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Obesity candidate genes, gestational weight gain and body weight changes in pregnant women

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Abstract

Objective—To examine the associations of two obesity associated genes, *FTO* (rs9939609) and *GNB3* (rs5443) single nucleotide polymorphisms (SNPs), with early pregnancy BMI, gestational weight gain, and postpartum weight retention.

Methods—Secondary data analysis of self-identified Caucasian (n = 580) and African American (n = 194) women who participated in a randomized controlled trial (2009-2014) and provided a saliva sample of DNA. Bivariate relationships were assessed using analysis of variance. Multiple regression models assessed the relationship between outcomes and gene SNPs, controlling for income, parity, and smoking status.

Results—*FTO* and *GNB3* gene associations with pregnancy weight were different by racial group and early pregnancy BMI. Obese African American women homozygote for the *FTO* risk allele (AA) had a higher gestational weight gain compared to non-risk homozygotes (TT) ($p = 0.006$). *GNB3* non-risk CC homozygotes trended on having a lower gestational weight gain compared to heterozygotes ($p = 0.05$). Caucasian *GNB3* C carriers trended to being heavier in early pregnancy ($p < 0.1$) and *GNB3* homozygote (TT) overweight women trended to lower postpartum weight retention than C carriers.

Conclusions—The *FTO* gene and possibly the *GNB3* gene are associated with high gestational weight gain in obese African American women. Obese carriers of the *FTO* risk allele gained 4.1 kg (AT) and 7.6 kg (TT) more than those without risk alleles. Overweight *GNB3* heterozygotes (CT) gained 6.6 kg less than homozygotes (CC). Overweight or obese African American women who have either risk variant are at risk for high gestational weight gain.

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Introduction

Obesity is a major issue for US women. Obesity and overweight are a common consequence of pregnancy if there is high gestational weight gain (GWG[1]) and high prepregnancy body mass index (BMI) [1]. How women respond to pregnancy depends on their genetics and environment [2]. Nearly 50% of women gain excessively [3] and over 50% enter pregnancy overweight/obese [4]. Interventions to decrease prepregnancy BMI and limit excessive GWG have had limited success [5]. To further our understanding of possible genetic effects on pregnancy-related weight we focus on the influence of two obesity associated genes, *FTO* (rs9939609) and *GNB3* (rs5443) single nucleotide polymorphisms (SNPs), on prepregnancy BMI, GWG, and postpartum weight retention.

Several studies have examined obesity and diabetes genes on prepregnancy weight, GWG and/or weight retention [2, 6–10] with inconsistent findings due to variations in sample size, methodology, racial/ethnic sample composition, and candidate gene SNP selection. The *FTO* gene was associated with high prepregnancy BMI in a sample from Brazil (73.5% self-reported black/mixed) [2] and in a sample from the United Kingdom of unreported racial/ethnic groups [8]. Lawlor et al. reported no gene effects on GWG or weight 8-weeks postpartum [8]. Stuebe et al. reported an interaction of the *FTO* gene with prepregnancy BMI on GWG in US Caucasian women [9]. In an African American sample the *FTO* gene was associated with GWG in obese women [6]. The *GNB3* gene has been associated with GWG in Caucasian, African American and Hispanic women [11], and postpartum weight retention in an unreported racial/ethnic group [12]. Conversely, the *GNB3* gene was not associated with prepregnancy BMI, GWG, or postpartum weight retention in US African American women [6].

A meta-analysis of *GNB3* gene studies of non-pregnant individuals reported the TT homozygote might increase susceptibility for overweight/obesity [13]. The *GNB3* and *FTO* genes have been associated with satiation, contributing to obesity [14]. The *GNB3* gene was associated with mood and hunger, potentially influencing obesity by behavioral regulation of food intake [15]. The *FTO* gene has consistently been associated with obesity [16].

The majority of genome wide association studies (GWAS) of obesity genes used European ancestral groups and generalizability to other racial/ethnic groups cannot be assumed: polymorphism allele frequencies differ by ancestral group [17]. For example, the *GNB3* risk allele frequency is approximately 70% in African Americans and 33% in Caucasians [18]. Variant effects are typically in the same direction in different ancestral groups, but effect sizes differ due to varied allele frequencies [17] and linkage disequilibrium structures [19].

