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Specific common variants of the obesity-associated *FTO* gene are not associated with psychological and behavioral eating disorder phenotypes

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Abstract

Extensive population-based genome-wide association studies have identified an association between the *FTO* gene and BMI; however, the mechanism of action is still unknown. To determine whether *FTO* may influence weight regulation through psychological and behavioral

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factors, seven single nucleotide polymorphisms (SNPs) of the *FTO* gene were genotyped in 1085 individuals with anorexia nervosa (AN) and 677 healthy weight controls from the international Price Foundation Genetic Studies of Eating Disorders. Each SNP was tested in association with eating disorder phenotypes and measures that have previously been associated with eating behavior pathology: trait anxiety, harm-avoidance, novelty seeking, impulsivity, obsessionality, compulsivity, and concern over mistakes. After appropriate correction for multiple comparisons, no significant associations between individual *FTO* gene SNPs and eating disorder phenotypes or related eating behavior pathology were identified in cases or controls. Thus, this study found no evidence that *FTO* gene variants associated with weight regulation in the general population are associated with eating disorder phenotypes in AN participants or matched controls.

Variations in the *FTO* gene have been implicated in obesity phenotypes in several genome-wide association studies (Dina et al., 2007; Frayling and McCarthy 2007; Grant et al., 2008; Hinney et al., 2007; Hunt et al., 2008; Loos et al., 2008; Scuteri et al., 2007; Thorleifsson et al., 2009; Willer et al., 2009). *FTO* has been associated with satiety responsiveness (Wardle et al., 2008) and is highly expressed in hypothalamic regions of the brain associated with appetite regulation (Stratigopoulos et al., 2008); however, the function of *FTO* and how it influences body mass is not yet understood. In a sample of Quebec, Canada families (n=908), *FTO* single nucleotide polymorphisms (SNPs) were associated with energy expenditure but not energy intake (Do et al., 2008), whereas in a smaller Scottish sample (n=151) the opposite was found (Speakman et al., 2008). Other evidence suggests that *FTO* may not affect body mass index (BMI) independently, but rather moderates the effect of energy expenditure (i.e., physical activity) on BMI (Andreasen et al., 2008; Berentzen et al., 2008).

Behavioral factors that might influence BMI have also been investigated. A study of children found *FTO* to potentially influence food choice and preference for energy-dense foods but not energy expenditure (Cecil et al., 2008). However, a study of children, adolescents and adults from European population cohorts found no association between *FTO* and eating behaviors including snacking, cravings, restriction, disinhibition, hunger, and binge-eating (Stutzmann et al., 2009). Although *FTO* may affect energy balance independent of appetite regulation (Frayling and McCarthy 2007), at this time there is no evidence suggesting an association of *FTO* with specific behavioral features of a hyperphagic phenotype in adults.

Examining populations with extreme phenotypes can facilitate identification of predisposing gene variants for complex disorders. To date, such efforts have been limited. Although single-nucleotide polymorphisms (SNPs) of *FTO* have been associated with BMI in several studies and appear to influence variation between normal weight and obesity (Dina et al., 2007; Frayling and McCarthy 2007; Hinney et al., 2007; Hunt et al., 2008; Loos et al., 2008; Scuteri et al., 2007; Thorleifsson et al., 2009; Willer et al., 2009), there are no observed associations of *FTO* SNPs with disordered eating behaviors (i.e., binge eating, snacking, craving, restriction, disinhibition, hunger, bulimia) in extreme obesity (Stutzmann et al., 2009), or a clinical diagnosis of anorexia nervosa (AN) (Brandys et al., 2010).

To limit the number of analyses in the current study, we focused on a set of candidate psychological and behavioral eating disorder phenotypes. Our group has previously described a multivariate approach to characterize intermediate behavioral phenotypes in persons with AN to identify gene-phenotype associations in this complex illness (Bacanu et al., 2005; Bulik et al., 2005). Three of the phenotypes—a composite measure of anxiety, obsessionality, and age at menarche—demonstrated heritability in both AN and bulimia nervosa (BN). Three others—lifetime minimum BMI, concern over mistakes, and food-related obsessions—showed extreme inter-individual variation and clustered in families. In

addition, several other quantitative traits, such as harm avoidance, novelty seeking, compulsions, and impulsivity, were presented as candidate phenotypes relevant to eating disorders pathology, published evidence for heritability (e.g. Holland et al., 1988; Keski-Rahkonen et al., 2005; Rutherford et al., 1993; Wade and Bulik 2007; Wilksch and Wade 2009), and showed an association with eating disorders in previous studies conducted by our group (Bacanu et al., 2005; Bulik et al., 2005; Bulik et al., 1995; Fassino et al., 2004; Halmi et al., 2003; Klump et al., 2000). These phenotypes may be behavioral mechanisms by which polymorphisms in the *FTO* gene exert an influence on body weight.

