# Deconstructing The Genetic Architectures Of BMI and Eating Behavior Phenotypes

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## Introduction

The modern food supply and sedentary lifestyle contribute significantly to the high prevalence of excess weight and obesity, but it is estimated that as much as 40-70% of the variability in body mass index (BMI) and adiposity is explained by genetics[1]. One of the most robust genetic associations predicting BMI is the *FTO* gene, as confirmed by experimental studies, yet mechanistic questions remain. Additionally, the broader polygenic architecture of BMI also implicates genes expressed in the central nervous system[2], suggesting mechanisms beyond individual differences in metabolism.

Indeed, psychological processes may partially explain the relationship between genetics and BMI. Both positive and negative emotional states have been shown to influence when and how much we eat[3]. Several studies have found that overweight individuals are more likely to overeat in response to negative emotions as compared to normal to underweight individuals[4]. Here, we examine the relationship between eating behavior, BMI, and genetics.

## Methods

The study population includes 354,787 survey respondents who were genotyped as part of the 23andMe Personal Genome Service and consented for research. The population characteristics are described in **Table 1**. Respondents completed a 21-item eating behavior questionnaire, which addressed various aspects of emotional eating, restrictive eating, situational eating, social eating, overeating, and passive screen-time eating. Only responses with non-missing data for age, sex, body mass index, race/ethnicity, and all 21-items in the questionnaire were included in analyses.

To evaluate the relationship between each behavior surveyed and body mass index, bivariate correlations were explored on a per-item basis (**Figure 1**). Next, we used principal components analysis to explore the dimensionality of eating behaviors constructs and to identify eating behavior endophenotypes (**Figure 2**). Finally, the genetic architectures of the two first principal components were explored in genome wide association studies (GWAS) (**Figures 3, 4**).

For the first two principle component GWAS shown in **Figures 3 and 4**, the sample was restricted to unrelated people of European descent, and was adjusted for age, sex, genotyping platform, and the first 5 genetic ancestry principal components—with and without adjusting for BMI. Statistical analyses were conducted in R.

## Results

**Table 1. Population characteristics, by BMI category.**

| | Full sample | BMI <25 | BMI 25-29.9 | BMI 30-34.9 | BMI 35+ |
|---|---|---|---|---|---|
| **Characteristic** | **N=354,787** | **N=63,012** | **N=64,721** | **N=128,434** | **N=98,620** |
| Age (mean(SD)) | 49.2(15.9) | 47.7(17.5) | 53.5(15.9) | 49.6(15.4) | 47.0(14.8) |
| % Female | 63% | 76% | 57% | 56% | 67% |
| **Body mass index** | | | | | |
| BMI (mean(SD)) | 31.7(6.9) | 22.2(1.9) | 27.3(1.4) | 32.2(1.4) | 40.2(4.9) |
| **Ancestry** | | | | | |
| European | 81% | 82% | 84% | 81% | 80% |
| African American | 3% | 2% | 2% | 3% | 4% |
| Asian | 1% | 3% | 1% | 1% | 1% |
| Other | 14% | 13% | 12% | 15% | 15% |
| Latino | 11% | 10% | 10% | 12% | 12% |

## Results

### Emotional and situational eating positively correlate with BMI

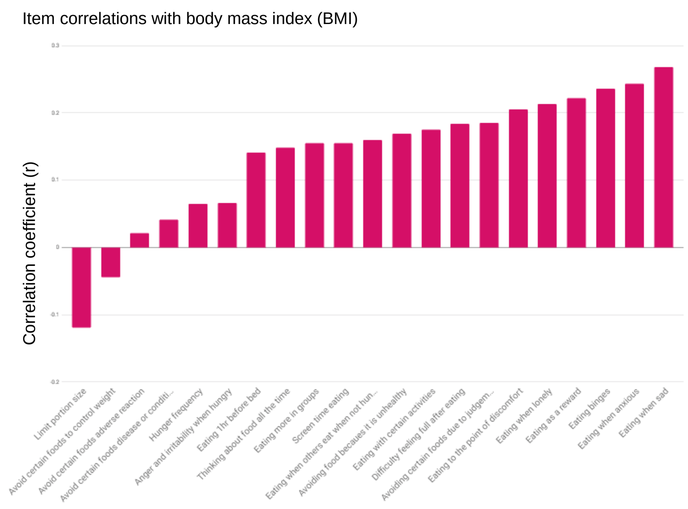


**Figure 1. Item level correlations with body mass index (BMI).** Correlation coefficients between each survey item and BMI.