The purpose of this study was to examine associations between the *GNB3* (rs5443) and *FTO* (rs9939609) single nucleotide polymorphisms (SNPs) and early pregnancy BMI, GWG and weight retention 6-months postpartum in a sample of self-identified Caucasian and African American women who participated in a randomized controlled trial (RCT) to limit GWG and weight retention [20]. The study was approved by the institutional review board.

[1]GWG: gestational weight gain

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Methods

Design

Secondary data analysis was conducted using data from the eMoms study conducted in New York state from 2009-2014 [20]. eMoms was a RCT that developed and tested electronically mediated interventions to slow weight accumulation during pregnancy and up to 12-months postpartum. Women were eligible for the RCT if aged 18–35, in the first 20 weeks of pregnancy, and had a BMI between 18.5–34.9 kg/m^2. Women pregnant with multiples, weight-affecting or psychiatric conditions, past or planned weight loss surgery or program, taking steroids, diabetic, hypertensive, or psychotropic medications, and without an e-mail address were excluded. Women (N =1689) were randomized within four early pregnancy BMI × income strata (two BMI groups: BMI 18.5–<25.0 and BMI 25.0–<35.0; and two income groups: above/below Medicaid eligibility) to three arms. The arms consisted of a control group exposed to electronic material unrelated to weight management; e-intervention1 received an electronic intervention during pregnancy with access to control content postpartum; and e-intervention2 received an electronic intervention during pregnancy and postpartum.

For these analyses, we used observations with complete data on GWG and weight at 6-months postpartum, self-identified as African American or Caucasian and provided a DNA sample. The sample was limited to these racial groups because allele frequencies vary by population and samples for other racial/ethnic groups were too small to analyze. There were 1088 Caucasian women and 421 African American women in the original sample. Of these, 847 provided DNA samples. The final African American sample for these analyses included 194 women with genetic data, after excluding 25 women who were underweight (early pregnancy BMI < 18.5 kg/m^2) or delivered preterm (< 37 weeks). The final Caucasian sample included 580 women with genetic data, after excluding 44 women who were underweight or delivered preterm.

Measures

***FTO* and *GNB3* Genotyping—**Genomic DNA was obtained using Oragene saliva collection kits (DNAGenotek Inc., Kanata, Canada). Analysis was done in the University Genomics Center using standard procedures. Briefly, saliva was purified using the DNA Genotek prepIT-L2P plate purification protocol. Extracted DNA was quantified on a NanoDrop 1000 spectrophotometer and normalized to 15 ng/uL. We used 30 ng for each polymerase chain reaction (PCR). Samples were run in single reactions for *FTO* and *GNB3* TaqMan SNP genotyping assay. TaqMan Universal PCR Master Mix (No AmpErase UNG) and TaqMan SNP genotyping assays were robotically plated into a 384-well plate. Real-time PCR reaction was run on Applied BioSystem's 7900HT real-time instrument using SDS 2.4.1 software. Immediately after real-time PCR, a post read was completed. SDS 2.4.1 was used to perform analysis and auto-call genotypes.

Gestational weight gain—Gestational weight gain was calculated as the difference between weight at the last prenatal visit after 37 weeks gestation and weight at the first prenatal visit (≤ 14 weeks gestation). Weights were abstracted from prenatal charts.

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Early pregnancy BMI—Early pregnancy BMI was calculated as kg/m^2 based on measured weights (≤14 weeks gestation) abstracted from prenatal charts, or study screening and heights measured by study staff, abstracted from prenatal charts, or self-reported at screening.

6-month postpartum weight retention—Study staff measured weight at 6-months postpartum. Weight retention was calculated as the difference between measured postpartum weight and weight at first prenatal visit.

Covariates

Parity—Parity was defined as number of live births (including study pregnancy).

Smoking—Smoking was collected in early and late pregnancy. Smoking was reported "Yes" or "No." Missing values were treated as "non-report" to capture missingness.

Income—Income was defined as high or low based on Medicaid eligibility (household income < 185% poverty line).

Study arms—Study arms were included as a covariate for the analyses of GWG and 6-month postpartum weight retention outcomes to improve predictive ability. This also adjusted for any imbalance in study arm distribution within the race, genetic and BMI categories of the groups that may confound gene effects.