As studies of *FTO* in extreme disturbances of eating behavior remain limited, we examined associations between a select panel of candidate phenotypes and *FTO* in a well-characterized case-control study of persons with AN. Exploring the association of *FTO* with eating disorder phenotypes could help us understand 1) the possible role of this gene in AN liability and phenotypic heterogeneity and 2) the behavioral factors that might mediate the association between the *FTO* gene and weight regulation.

MATERIALS AND METHODS

Participants

Female participants for the current study (1085 AN cases and 677 controls) were selected from three studies that were part of the international Price Foundation Genetic Studies of Eating Disorders: the Anorexia Nervosa Affected Relative Pair Study (Kaye et al., 2000), the Bulimia Nervosa Affected Relative Pair Study (Kaye et al., 2004), and the Anorexia Nervosa Trios Study (Reba et al., 2005). The affected participants were chosen based on availability of adequate genomic DNA. All participants were then ordered using a diagnostic hierarchy (highest to lowest): 1) restricting AN (RAN), 2) AN with purging but no binge eating (PAN), 3) AN with binge eating with or without purging (BAN), 4) a lifetime history of both AN and BN (ANBN), 5) subthreshold AN with no binging or purging, 6) purging BN, and 7) subthreshold BN. From each family, the individual with the diagnosis highest in the hierarchy was selected. Using these same criteria, a secondary set of samples was selected; each of these participants was related to one individual in the primary sample. For complete details of the sample selection and diagnostic criteria, see Pinheiro et al. (2010). Briefly, our analysis sample had 10 families with two second-degree relatives, 15 families with two third-degree relatives, and three families with two fourth-degree relatives. All sites received approval from their local Institutional Review Board and informed consent was obtained from all study participants. Brief descriptions of each study are provided below.

AN Affected Relative Pair Study—Probands and affected relatives were ascertained for this study. Probands were required to meet the following criteria: modified DSM-IV criteria for AN, amenorrhea not required; low weight that is/was less than the 5th percentile of body mass index (BMI) for age and gender according to the Hebebrand et al. (1996) The National Health and Nutrition Examination Survey (NHANES) chart; age between 13 and 65 years at the time of study; eating disorder onset prior to age 25; and having met criteria for AN not less than three years prior to ascertainment. Affected relatives were required to be biological family members who were between the ages of 13 and 65 years at the time of study and had lifetime eating disorder diagnosis of DSM-IV AN excluding amenorrhea, a lifetime eating disorder diagnosis of DSM-IV BN, or a diagnosis of eating disorder not otherwise specified. For the complete list of inclusion and exclusion criteria for probands and relatives, see Kaye et al. (2000).

BN Affected Relative Pair Study—Participants for this study included probands and affected relatives. Probands were required to meet the following criteria: a lifetime DSM-IV

diagnosis of BN with the additional criterion of at least a six-month period of binge eating and vomiting at least twice a week and between the ages 13 and 65 at the time of study. Affected relatives had to meet the same criteria as for the AN Affected Relative Pair Study. A complete list of inclusion and exclusion criteria for both probands and relatives can be found in Kaye et al. (2004).

AN Trios Study—Individuals with AN, their parents, and a sample of control women were ascertained for this study. Probands were required to meet the same criteria as the probands in the AN Affected Relative Pair Study with the additional criterion of weight that is/was controlled through restricting and/or purging. In order to limit any potential genetic confounds from obesity, female participants were excluded if they reported maximum BMI since puberty > 27 kg/m^2.

All participating sites in the AN Trios Study recruited healthy women between the ages of 18 and 65 to serve as a control group. Thus, control and affected participants were matched by site, age range, ancestry, and education. Control women were required to be at normal weight with a lifetime adult minimum BMI above 19 and maximum BMI below 27 kg/m^2. BMI exclusions were designed to screen for eating disorders (on the low end) and obesity on the upper end to be consistent with exclusion criteria in the eating disorders groups. Additional exclusion criteria for the control women included a score of 20 or higher on the Eating Attitudes Test (Garner et al., 1982), indicating a history of an eating disorder or eating disordered behaviors; a first degree relative with an eating disorder; and a history of any disorder assessed using the Structured Clinical Interview for DSM-IV (SCID) Screen Patient Questionnaire (First et al., 1997). The control group participants completed the same battery of self-report questionnaires as probands, assessing personality and symptom measures.