### PCA identifies two broad constructs: Emotional or situational eating and avoidant eating

A)

| Item | PC 1 | PC 2 |
|---|---|---|
| **Limit portion size** | -0.11 | **0.40** |
| **Avoiding food becaues it is unhealthy** | -0.07 | **0.47** |
| **Avoid certain foods disease or condition** | -0.02 | **0.40** |
| **Avoid certain foods to control weight** | -0.02 | **0.49** |
| **Avoid certain foods adverse reaction** | 0.01 | **0.35** |
| **Avoiding certain foods due to judgement** | 0.14 | **0.22** |
| Hunger frequency | 0.16 | 0.03 |
| Screen time eating | 0.17 | -0.07 |
| Eating 1hr before bed | 0.18 | -0.10 |
| Anger and irritability when hungry | 0.19 | 0.05 |
| **Difficulty feeling full after eating** | **0.22** | 0.01 |
| **Eating more in groups** | **0.24** | -0.01 |
| **Eating to the point of discomfort** | **0.25** | -0.07 |
| **Thinking about food all the time** | **0.27** | 0.05 |
| **Eating with certain activities** | **0.27** | -0.01 |
| **Eating with others eat when not hungry** | **0.28** | 0.05 |
| **Eating as a reward** | **0.29** | 0.05 |
| **Eating binges** | **0.29** | -0.04 |
| **Eating when lonely** | **0.30** | 0.07 |
| **Eating when anxious** | **0.31** | 0.09 |
| **Eating when sad** | **0.32** | 0.08 |

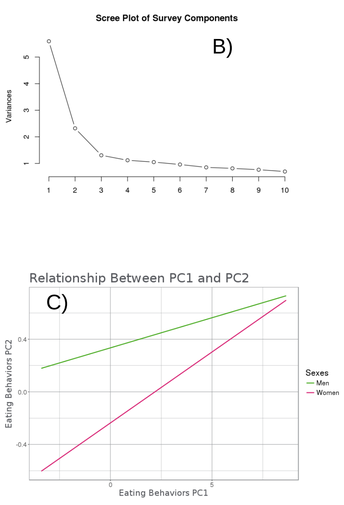


**Figure 2. Principal components.** A) Factor loadings for PC1 and PC2 B) Scree plot of PCA analysis showing two major latent dimensions, C) Relationship between (non-orthogonal) PC1 and PC2, by sex. The dimensional structure of the survey items suggested one broad construct of emotional and situational eating, as well as a common factor of avoidant behavior. When allowed to be non-orthogonal, the relationship between these PCs was stronger among women than among men.

