attenuates the effect of FTO genotype on BMI and WC. This may have important public health implications because genetic susceptibility to obesity in the presence of FTO variants may be reduced by adopting a physically active lifestyle.
INTRODUCTION

Changes in lifestyle, including higher energy intake and lack of physical activity (PA), have been the driving force behind the dramatic increase in obesity prevalence over the past three decades (1, 2). The prevalence of obesity has increased markedly, with 16.6% of European adults (3) and 9.3% of adults globally now having obesity (4). However, epidemiological studies show that genetic factors play an important role in the development of obesity (5), suggesting that obesity is a multifactorial condition influenced by a complex interplay between lifestyle and genetics (2, 5, 6).

Recent genome wide association studies have identified single nucleotide polymorphisms (SNPs) in genes (7), including the fat mass and obesity-associated gene (FTO), that are strongly associated with the development of obesity (7, 8, 9, 10). A study of 38,759 individuals revealed that subjects homozygous for the FTO (rs9939609) risk allele weighed on average 3kg more and had 1.7-fold increased odds of being obese compared with individuals homozygous for the lower-risk allele (10). Although the evidence for an effect of FTO, or other obesity-related loci, on obesity is strong, the variance in BMI explained by genetic variants is small (2.7%) (11, 12). This is in stark contrast with earlier studies of the heritability of BMI, which was estimated to be 40-70% (5, 13). Gene-lifestyle interactions may contribute to the unexplained heritability of BMI and obesity (14, 15), and numerous such interactions for many different cardio-metabolic phenotypes, including obesity anthropometrics, were recently catalogued from 386 published scientific reports (16). Much work remains to determine how robust these interactions are. Still, modulation of FTO-obesity associations by self-reported (SR) PA is one of the most replicated (16).
Although genetically predisposed individuals may be more susceptible to obesity in an obesogenic environment, with a higher risk of over-consumption as was shown in twin studies (13), there has been limited evidence of genotype-lifestyle interactions on adiposity outcomes (6, 17). Importantly, most of the studies to date have focused on the interplay between genes and self-reported (SR) PA, where measurement error in SR PA may have attenuated the true strength of the gene-PA interaction (18). To date, only very few studies have used objectively measured PA to examine the FTO-PA interaction in adults (19, 20). Therefore, in the current study, we investigated whether the effect of the FTO loci on obesity-related traits was modified by objectively measured PA in European adults from the Food4Me study.

**METHODS**

**Study population**

The Food4Me Proof of Principle (PoP) study was a 6-month, 4-arm, internet-based, randomised controlled trial (RCT) conducted across 7 European countries ([www.food4me.org](http://www.food4me.org)) (21). 1,607 participants from the following recruitment sites: University College Dublin (Ireland), Maastricht University (The Netherlands), University of Navarra (Spain), Harokopio University (Greece), University of Reading (United Kingdom, UK), National Food and Nutrition Institute (Poland), and Technical University of Munich (Germany), were randomised into the RCT. Participants recruited and randomised per country has been described elsewhere(21, 22). Participants aged ≥18 years of age were included in the study. To keep the cohort as representative as possible of the adult European population, a minimal set of exclusion criteria were applied as described elsewhere (21).
Study measures

Participants consented to self-report their measures via the internet and to send biological samples (Dried Blood Spot cards and buccal swabs) by post, using pre-paid, stamped addressed envelopes. To ensure that procedures were similar in all recruiting centres, standardised operating procedures were prepared for all measurements, and researchers underwent centralised training. Moreover, to enable participants to collect and report the required information and to collect, process and dispatch the biological samples correctly, participants were given printed detailed instructions, and video demonstrations of key procedures were available online. All instructions were provided in the language of the country of recruitment (21).

Collection of demographic and anthropometric data

An online screening questionnaire collected detailed SR information on demographic, food choices, health-related and anthropometric data. At baseline, body weight, height and waist circumference (WC) were self-measured and self-reported by participants via the internet. Participants were instructed to measure body weight after an overnight fast, without shoes and wearing light clothing using a home or commercial scale, and to measure height, barefoot, using a standardised measuring tape provided by Food4Me (21). WC was measured at the mid-point between the lower rib and the iliac crest using the provided tape measure. Central obesity was defined as WC >88 cm for women and >102 cm for men. BMI was calculated from body weight and height. Adiposity status was defined using WHO criteria for BMI
(underweight<18.5 kg.m\(^{-2}\), normal weight $\geq$18.5 kg.m\(^{-2}\) to $\leq$24.9 kg.m\(^{-2}\), overweight $\geq$25.0kg.m\(^{-2}\) to $\leq$29.9 kg.m\(^{-2}\) and obese $\geq$30.0 kg.m\(^{-2}\)). SR measurements were validated in a sub-sample of the participants ($n$=140) and showed a high degree of reliability (23).