Assessment Instruments

Many of the same assessment instruments were used in all three studies. The differences among studies are noted below.

General Clinical Information—A modified version of the Structured Interview for Anorexia Nervosa and Bulimic Syndromes [SIAB; (Fichter et al., 1998)] was used to obtain data for minimum and maximum BMI, age at menarche, and a history of menstrual irregularity. Women who reported oligomenorrhea, primary amenorrhea, or secondary amenorrhea were classified as having irregular menses; those with normal cycles were scored as having normal menses; and no score was given to women reporting pregnancy or hormone use during time of low weight.

Eating Disorder Diagnosis—Lifetime diagnoses of eating disorders were determined using responses to the SIAB (Fichter et al., 1998). In the BN Affected Relative Pair and AN Trios studies, the SIAB diagnosis was validated using the Module H of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I). SCID I was also used to obtain information about age of onset, severity of illness, recovery status and months since last eating disorder symptom.

Disordered Eating Behaviors—Binge eating, vomiting, fasting, excessive exercising, and eating more when stressed or overburdened, as assessed by the SIAB, were examined in the current study. Below is a brief description of the scoring used; a detailed description of the questions and response options are available elsewhere (Pinheiro et al., 2010).

Binge eating behavior was defined as episodes of eating in which the participant ate a large amount of food (>1000 k cal) in a relatively short period of time with loss of control over the eating behavior. If the participant endorsed binge eating at least an average of twice a week (no minimum duration) and had at least slight loss of control, she was scored as positive for binge eating behavior. For both vomiting and fasting, participants who endorsed the "never" response option were considered to not engage in the respective behavior. Those who endorsed any of the other response options were considered to have engaged in the behavior. Participants were considered excessive exercisers if they reported that their exercise severely interfered with important activities, they exercised more than three hours per day and experienced distress if unable to exercise, they frequently exercised at inappropriate times and places with little or no attempt to suppress the behavior, or they exercised despite more serious injury, illness or medical complication. All other participants were categorized as not excessive/regular exercisers. For eating more when stressed or overburdened, participants who responded "never" were scored as 0 and those who responded "rarely," "sometimes," "frequently," or "very frequently" were scored as 1.

Personality and Symptom Assessments—From all three studies, personality and symptom variables included the harm avoidance and novelty seeking scales from the Temperament and Character Inventory (TCI; Cloninger et al., 1993), the concern over mistakes scale from the Frost Multidimensional Perfectionism Scale (MPS; Frost et al., 1990), trait anxiety from the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970), total obsessions and compulsions from the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989), and worst total score from the Yale-Brown-Cornell Eating Disorder Scale (YBC-EDS; Sunday et al., 1995)

The drive for thinness, body dissatisfaction and bulimia subscales of the Eating Disorder Inventory-2 (EDI-2; Garner 1990) were assessed in both the AN Affected Relative Pairs and AN Trios studies. The Barrett Impulsivity Scale-11 (BIS-11; Barrett 1983) was administered in the BN Affected Relative Pairs and AN Trios studies. The scales used from the BIS-11 were cognitive, motor, and non-planning.

SNP selection—A detailed description of candidate gene and SNP selection for the initial study is available elsewhere (Pinheiro et al., 2010). In brief, genes residing under reported eating disorders linkage peaks, plausible candidate genes based on previous findings reported in the eating disorders literature, published findings in other related disorders, and genes involved in pathways thought to be implicated in AN were identified, including *FTO*. This inclusive list was then reduced and genes were selected that had evidence of expression in the brain and were shown to be estrogen responsive in microarray assays. Seven *FTO* SNPs (rs7193144, position=52368187; rs8043757, position=52370951; rs3751812, position=52375961; rs11075990, position=52377394; rs9941349, position=52382989; rs17817964, position=52385567; rs9930506, position=52387966) passed all quality control steps and were selected to test the specific hypothesis for the current study.