Statistical Analyses

Statistical analyses were performed using R version 3.3.2 [21]. Descriptive statistics include frequencies and percentages for categorical measures, and means and standard deviations for continuous measures. Analysis of variance (ANOVA) was used to assess the bivariate relationships between each outcome and gene SNP. Subsequent multiple regression models assessed the relationship between outcomes and each gene, separately, while controlling for income, parity, and smoking status. When fitting models for GWG and 6-month weight retention, we controlled for smoking status late in pregnancy, which is most proximal to time of delivery, while for early pregnancy BMI, we controlled for smoking measured early in pregnancy. In the models for GWG and 6-month weight retention we controlled for early pregnancy BMI and study arm. Anticipating complex genetic differences across race, all analyses were performed on subsamples of African American and Caucasian women, separately. Within each race, we analyzed the overall subsample and also separated by early pregnancy BMI categories: Normal (18.5 – 24.9 kg/m^2), Overweight (25.0 – 29.9 kg/m^2), and Obese (≥ 30.0 kg/m^2) for GWG and weight retention analyses. For each model, we used the F test to assess goodness of fit and the Type 3 test to determine the significance of the relationship between each of the covariates and outcomes.

Results

The sample consisted of 774 women: 194 African American and 580 Caucasian (Table 1). Allele frequencies for the *FTO* gene were similar across racial groups. *GNB3* allele frequencies differed between groups, with African American women having a higher

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prevalence of the risk allele (T). The majority of women were in the normal BMI category in early pregnancy (> 50%). The GWG for a large percentage of African American and Caucasian women was above IOM guidelines (47% and 50%, respectively). More Caucasian women in the overweight and obese BMI categories gained above IOM guidelines (72.7% and 59.3%) compared to of African American women (47.7% and 41%) (Table 2).

African American Subsample

There was no deviation from the Hardy Weinberg equilibrium in the FTO (χ^2=0.0042, p=0.948) or GNB3 genes (χ^2=1.098, p=0.295) [22].

Early Pregnancy BMI—There was no statistically significant association of the *FTO* and *GNB3* alleles with early pregnancy BMI overall and by BMI category in African American women with one exception (Table 3). Women in the normal BMI category and carriers of the *FTO* AT allele combination were 0.9 BMI units more than the *FTO* TT combination (p <. 05). Parity was associated with early pregnancy BMI, with multiparous women having a higher BMI.

Gestational Weight Gain—There was no statistically significant association of *FTO* and *GNB3* alleles with GWG in the overall African American sample. However, in the obese subsample, the relationship between GWG and the *FTO* gene was statistically significant (*p=0.022*), controlling for early pregnancy BMI, income, parity, intervention arm, and smoking status (Table 3), while the overall relationship between *GNB3* was trending on significant (*p=0.097*) (Table 4). The *FTO* risk allele homozygotes (AA), experienced increased GWG compared to AT/TT combinations (est. differences = 4.1 and 7.6 kg, *p=0.073 and p=0.006*, respectively). The *GNB3* non-risk homozygotes CC combination experienced decreased GWG compared to those with at least one risk allele, CT/TT (est. differences = −7.3 and −6.0 kg, *p=0.051* and *p=0.107*, respectively), although the overall *GNB3* effect was not significant.

These models demonstrated a significant association between GWG and parity (multi- vs. single); obese women gained significantly more weight if it was a first child (about 10 kg, *p<0.0001* for each gene group). Income trended on significant in *FTO* and *GNB3* models (*p=0.049*, and *p=0.056*, respectively), with obese low-income women gaining about 4.4 kg more than high-income women in each model. The overall African American sample also revealed significance of early pregnancy BMI predicting GWG in *FTO* and *GNB3* multivariable models (*p < 0.0001*).

In overweight women, the relationship between GWG and *GNB3* was significant (*p=0.032)*, controlling for early pregnancy BMI, income, parity, intervention arm, and smoking status. Women with the *GNB3* CT allele combination had decreased GWG compared to those with the TT allele combination (est. difference = −6.6 kg., *p=0.011*), while decreased GWG in CC compared to those with the TT combination was trending on significant (est. difference = −4.7 kg., *p=0.110*).