Physical activity measures and analysis

Physical activity levels (PAL) and time spent in sedentary behaviours were measured objectively using triaxial accelerometers (TracmorD, Philips Consumer Lifestyle, The Netherlands) (24). All participants were instructed to wear the accelerometer every day during waking hours, except when taking a shower, for the whole duration of the study. For the analyses reported in this paper, data collected over 2 weeks at baseline were used. Participants were instructed to upload their PA data into the study server via the internet.

Data were recorded with a time sampling interval of 1 min (i.e. 1-min epochs). A day was considered valid if the volunteer had worn the TracmorD for at least 10 hours, but not longer than 18 hours. Wear time was defined as 24 hours minus non-wear time. To define non-wear time, we adapted the recommendations of Choi et al. (25) to the TracmorD. The R software version 3.1.2 was used for PA data processing.

PA domains were based on application of thresholds for activity energy expenditure (AEE) and included time spent in sedentary behaviours (corresponding to $<1.5$ METs), light (1.5 to $<3$ METs), moderate (3 to $<6$ METs), vigorous ($\geq 6$ METs) or moderate-equivalent intensity PA (26). Moderate-equivalent PA was derived using the following equation \([\text{moderate PA} + (\text{vigorous PA} \times 2)]\) (27).
Adherence to the WHO physical activity recommendations was examined by estimating the proportion of volunteers who accumulated at least 150 minutes per week of moderate PA or 75 minutes of vigorous PA or an equivalent combination of moderate and vigorous PA, in bouts of at least 10 minutes (27). This translates to at least 150 minutes per week of moderate-equivalent PA. Three-categorical variables were created for all PA variables. For the moderate-equivalent PA variable, 150 and 300 min.week\(^{-1}\) of moderate-equivalent PA were used to create 3 relevant categories. Similarly, for the moderate PA variable, 150 and 300 min.week\(^{-1}\) of moderate PA were used to create the 3 categories. For all other PA variables, categories were tertiles derived from STATA.

Genotypic analyses

Buccal cell samples were collected from participants at baseline using Isohelix SK-1 DNA buccal swabs and Isohelix dried-capsules and posted to each recruiting centre for shipment to LGC Genomics (Hertfordshire, United Kingdom). LGC Genomics extracted DNA and genotyped specific loci using KASP\(^{TM}\) genotyping assays. FTO SNPs (rs9939609 and rs1121980) were genotyped and showed a high linkage disequilibrium (\(r^2=0.96\)). Therefore, results for rs1121980 are not reported. Accuracy of the genotyping analysis has been assessed and reported elsewhere(23).

A goodness-of-fit chi-square test was performed to examine if the observed genotype counts were in Hardy-Weinberg equilibrium. Genotype frequency for the FTO rs9939609 variant did not deviate from Hardy-Weinberg equilibrium (TT=469, TA=739 and AA=264, \(P=0.345\)).
Ethics approval and participant consent

The Research Ethics Committees at each University or Research Centre delivering the intervention granted ethics approval for the study. The Food4Me trial was registered as a RCT (NCT01530139) at www.clinicaltrials.gov. All participants who expressed an interest in the study were asked to sign online consent forms at two stages in the screening process. These forms were automatically directed to the local study investigators to be counter-signed and archived (21).

Statistical analysis

Baseline data were used for the present analyses. Results from descriptive analyses are presented as means and SD for continuous variables and as percentages for categorical variables.