Statistical analyses

Statistical software R 2.9.1 (R Development Core Team 2009), JMP 7.0 (SAS Insititute Inc. 1989–2007), and PLINK (Purcell et al., 2007) were used to conduct all analyses. For each phenotype, we ran a model testing for the main effect of the individual SNP genotypes under various models including additive, dominant, and recessive. Each model also included affection status and the interaction between the SNP and affection status. Logistic regression was used for binary variables and linear regression for continuous variables. The best model for each analysis was selected using a step-wise procedure based on the AIC criterion (Akaike 1987). We present only the results based on the additive model because 1)

previously published work had demonstrated that *FTO* SNPs were associated with BMI primarily in the additive model; 2) for our data, the additive model demonstrated the best or comparable fit to all other models; and 3) no SNP reached genome-wide significance under recessive or dominant models. We also performed stratified association analysis separately for cases and for controls and obtained similar results. For each analysis, correction for multiple testing was accomplished using the local false discovery rate (FDR) approach (Efron et al., 2001) that is implemented in R/fdrtool (Strimmer 2008). The local FDR is an empirical Bayesian posterior probability and is more readily interpretable than the classical FDR.

Power analysis—Power analysis was conducted using the R/gap genetic analysis package (Zhao 2007), and Genetic Power Calculator (Purcell et al., 2003). Under an additive genetic model assuming disease prevalence of 0.009 and disease allele frequency of 0.4, and assuming type I error rate at 10^{-8} level, our sample has 80% power to detect effect sizes of at least 2.3 relative risk for binary traits or at least 2.2% variance for quantitative traits.

Standard quantitative trait loci analysis assumes that the data are normally distributed. Violations of this assumption can decrease the power and increase the type I error rate. We examined the distributions of quantitative phenotypes within the total sample that showed various degrees of departure from normality. In order to deal with non-normal distribution of these traits, we explored a number of data transformation methods and used a goodness-of-fit test to assess normality of transformed data. We found that log and square root methods did not transform data to a normal distribution and that the qualitative conclusions of the association test were unchanged when transformed data were used (data not shown). Other methods, including a rank-based method or converting a quantitative measure to a dichotomous or categorical variable, would result in a loss of information and therefore were not implemented.

RESULTS

The *FTO* SNPs passed all quality control screening (see Pinheiro et al., 2010). Minor allele frequencies of the *FTO* SNPs ranged from 0.41 to 0.45. Missing genotypes were found for four AN cases in two SNPs and the difference in missingness was not significant between cases and controls ($p>0.50$). All seven SNPs satisfied Hardy Weinberg equilibrium ($p>0.24$ in controls). All pair-wise linkage disequilibrium (r^2) values among the seven SNPs ranged between 0.81 and 1.

Table 1 presents the uncorrected and corrected p-values for the most significant SNPs from the association analyses, accounting for affection status and the interaction between SNP and affection status. (Since all SNP pairs have high linkage disequilibrium, the results for the SNPs not shown are similar). The lowest uncorrected p-value obtained for all SNP analyses was 0.021, which corresponds to an FDR of 0.47, suggesting no significant phenotype-genotype association.

After FDR correction for multiple comparisons, no significant associations were found for any of the *FTO* SNPs genotyped with eating disorder phenotypes or measures of trait anxiety, harm-avoidance, novelty seeking, impulsivity, obsessionality, compulsivity, or concern over mistakes, in cases or controls. Among the cases only, there were also no significant associations between *FTO* SNPs and the drive for thinness, body dissatisfaction, or bulimia scales.

Given the preliminary nature of this study, we sought to inform future research in this area by exploring some of the non-significant trends identified in the current sample that may

warrant examination in subsequent studies. In uncorrected tests, highest lifetime BMI was significantly higher for individuals with one or two copies of the rs7193144 at-risk C allele as compared to those homozygous for the T allele ($p<.033$). Similarly, lowest lifetime BMI was significantly higher among individuals carrying one or two copies of the rs3751812 at-risk T allele as compared to individuals homozygous for the G allele ($p<.021$). These results are consistent with the expected effects of these SNPs on BMI and obesity risk based on previous evidence (Dina et al., 2007; Grant et al., 2008; Hinney et al., 2007; Scuteri et al., 2007); however, the non-significant corrected FDR values for these effects suggest the findings may be spurious.