### GWAS of PC1: Emotional and situational eating

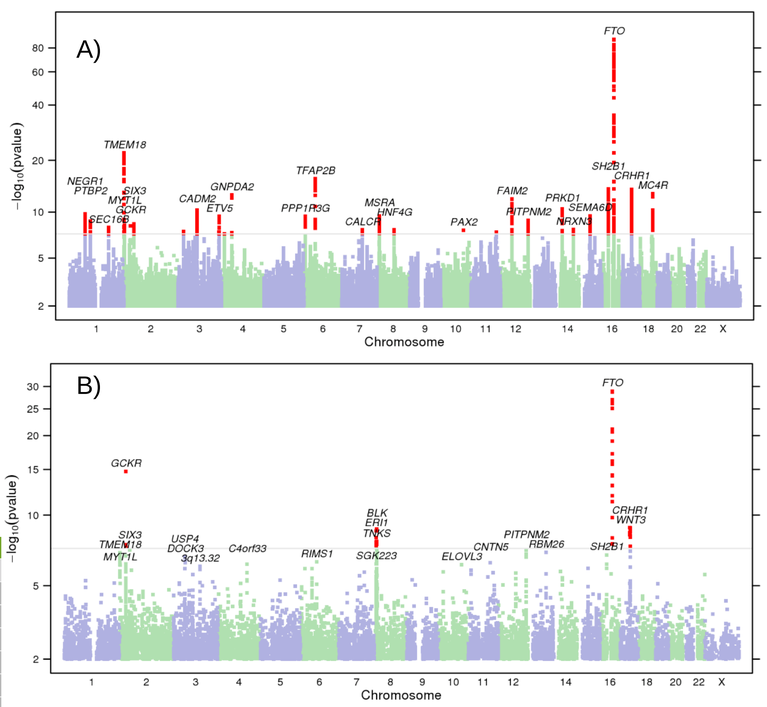


**Figure 3. GWAS of PC1.** A) Manhattan plot of the GWAS for PC1 adjusting for age, sex, and population structure B) Controlling for all factors in plot A with the addition of BMI.

### GWAS of PC2: Avoidant eating

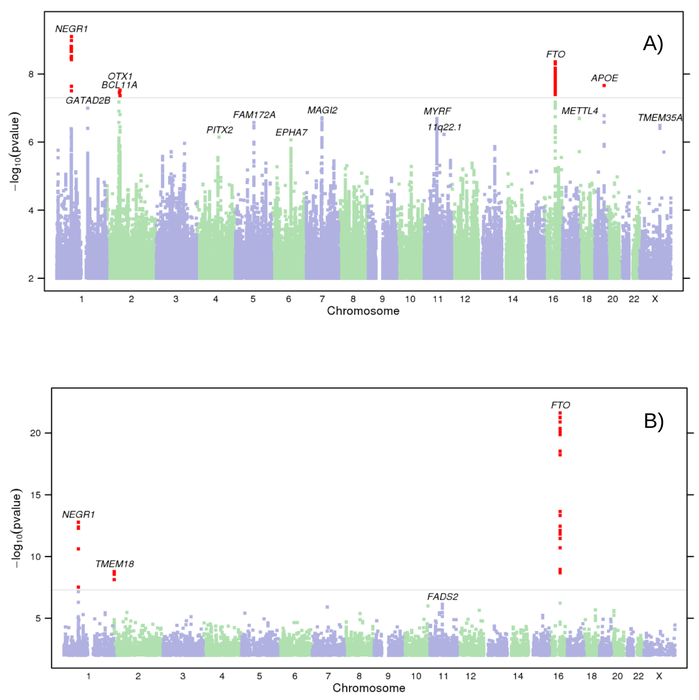


**Figure 4. GWAS of PC2.** A) Manhattan plot of the GWAS for PC2 adjusting for age, sex, and population structure B) Controlling for all factors in plot A with the addition of BMI

## Discussion

These findings support a long-standing body of research associating *FTO* with behaviors contributing to elevated weight. Furthermore, we extend previous analyses by examining the genetic architecture of emotional/situational and avoidant eating behavior that is independent of BMI. Indeed, *FTO* and several additional loci may play a role in the way we choose to eat or not eat in response to negative emotional states and situations as well as food avoidant behaviors independent of their direct effect on BMI.

Our results suggest that there may be genetic vulnerability to emotional/situational and avoidant eating that may enhance the feedback loop between BMI and these constructs. In light of the limited success of dieting and exercise interventions to control weight, and the strong feedback cycles associating negative emotional states (e.g. sadness, anxiety, and loneliness) with increased food intake behaviors, cognitive and behavioral strategies specifically designed to aid emotional and situational eating should be explored to minimize the health impacts of these common emotional states. Individuals with enhanced genetic vulnerability to situational eating may especially benefit from such interventions.

## Acknowledgments

We thank 23andMe customers who consented to participate in research for enabling this study. We also thank employees of 23andMe who contributed to the development of the infrastructure that made this research possible.

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