Robust Linear Regression analyses were used to test for associations between the main outcomes (weight, BMI and WC) and FTO genotype. FTO was coded using an additive genetic model (TT=0, AT=1, AA=2) and PA was categorized and coded as ordinal variable (0=Lower, 1=Middle, 2=Higher). The interplay between PA and FTO genotype was investigated by including an interaction term in the models, with PA and FTO variables coded as specified above. For categorical outcomes (% of participants with overweight or obesity), Robust Logistic Regression was used and FTO and PA (coded as ordinal variables) were included in the model using an interaction term. Analyses were adjusted for age, sex, country, season and monitor wearing time, as appropriate. Results were deemed significant at $P<0.05$. Data were analysed using Stata (version 13; StataCorp. College Station, TX, USA).
RESULTS

Cohort characteristics

Of the 1,607 individuals randomised into the Food4Me study, data at baseline on FTO genotype and PA were available for 1,280 participants (58% were women and 97% were Caucasians). As summarised in Table 1, 30% of individuals had overweight and 16% had obesity. In addition, WC was above the healthy limit (>102 cm for males and 88 cm for females) for 23% of males and 26% of females. Although 57% of men and 40% of women met the PA recommendation (≥150 minutes of moderate-equivalent PA a week), 28% of the participants recorded less than 1 minute of vigorous intensity PA daily. All PA variables were significantly associated with obesity–related markers (Table S5).

Association of FTO genotype with obesity measures

Carriage of the A allele of the FTO rs9939609 variant was associated with higher body weight [β: 1.09 kg increase per risk allele, 95%CI (0.14 to 2.04), \( P=0.024 \)], BMI [β: 0.54 kg.m\(^{-2}\), 95%CI (0.23 to 0.83), \( P<0.0001 \)], and WC [β: 1.07 cm, 95%CI (0.24 to 1.90), \( P=0.011 \)] (Figure 1). Participants with the FTO risk allele (A) had significantly higher odds of having overweight (OR: 1.27 (1.06 to 1.51), \( P=0.007 \)) or obesity (OR: 1.41 (1.13 to 1.75); \( P=0.003 \)) than individuals with the T allele, but no significant association was found for central obesity (Table 2).

Interaction between FTO genotype and PA levels on adiposity

We found a significant interaction between FTO genotype and category of moderate-equivalent PA on body weight, BMI and WC (Table 3 and Figure 2). The strength of the association between FTO and body weight decreased with increasing moderate-equivalent PA: the
relationship declined from 3.53 kg (95%CI: 0.93 to 6.11) per copy of the *FTO* risk allele in participants with lower levels of PA (≤150 min.week\(^{-1}\)) to -0.28 kg (95%CI: -1.48 to 0.91) in participants with higher levels of PA (>300 min.week\(^{-1}\)), as shown in Table 3 and Figure 2. Similar results were found for BMI (lower PA: 1.06 kg.m\(^{-2}\) vs higher PA: 0.16 kg.m\(^{-2}\) per copy of the risk allele, \(P_{(interaction)}=0.020\) and WC (lower PA: 2.72 cm vs higher PA: -0.49 cm per copy of the risk allele, \(P_{(interaction)}=0.005\)). When the relationship between *FTO* genotype and other PA domains (vigorous, moderate and light intensity PA) were studied, we observed significant interactions between *FTO*\(^{\ast}\)vigorous intensity PA (Table S1 and Figure S1) and *FTO*\(^{\ast}\)moderate intensity PA (Table S2 and Figure S2) on body weight, BMI and WC. However, no significant *FTO*\(^{\ast}\)light intensity PA interactions were identified (Table S3 and Figure S3). Although there were no significant interactions between *FTO* genotype and sedentary behaviour on obesity measures (body weight, BMI and WC), these increased with increasing time spent in sedentary behaviour (Table S4 and Figure S4). The effect size of *FTO* on BMI and WC was 60% and 320% greater in individuals with longer, than shorter, time spent in sedentary behaviour, respectively. When additional analyses were performed and PA was included in the interaction models as a continuous variable, we saw a similar trend for the interaction effect between FTO and PA-related variables but these interaction were no longer significant (\(P>0.05\)) for any of the outcomes. Additionally, no association were found between PA variables and FTO genotype (Table S6). Sensitivity analysis where participants of non-white ethnic origin (<3%) were removed from the analysis did not modify any of our findings.
Discussion

Main findings

Our main findings are that, on average, each additional copy of the FTO risk allele at rs9939609 was associated with significant increases in body weight, BMI and WC of 1.09 kg, 0.54 kg.m\(^{-2}\) and 1.07 cm, respectively. Consistently, each copy of the risk allele increased the odds of having overweight or obesity by 32%. Our results provide further evidence to support the interplay between genes and lifestyle. We showed that the effect sizes of the FTO associations on BMI and WC for active individuals (moderate-equivalent PA >300 min.week\(^{-1}\)) were 85% and 118% lower, respectively, than for inactive individuals (moderate-equivalent PA <150 min.week\(^{-1}\)). These findings emphasise the importance of PA in the prevention of obesity especially in subjects carrying the FTO risk allele.