DISCUSSION

The purpose of this study was to explore the association of *FTO* with eating disorder phenotypes to inform our understanding of the possible influence of this gene on AN phenotypic expression and to elucidate potential behavioral mechanisms linking the *FTO* gene to weight regulation. Seven *FTO* SNPs were genotyped in a sample of 1085 AN cases and 677 controls with well-characterized eating disorder related phenotypes. There were no allele frequency differences between cases and controls, suggesting that *FTO* is not associated with the syndrome of AN. After appropriate correction for multiple comparisons, we found no evidence for any association among *FTO* SNPs and eating disorder phenotypes or measures of trait anxiety (STAI), harm-avoidance, novelty seeking (TCI), impulsivity (BIS-11), obsessionality, compulsivity (Y-BOCS), or concern over mistakes (MPS)—variables that have previously been associated with eating disorders (Bulik et al., 2005). Further, by including affection status and the interaction of affection status with genotype in the analyses, we considered whether the effect of *FTO* on eating disorder related phenotypes might be specific to cases or controls. These analyses revealed an absence of any affection status specific SNP associations with eating disorders related phenotypes. There was also no association between *FTO* and the drive for thinness, body dissatisfaction, or bulimia scales (EDI-2) among the cases.

Although not significant post correction, two SNPs previously associated with BMI and obesity in population samples were also associated with increased highest (rs7193144 C allele) and increased lowest (rs3751812 T allele) lifetime BMI in the current sample. Two genome-wide association studies (Hinney et al., 2007; Scuteri et al., 2007) independently reported the associations of the same *FTO* genetic variant, the rs7193144 C allele, with increased obesity and obesity-related traits in European and Hispanic populations. Similarly, the T allele of SNP rs3751812 has been associated with severe obesity in both adults and children of European ancestry (Dina et al., 2007) and childhood obesity in a cohort consisting of both Caucasians and African Americans (Grant et al., 2008). The potential association between *FTO* and BMI in the current female-only sample appears to be in line with previous larger scale studies showing an association between the *FTO* gene and weight regulation in both males and females. The association between *FTO* variants and BMI—albeit non-significant post statistical correction—that is consistent with previous published studies helps substantiate the examination of possible psychological and behavioral mechanisms linking *FTO* to weight regulation in the current study sample.

Overall, our findings do not support the hypothesis that previously reported associations between *FTO* and elevated BMI are reflected in intermediate behavioral phenotypes that have shown to be important in eating disorders, AN and BN. The effect of *FTO* on weight regulation might be more biological in nature—related to metabolic dynamics of energy regulation, for instance—than due to behavioral patterns or psychological factors. This would be consistent with previous findings in adults showing no association between *FTO* and eating behaviors (Stutzmann et al., 2009) and caloric intake, but a significant effect of

FTO on measures of energy regulation—insulin sensitivity, resting metabolic rate, and plasma leptin levels (Do et al., 2008). The association of *FTO* with energy regulation reported by Do and colleagues (2008), however, was non-significant when accounting for fat-free mass. Further, the cross-sectional nature of the study makes it difficult to determine whether body mass is a cause of poor energy regulation or mediates the association between *FTO* and energy regulation.

To determine the mechanistic role of *FTO*, more research examining the link between *FTO* and the biological and behavioral risk factors for poor weight regulation will be needed. This may be more easily accomplished using mouse models, since these studies allow functional testing of candidate genes for selected phenotypes in a controlled genetic and environmental background. For instance, a study characterizing body weight regulation in mice found that although *FTO* gene deficient mice exhibited less locomotor activity and relatively normal caloric intake, they were leaner and had increased levels of energy expenditure compared to mice with one or two copies of the active *FTO* allele (Fischer et al., 2009). This evidence further suggests that *FTO* may influence body weight via energy regulation.

Limitations of the current study include its small sample size and the number of comparisons conducted, reducing power. Increased sample size improves power in general and provides more robust results. To detect an effect size similar to what has been reported (odds ratio 1.07–1.67) for BMI in previous studies (Dina et al., 2007; Frayling and McCarthy 2007; Hinney et al., 2007; Hunt et al., 2008; Loos et al., 2008; Scuteri et al., 2007; Thorleifsson et al., 2009; Willer et al., 2009), the current study would need to significantly relax type I error rate for all tests, setting the error rate to 0.005. With this more liberal type I error rate, our sample would have sufficient power (80%) to identify an odds ratio of at least 1.5 under an additive genetic model assuming disease prevalence of 0.009 and disease allele frequency of 0.4.

In conclusion, we found no evidence for large effects of *FTO* genetic variants on selected eating disorders phenotypes in AN cases or controls. However, the potential for small effects of *FTO* genetic variants on behavioral phenotypes should be considered. We cannot exclude the possibility that some associations might be found with a considerable increase in sample size—particularly the number of individuals presenting with clinically significant eating disorder phenotypes—density of *FTO* SNPs examined, or number and diversity of eating disorder phenotypes examined.