Postpartum Weight Retention—There was no statistically significant association of the *FTO* and *GNB3* with 6-month postpartum weight retention overall and by BMI category

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with one exception. Women in the overweight subsample with the *FTO* AT allele combination had a nearly significant increase in weight retention than AA and TT allele combinations (est. differences = 6.0 and 5.2 kg., *p=0.084* and *p=0.074, respectively*), even though the overall effect was not significant (*p=0.152*). Women in the overweight subsample with the *GNB3* TT allele had a nearly significant increase in weight retention than CC/CT allele combinations (est. differences = 5.6 and 4.4 kg, *p=0.079* and *p-0.168*), even though the overall effect was not significant (*p=0.176)*.

Caucasian Subsample

There was no deviation from the Hardy Weinberg equilibrium in the *FTO* (χ^2=0.3267, *p=0.568*) or *GNB3* (χ^2=0.013, *p=0.910*) genes [22].

Early pregnancy BMI—There was no statistically significant association of *FTO* and *GNB3* alleles with early pregnancy BMI overall and by BMI category except in the overall Caucasian subsample; there was a trend ($p < 0.1$) toward carriers of the *GNB3* C allele being heavier early in pregnancy (Table 4). Low-income women tended to have higher early pregnancy BMIs (about 0.9 kg/m^2, *p=0.03* for both models) (Tables 3 and 4) as did multiparous women (0.78 kg/m^2 and *p=0.030, 0.029* for *FTO* and *GNB3* models, respectively).

Gestational Weight Gain—There were no differences in GWG among the *FTO* and *GNB3* alleles for Caucasian women. There was a significant negative relationship between GWG and early pregnancy BMI (estimated coefficient =−0.3 kg, *p<0.0001)* for both models) (Tables 3 and 4). Multiparous women had reduced GWG compared to primiparous women (estimated coefficient =−1.4 kg, *p=0.003* for both models). For normal BMI women there were significant associations of GWG, income and parity. Higher income and multiparous women saw reduced weight gain for *FTO* and *GNB3* (Tables 3 and 4).

Postpartum Weight Retention—There were no differences in weight retention at 6-months postpartum among *FTO* and *GNB3* overall and by BMI categories with one exception. In the overweight sample there was a trending [effect] for women with the *GNB3* TT combination having less weight retention than CC combination (−2.6 kg., p=0.097). The *FTO* gene was significantly associated with weight retention in overweight women, with risk allele homozygotes, AA, experiencing less weight retention compared to AT/TT combinations (estimated differences = −2.7 and −1.9 kg, *p=0.038* and *p=0.162*, respectively). The overall effect of the *FTO* was not significant (*p=0.115*).

Six-month weight retention was significantly associated with the income: low-income women had a higher weight retention (Tables 3 and 4) in *FTO* and *GNB3* models, an effect seen particularly in normal and overweight women. In the normal weight subsample, increasing early pregnancy BMI was associated with increasing weight retention.

Discussion

In the current study *FTO* and *GNB3* gene associations with pregnancy weight were different by racial group and early pregnancy BMI. For African American women *FTO* risk alleles

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were associated with GWG if women were obese in early pregnancy: obese women homozygous for the risk allele (AA) had higher GWG compared to alternative allele combinations (AT, TT). There was a trend for an association of the *GNB3* gene with GWG in obese African American women with non-risk CC homozygotes having a lower weight gain. In overweight African American women the *GNB3* gene was associated with GWG: women with the CT combination had lower weight gains than the TT combination. For Caucasian women, there were trends toward *GNB3* C carriers being heavier in early pregnancy and *GNB3* homozygote (TT) overweight women having less weight retention than those with CT or CC combinations.

Early pregnancy BMI

Early pregnancy BMI was not associated with gene SNPs in our study. Out of four studies that examined an *FTO* association with prepregnancy BMI, three found an association [2, 8, 10]: in a Brazilian sample (primarily self-reported black skin) [2]; in a UK sample (unknown racial/ethnic group) [8]; and in Danish women [10]. In the fourth study, in a US African American sample no association was found [6]. The most likely explanation for differences is race/ethnicity admixtures and limited sample sizes.