Comparison with other studies

Our results are consistent with the findings of previous studies showing associations between FTO variants and obesity-related traits (10, 28, 29). Although the effect size of the FTO rs9939609 is relatively modest, it is consistent across studies conducted in Caucasian populations (10, 28, 29, 30, 31). Our FTO effect size estimates are in agreement with previous findings where each copy of the risk allele was associated with an increase in adiposity measures ranging from 0.76 to 2.4 cm for WC, and from 0.31 to 0.66 kg.m\(^{-2}\) for BMI, which is equivalent to ~1.3 to 2.1 kg in body weight for an individual 1.80 m tall (8, 9, 10, 28, 30). Similarly, the odds of having overweight or obesity reported in previous studies ranged from ~1.19 to 1.69 per additional copy of the risk allele (8, 9, 10, 28, 29), which is in agreement with
our estimates (OR: 1.27 (1.06 to 1.51) for overweight and OR: 1.41 (1.13 to 1.75) for obesity per copy of the risk allele).

Furthermore, our study suggests that an active lifestyle may attenuate the *FTO* genetic susceptibility to obesity (19, 20, 32, 33). A meta-analysis of cross-sectional studies, including 218,166 adults (19), reported a significant *FTO*PA interaction (*P*=0.001), where the minor A *FTO* allele of the rs9939609 variant increased the odds of being obese less in physically active individuals [OR: 1.22 (95%CI 1.19-1.25)] than among inactive individuals (OR: 1.30 (1.24-1.36)). Moreover, the latter meta-analysis reported that the association of the *FTO* genotype with BMI and WC was attenuated in physically active individuals (0.32 kg.m\(^{-2}\) and 0.68 cm per copy of the risk allele, respectively) compared with inactive individuals (0.46 kg.m\(^{-2}\) and 1.01 cm per copy of the risk allele). Although our study showed qualitatively similar findings, we observed a bigger attenuation by PA of the effect of *FTO* on obesity-related traits. This quantitative difference between studies may be explained by the relative precision of PA measurements.

Our results are based on objectively measured PA data whereas the earlier meta-analysis (19) used primarily SR PA data. SR PA can be subject to optimistic bias leading to PA overestimation (34). Furthermore, SR PA is prone to random error, which leads to regression dilution bias (35). This can obscure the true effect of PA on the interplay between genes and environment (36). Moreover, the use of categories of PA may provide better knowledge of the dose-response relationship between *FTO* genotype and PA on adiposity, which may assist in identifying the minimum amount of PA necessary to overcome the genetic effect of *FTO* genotype on obesity-related traits. We found that the influence of the *FTO* risk allele on BMI was 36% and 84% lower in individuals achieving between 150-300 min.week\(^{-1}\) or above 300 min.week\(^{-1}\) of moderate
equivalent PA, respectively, than in inactive individuals (<150 min.week\(^{-1}\)). The attenuating effect of PA on FTO related adiposity was similar when WC was used as an outcome (the FTO risk allele effect on WC was 1.5 and 6.5-fold lower for active and highly active individuals than in inactive individuals).

Although previous studies have reported a significant FTO*PA interaction (20, 30, 31, 32, 33, 37), most of these studies used SR PA (19). Objectively measured PA allowed us to investigate whether sedentary behaviours or other PA domains, such as light, moderate and vigorous intensity PA, modulate the effect of the FTO genotype on obesity-related traits. We identified that achieving between 10 to 90 minutes of vigorous PA per week mitigated the effect of FTO genotype on obesity measures. However, higher levels of moderate intensity PA appear to be needed (150 to 300 min.week\(^{-1}\)) to achieve similar attenuating effects on the association between FTO genotype and obesity.