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Table 1

Results (p-value, uncorrected) and FDR corrections for multiple comparisons (p_{fdr}-value) from association analysis for the top *FTO* SNPs[1].

Variable	N	SNP	SNP p-value (p_{fdr}-value)	Affection Status p-value (p_{fdr}-value)	Interaction p-value (p_{fdr}-value)
Age of Onset of Eating Disorder[2]	Cases=1084 Controls=NA	rs9941349	0.23 (1)	NA	NA
Duration of Eating Disorder[2]	Cases=933 Controls=NA	rs9930506	0.42 (1)	NA	NA
Lifetime Highest BMI[3]	Cases=1085 Controls=677	rs7193144	0.033 (0.47)	$<10^{-8}$ ($<10^{-8}$)	NA
Lifetime Lowest Illness-Related BMI[3]	Cases=1085 Controls=677	rs3751812	0.021 (0.47)	$<10^{-8}$ ($<10^{-8}$)	NA
Structured Interview on Anorexic and Bulimic Disorders					
Age at Menarche[3]	Cases=1065 Controls=667	rs9941349	0.66 (1)	$<10^{-8}$ ($<10^{-8}$)	NA
Menstrual Status[3]	Cases=1053 Controls=667	rs9930506	0.33 (1)	$<10^{-8}$ ($<10^{-8}$)	NA
Eating Stress[2]	Cases=1065 Controls=NA	rs17817964	0.73 (1)	NA	NA
Excessive Exercise[2]	Cases=1067 Controls=NA	rs7193144	0.37 (1)	NA	NA
Fasting[2]	Cases=1066 Controls=NA	rs8043757	0.20 (1)	NA	NA
Binge Eating[2]	Cases=1064 Controls=NA	rs9941349	0.64 (1)	NA	NA
Vomiting[2]	Cases=1066 Controls=NA	rs9941349	0.23 (1)	NA	NA
State-Trait Anxiety Inventory – Form Y					
Trait anxiety[3]	Cases=1055 Controls=669	rs17817964	0.30 (1)	$<10^{-8}$ ($<10^{-8}$)	NA
Temperament and Character Inventory					
Harm avoidance[4]	Cases=1067 Controls=671	rs8043757	0.13 (0.66)	$<10^{-8}$	0.14 (0.66)
Novelty seeking[3]	Cases=1067 Controls=671	rs8043757	0.69 (1)	$<10^{-8}$ ($<10^{-8}$	NA
Multidimensional Perfectionism Scale					

Variable	N	SNP	SNP p-value (p_{fdr}-value)	Affection Status p-value (p_{fdr}-value)	Interaction p-value (p_{fdr}-value)
Concern Over Mistakes[3]	Cases=1071 Controls=673	rs17817964	0.42 (1)	$<10^{-8}$ ($<10^{-8}$)	NA
Yale-Brown-Cornell Eating Disorder Scale					
Worst Total Score[2]	Cases=1081 Controls=NA	rs9941349	0.063 (0.66)	NA	NA
Yale-Brown Obsessive Compulsive Scale					
Obsessions[2]	Cases=1029 Controls=NA	rs9941349	0.58 (1)	NA	NA
Compulsions[2]	Cases=1029 Controls=NA	rs7193144	0.72 (1)	NA	NA
Eating Disorder Inventory – 2					
Bulimia[4]	Cases=786 Controls=676	rs9941349	0.34 (1)	$<10^{-8}$ ($<10^{-8}$)	0.16 (0.66)
Body Dissatisfaction[3]	Cases=786 Controls=676	rs9941349	0.74 (1)	$<10^{-8}$ ($<10^{-8}$)	NA
Drive for Thinness[3]	Cases=784 Controls=677	rs9941349	0.49 (1)	$<10^{-8}$ ($<10^{-8}$)	NA
Barrett Impulsivity Scales					
Cognitive[4]	Cases=751 Controls=670	rs9941349	0.11 (0.66)	$<10^{-8}$	0.055
Motor[3]	Cases=745 Controls=664	rs17817964	0.69 (1)	0.051 (0.47)	NA
Non-planning[3]	Cases=750 Controls=671	rs9941349	0.62 (1)	0.007 (0.47)	NA

[1] Linkage disequilibrium values among the 7 SNPs are between .81 and 1.00, thus the results for the other SNPs are similar, confirming no association.

[2] Data are available for cases only.

[3] Best models include SNP and affection status.

[4] Best models include SNP, affection status, and interaction.