Gestational weight gain

The finding that obese African American women homozygous for the FTO risk allele had a significantly higher GWG than non-carriers (7.6 kg) is consistent with our prior study [6]. A study that examined interaction effects of the *FTO* gene with prepregnancy BMI on GWG in Caucasian women also reported no main effect, yet a gene interaction with prepregnancy BMI [9]; an effect not found in their African American sample. No main effect of the *FTO* gene on GWG is consistent with other studies [2, 8, 9].

In the current study, the *GNB3* gene was marginally associated with GWG in African American overweight/obese women. Heterozygotes gained more weight than non-risk allele carriers. In our prior study there were no significant associations in African American women [6], however, the small sample may have compromised power. In a study of US women (294 Hispanic, Caucasian and African American), those homozygous for the risk allele gained significantly more weight than carriers of the C allele [11].

Postpartum weight retention

In this study, *FTO* and *GNB3* gene effects were evident in overweight Caucasians. This is similar to a study where inactive women with the *GNB3* risk allele retained more weight [12]. We did not include a physical activity measure. Studies of postpartum weight retention and the *FTO* gene did not report an effect [2, 6, 8]. The women in those studies self-identified as African American, black, or race was not indicated. Reports did not include examination of gene effects by prepregnancy BMI category in two of the studies, and measurement of weight retention was at or before six weeks postpartum, when weight stabilization is questionable [2, 8]. The small sample size of the third study may have compromised power [6].

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Non-genetic findings

Parity was associated with early pregnancy BMI with multiparous women starting pregnancy at a higher BMI. This is consistent with literature indicating women retain weight postpartum and start subsequent pregnancies at a higher BMI [1]. Income was associated with early pregnancy BMI in Caucasians. Low-income women had a higher early pregnancy BMI, consistent with current evidence [23]. It is unclear why this was different for African Americans. In our sample, 80% of African Americans and 27% of Caucasians were low-income and early pregnancy BMI was higher in African Americans.

All women gained more weight if this was their first baby consistent with the literature [24, 25]. Postpartum weight retention was higher in Caucasian but not African American low-income women if initially at a normal weight. This finding is consistent with a study reporting that normal weight black women were at greater risk of overweight/obesity if they had high GWG compared to women who were already overweight/obese [26]. Alternatively, the risk for weight retention has been found to increase with high GWG irrespective of prepregnancy BMI [25].

Implications

The implications of this study from a clinical perspective are substantial. There was not a clear association between gene SNPs and early pregnancy BMI. However, there were associations of the *FTO* gene, particularly in African American obese women, with GWG. Women with the risk allele gained 4.1 kg (AT) and 7.6 kg (TT) more than those without risk alleles. A similar pattern occurred for the *GNB3* gene in overweight women; women with one copy of the risk allele gained 6.6 kg less than those with two copies. These findings provide evidence that African American women who start pregnancy overweight/obese and have one of these gene variants are at risk of higher GWG. This study provided less evidence of a clinical impact for Caucasian women. Nonetheless, there were trends for overweight women to retain more weight (2.6 kg) if they carried a *GNB3* risk allele.

A limitation of the current study is the small sample size. We were able to detect an association of the *FTO* gene with GWG in obese African Americans, a trend in association of the *GNB3* gene with GWG in African Americans, and trends in Caucasians of an association of the *GNB3* gene with early pregnancy BMI and postpartum weight retention. Another limitation is the lack of ancestry informative markers to precisely categorize women into racial/ethnic groups. The effect of the intervention on GWG and weight retention should be interpreted with caution. In the original study, women were randomized to intervention and control conditions. For this secondary analysis, randomization was broken because the interest was to observe association of the genes by race. Thus, an observed intervention effect can be confounded by unknown characteristics being unbalanced within racial groups. Therefore we did not discuss intervention effects.

Conclusion

Results from the current study provide evidence that the *FTO* gene and possibly the *GNB3* gene are associated with increased GWG in obese African American women. Further study

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is needed of obesity gene SNPs and pregnancy weight in larger samples of different racial/ethnic groups to further characterize genetic effects on pregnancy weight gain and retention.