The mechanism how the FTO gene may have an impact on obesity outcomes remains unclear. Recent evidence suggests that genetic variants within introns 1 and 2 of FTO may change the basic function of human adipocytes from substrate storage to fuel utilization through enhanced thermogenesis (38). Claussnitzer et al. proposed that noncoding variants in FTO influence the thermogenic capacity of beige cells, which results in phenotypic differences in BMI. They identified a large enhancer region in the FTO locus of adipocytes that has long-range control over two homeobox regulatory genes, IRX3 and IRX5, and demonstrated cell-autonomous effects of these genes by means of genetic knockdown of IRX3 and IRX5 to restore thermogenesis in adipocytes from persons at high genetic risk for obesity. In contrast, overexpression of these proteins in adipocytes from persons without this genetic risk resulted
in decreased mitochondrial function and thermogenesis (38). Some attempts have been made
to explain the relationship between FTO and PA energy expenditure (39), but there is
inconclusive evidence on whether this may be due to epistatic gene interactions with other
genes that may control PA or dietary intake, or to gene-environment interaction (39).

The strengths of our study include the objective measure of PA in a large European cohort,
which is important because the identification of convincing gene-lifestyle interactions requires
accurate measures of the environmental exposure (18) to make them as robust basis for public
health action. Moreover, our estimate of PA allowed us to create categories of PA domains
which revealed the dose-response relationship for gene-environment interaction. A potential
limitation of our study is that anthropometric data were self-measured and self-reported via
the internet, which may have introduced measurement error. Nonetheless, the accuracy of
internet-based, self-reported anthropometric data is high (40) and this has been confirmed in
our study (23). However, we cannot completely discard any confounding effect of self-reported
data on our main outcomes. Another factor that should be considered as a limitation is the lack
of information on relatedness of the individuals. Additionally, when interactions between
FTO and PA were assessed by fitting PA as a continuous variable in the interaction term, the
trend remained similar but the interactions were no longer statistically significant (P>0.05).
A larger sample size will be needed to confirm our findings using PA as a continuous
variable. Furthermore, by design, we recruited individuals interested in taking part in a
personalized intervention on nutrition and lifestyle, which is less representative than a
European-wide survey. Nonetheless, our participants were broadly representative of the
European adult population, most of whom had adequate nutrient intakes but could benefit
from improved dietary choices and greater PA [41]
Implications of findings

Considering the current prevalence of overweight and obesity worldwide (4), our findings are highly relevant for improving public health. They emphasise that PA may be a particularly effective way of controlling body weight in individuals with a genetic predisposition towards obesity and thus contrast with the deterministic view that genetic influences are unmodifiable. The apparent effect of an active lifestyle on genetic predisposition to obesity (~4kg differences in the FTO-related effect size on body mass for inactive vs active individuals) is large enough to be clinically relevant. Evidence of such gene–lifestyle interactions may empower and motivate individuals to adopt healthier lifestyle behaviours through knowledge that such behaviour change can be effective in preventing obesity and, therefore, risk of obesity-related non-communicable diseases. Gene*environment interactions for cardio-metabolic phenotypes involve physical activity more often than any other lifestyle factor, including dietary fat intakes (16).

In conclusion, despite the fact that FTO genotype is robustly associated with BMI and WC, our results show that higher PA attenuates this genetic predisposition to obesity-related traits. These finding are relevant for public health and suggest that promoting PA, particularly in those who are genetically susceptible, is an important strategy for addressing the current obesity epidemic.

ACKNOWLEDGMENTS
The authors thank Dr Annelies Goris and Dr Jettie Hoonhout from Philips for their support during physical activity data collection.

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40. Pursey K, Burrows TL, Stanwell P, Collins CE. How Accurate is Web-Based Self-Reported Height, Weight, and Body Mass Index in Young Adults? *Journal of Medical Internet Research* 2014;16.
Figure 1. Association between FTO rs9939609 genotype and adiposity measures.

Least-squares means of genotypes were calculated by using Robust Linear Regression, with adjustment for age, sex and country.
\[ P_{(FTO^{PA})} = 0.003 \]

**Body Weight (kg)**

<table>
<thead>
<tr>
<th>Category of Moderate-equivalent PA</th>
<th>TT</th>
<th>TA</th>
<th>AA</th>
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<tbody>
<tr>
<td>Lower (&lt;150 min.week⁻¹)</td>
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<td></td>
</tr>
<tr>
<td>Middle (150-300 min.week⁻¹)</td>
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<tr>
<td>Higher (&gt;300 min.week⁻¹)</td>
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\[ P_{(FTO^{PA})} = 0.020 \]

**Body Mass Index (kg.m⁻²)**

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<th>TA</th>
<th>AA</th>
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<td>Lower (&lt;150 min.week⁻¹)</td>
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<tr>
<td>Middle (150-300 min.week⁻¹)</td>
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<tr>
<td>Higher (&gt;300 min.week⁻¹)</td>
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\[ P_{(FTO^{PA})} = 0.005 \]

**Waist Circumference (cm)**

<table>
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<th>AA</th>
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<td>Middle (150-300 min.week⁻¹)</td>
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<tr>
<td>Higher (&gt;300 min.week⁻¹)</td>
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Figure 2. Effect of the FTO rs9939609 genotype on adiposity-measures by category of moderate-equivalent physical activity.