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Table 1

Maternal characteristics and gene allele frequencies by racial group

Covariate	African American N (%)	Caucasian N (%)
Age		
< 20	33 (17%)	16 (3%)
20 - 30	129 (66%)	295 (51%)
>= 30	32 (16%)	269 (46%)
BMI Category		
Normal	87 (45%)	317 (55%)
Overweight	61 (31%)	173 (30%)
Obese	46 (24%)	90 (16%)
Gestational Weight Gain in Institute of Medicine Ranges		
Below	40 (27%)	92 (17%)
Within	38 (26%)	172 (33%)
Above	68 (47%)	263 (50%)
Smoking (Time 1)		
Yes	11 (6%)	31 (5%)
No	114 (59%)	495 (85%)
Non Report	69 (36%)	54 (9%)
Smoking (Time 2)		
Yes	7 (4%)	19 (3%)
No	81 (42%)	433 (75%)
Non Report	106 (55%)	128 (22%)
Parity		
Single	85 (45%)	258 (45%)
Multiple	103 (55%)	316 (55%)
Income		
High	38 (20%)	426 (73%)
Low	156 (80%)	154 (27%)
Treatment Arm		
Placebo	57 (29%)	196 (34%)
Pregnancy	68 (35%)	185 (32%)
Pregnancy + Postpartum	69 (36%)	199 (34%)
***FTO* Allele Frequencies**		
AA	39 (20%)	84 (14%)
AT	95 (49%)	286 (49%)
TT	60 (31%)	210 (36%)
***GNB3* Allele Frequencies**		
CC	19 (10%)	263 (45%)
CT	75 (39%)	255 (44%)
TT	100 (52%)	62 (11%)
	Mean (SD)	

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Covariate	African American N (%)	Caucasian N (%)
Early pregnancy BMI	26.4 (4.9) n=194	25.3 (4.2) n=580
Gestational Weight Gain	12.7 (6.6) n=147	14.4 (5.3) n=529
6-Month Weight Retention	4.7 (6.2) n=111	2.3 (5) n=460

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Table 2

Percent of women with gestational weight gain within Institute of Medicine (IOM) guidelines based on prepregnancy BMI category

	Normal		Overweight		Obese	
	African American	Caucasian	African American	Caucasian	African American	Caucasian
Below IOM guidelines	25	22.4	25	8.4	33.3	16
Within IOM guidelines	26.6	42.5	27.3	18.8	23.1	22.2
Above IOM guidelines	48.4	35	47.7	72.7	41	59.3

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Table 3

Estimated coefficients for each model including *FTO*. A is the risk allele, so the wild genotype, TT, is used as a reference

	Overall		Normal		Overweight		Obese	
	AA	**Cauc**	**AA**	**Cauc**	**AA**	**Cauc**	**AA**	**Cauc**
Early pregnancy BMI								
*FTO*AA	0.2	0.3	1†	0.2	0.2	0.5	−1.3	−1.5†
*FTO*AT	−0.2	0	0.9*	0.1	0.7	0.4†	−1.5†	−0.3
Income	−0.8	0.9*	0	−0.1	0	−0.1	0.1	0
Multiparity	1.6*	0.8*	−0.3	0	0.4	0.3	0.2	0.8†
Smoked: No	−1.5	−1	0.1	0.5	0	0.4	0.4	−1.9*
Smoked: Non Report	−1.8	−0.5	−0.1	0.9	0.3	−0.3	0.2	−1.9†
Gestational Weight Gain								
*FTO*AA	1.9	−0.3	1	0.8	0.9	−2	7.6*	0.1
*FTO*AT	0.8	0.5	0.7	0.8	−1	−0.1	3.6	1.1
Early pregnancy BMI	−0.5***	−0.3***	−0.2	0.3	−0.3	−0.6†	−0.1	0.1
Treatment arm	−2†	1.2*	−2.8	0.1	−0.4	1.8†	−4*	3.3*
Income	0.1	0.7	1.5	1.9**	−3.2	0.2	4.4*	−1.1
Multiparity	−2.1*	−1.4**	0.5	−1.4**	−1.7	−1.2	−10***	−1.7
Smoked: No	−0.5	1	4.8	−1.9		3.8	−5.2	4.2
Smoked: Non Report	0.6	0.6	4.4	−1.7	3	3.1	−4	1.2
6 Mo. Weight Retention								
*FTO*AA	−0.6	−0.6	0	−0.4	−0.8	−1.9	−2	3.6
*FTO*AT	−1.2	0.4	−3.2	0.3	5.2†	0.8	−0.4	0.5
Early pregnancy BMI	−0.2	0	0.8	0.3*	0.3	−0.3	0	−0.3
Pregnancy arm	0.7	−0.1	−0.4	−0.2	0.9	0.1	−3.1	−1.2
Pregnancy +Postpartum	−1.7	0.1	−6**	0.1	2.3	0.9	0	−2.8
Income	1.2	2.5***	4.6*	2.4**	1.5	2.2*	3.2	1.7
Multiparity	−1.7	−0.7	1.1	−0.4	−4.4†	0.1	−3.7	−3.4†
Smoked: No	−0.3	2.1	5.5	0.9		4.1	−3	2.9

	Overall		Normal		Overweight		Obese	
	AA	Cauc	AA	Cauc	AA	Cauc	AA	Cauc
Smoked: Non Report	−1	2.4	5	1.1	1.9	6†	−8†	2.3

† p<0.1,

* p<0.05,

** p<0.01, and

*** p<0.0001

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Table 4

Estimated coefficients for each model including *GNB3*. T is the risk allele, so the wild genotype, CC, is used as a reference

	Overall		Normal		Overweight		Obese	
	AA	**Cauc**	**AA**	**Cauc**	**AA**	**Cauc**	**AA**	**Cauc**
Early pregnancy BMI								
*GNB3*CT	−0.6	0.7†	0.3	0.1	−0.7	−0.2	−0.6	0.8
*GNB3*TT	−0.8	1†	0.5	−0.2	−0.7	0.1	−0.8	0.9
Income	−0.7	0.9*	0	−0.1	0	−0.1	0.4	−0.1
Multiparity	1.5*	0.8*	−0.2	0	0.4	0.3	0.4	0.8†
Smoked: No	−1.5	−0.9	0.1	0.5	−0.1	0.4	0	−1.8†
Smoked: Non Report	−1.7	−0.3	−0.3	0.8	0.3	−0.3	−0.1	−1.9†
Gestational Weight Gain								
*GNB3*CT	0.7	0.4	−1.4	−0.3	−1.9	1.5	7.3†	0.2
*GNB3*TT	2	0.8	−0.7	1.2	4.7	0.7	6	−0.2
Early pregnancy BMI	−0.5***	−0.3***	−0.2	0.3†	−0.5	−0.6†	−0.3	0.1
Treatment arm	−1.7	1.2*	−2.6	0.2	1.1	1.4	−2.9	3.3*
Income	0	0.7	1.6	1.8**	−4†	0.2	4.5†	−0.9
Multiparity	−2.2*	−1.4**	0.5	−1.4**	−4.4*	−1.2	−10.4***	−1.6
Smoked: No	−0.5	1	4.2	−1.6		4.1	−5.3	3.8
Smoked: Non Report	0.4	0.7	3.9	−1.3	2.6	3.7	−4.4	0.6
6 Mo. Weight Retention								
*GNB3*CT	0.4	0	−5.6	−0.4	1.2	−1	5.8	2.1
*GNB3*TT	−0.3	−0.3	−6.2	1.3	5.6†	−2.6†	2.7	0.3
Early pregnancy BMI	−0.2	0	0.9†	0.4*	0.4	−0.4	0.2	−0.5
Pregnancy arm	0.4	−0.1	−2.2	−0.2	2.6	−0.4	−2.8	−1
Pregnancy +Postpartum	−2	0.1	−7.3**	0.2	5.2†	0.8	−0.8	−2.8
Income	1.3	2.5***	4.4†	2.2**	0	1.9†	3	2.8
Multiparity	−1.7	−0.7	0.7	−0.4	−5†	0.5	−5.1	−2.6

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	Overall		Normal		Overweight		Obese	
	AA	Cauc	AA	Cauc	AA	Cauc	AA	Cauc
Smoked: No	−0.2	2.1	6†	1.1		4	−6.6	3.3
Smoked: Non Report	−0.8	2.4	6.2†	1.3	1.2	6.2†	−8.8†	3

† p<0.1,

* p<0.05,

** p<0.01, and

*** p<0.0001