P values are for the interaction between the FTO variant and PA category; Least-squares means of different genotypes across all PA groups were calculated by using Robust Linear Regression Analysis, with adjustment for age, sex, country, monitor wear time and season. Allele frequency by PA category were (Lower: 71/158/59; Middle: 103/142/61; Upper: 231/342/113) for TT, TA and AA genotypes, respective.
Table 1. Characteristics of Food4Me Study participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall</th>
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<th>Women</th>
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<tbody>
<tr>
<td>n</td>
<td>1280</td>
<td>537</td>
<td>743</td>
</tr>
<tr>
<td>Age (years)</td>
<td>39.9 (13.0)</td>
<td>41.6 (13.4)</td>
<td>38.7 (12.5)</td>
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<tr>
<td><strong>Anthropometric</strong></td>
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<tr>
<td>Height (m)</td>
<td>1.71 (0.09)</td>
<td>1.79 (0.07)</td>
<td>1.65 (0.06)</td>
</tr>
<tr>
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<tr>
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<td>26.1 (4.1)</td>
<td>24.9 (5.2)</td>
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<td>3.8</td>
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<tr>
<td>Normal weight (≥18.5 to &lt;25.0 kg.m(^{-2}); %)</td>
<td>51.3</td>
<td>44.7</td>
<td>56.0</td>
</tr>
<tr>
<td>Overweight (≥25.0 to &lt;30.0 kg.m(^{-2}); %)</td>
<td>30.3</td>
<td>38.4</td>
<td>24.6</td>
</tr>
<tr>
<td>Obese (≥30.0 kg.m(^{-2}); %)</td>
<td>15.8</td>
<td>16.1</td>
<td>15.6</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>85.7 (13.8)</td>
<td>92.7 (12.1)</td>
<td>80.7 (12.8)</td>
</tr>
<tr>
<td>Central obesity* (% )</td>
<td>24.3</td>
<td>22.8</td>
<td>25.6</td>
</tr>
<tr>
<td><strong>Physical Activity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAL</td>
<td>1.73 (0.18)</td>
<td>1.74 (0.2)</td>
<td>1.72 (0.2)</td>
</tr>
<tr>
<td>Sedentary time (min.day(^{-1}))</td>
<td>744.8 (76.6)</td>
<td>738.9 (82.3)</td>
<td>749.1 (71.5)</td>
</tr>
<tr>
<td>Light PA (min.day(^{-1}))</td>
<td>73.9 (30.4)</td>
<td>74.0 (29.8)</td>
<td>73.9 (30.9)</td>
</tr>
<tr>
<td>Moderate PA (min.day(^{-1}))</td>
<td>33.3 (20.4)</td>
<td>37.3 (21.1)</td>
<td>30.3 (19.4)</td>
</tr>
<tr>
<td>Vigorous PA (min.day(^{-1}))</td>
<td>11.8 (16.1)</td>
<td>16.7 (18.1)</td>
<td>8.17 (13.1)</td>
</tr>
<tr>
<td>Moderate-equivalent PA (min.day(^{-1}))</td>
<td>56.9 (45.0)</td>
<td>70.9 (49.1)</td>
<td>46.7 (38.4)</td>
</tr>
<tr>
<td>Moderate-equivalent PA 10min bouts (min.day(^{-1}))</td>
<td>29.2 (32.3)</td>
<td>36.5 (35.9)</td>
<td>23.8 (28.1)</td>
</tr>
<tr>
<td>Active individuals (≥150 min.week(^{-1}) moderate-equivalent PA in bouts; %)</td>
<td>47.0</td>
<td>56.5</td>
<td>40.0</td>
</tr>
</tbody>
</table>

Data presented as Mean (SD) for continuous variables and as % for categorical variables.

PAL - Physical activity level. *Central obesity was defined as WC >88 cm for women and >102 cm for men.