Sensitivity Genotype Moderates the Link between Objective Weight and Perceived Weight Status among Young Women in the U.S.

Robbee Wedow, BS[1, 2, 3*]
Jason D. Boardman, PhD[1, 2, 3]

[1] Department of Sociology, University of Colorado, Boulder, Colorado
[2] Health and Society Program, Institute of Behavioral Science, University of Colorado, Boulder, Colorado
[3] Institute for Behavioral Genetics, University of Colorado, Boulder, Colorado
*Direct correspondence to Robbee Wedow, Institute of Behavioral Science University of Colorado Boulder, rwedow@alumni.nd.edu

Key Words: genetic sensitivity, perceived weight status, body mass index, social cues, 5HTTP

Running title: Sensitivity Genotype and Perceived Weight Status

Manuscript Word Count (Introduction, Methods, Results, Discussion): 1,498

Funding: This research was supported, in part by a grant from The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NIH/NICHD R01HD061622), from the NICHD supported University of Colorado Population Center (R24 HD066613), and the National Science Foundation's Graduate Research Fellowship Program (DGE 1144083). Any opinion, findings, and conclusions or recommendations expressed in this material are those of the authors(s) and do not necessarily reflect the views of the National Science Foundation. This research uses data from Add Health, a program project directed by Kathleen Mullan Harris and designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris at the University of North Carolina at Chapel Hill, and funded by grant P01-HD31921 from The Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 23 other federal agencies and foundations. Special acknowledgment is due to Ronald R. Rindfuss and Barbara Entwisle for assistance in the original design. Information on how to obtain the Add Health data files is available on the Add Health website (http://www.cpc.unc.edu/addhealth). No direct support was received from grant P01-HD31921 for this analysis.

Abstract

Objective

To date, only a limited body of work has evaluated the pathways through which the same objective weight leads to different perceived weight status assessments. The objective of this article is to evaluate the role of a common genetic polymorphism of the 5HTTLPR gene as a potential link between objective body mass index (BMI) and perceived weight using a nationally representative sample of adolescents as they age to adulthood.

Methods

Genetic data from Waves I- IV of the National Longitudinal Study of Adolescent Health is used to investigate whether the short allele genotype of 5HTT, a genotype associated with environmental sensitivity, moderates the association between measured body-mass index and perceived, self-reported weight (reported on a 5-point Likert scale).

Results

Results confirm significant sensitivity for women in Waves I and II at heavier BMI values. Importantly, it is only once BMI exceeds levels approaching clinical obesity that we see a significant departure in the predicted values.

Conclusions

This study shows a link between a specific polymorphism and sensitivity to social cues about body size. It may therefore provide the foundations for important future work that investigates the forces that lead young women in America to characterize their "ideal weight".

Introduction

Overestimating body size is more common among women compared to men in the United States[1, 2]. Overestimating body size has been shown to be one potential pathway toward the development of disordered eating behaviors for young women[3]. As such, understanding the factors responsible for the links between perceived and objective physical weight has critical public health implications. To date, a limited number of studies have evaluated the pathways through which the same objective weight leads to very different perceived weight statuses and most of this work has focused on social demographic factors such as race, class, and marital status[4].

This brief report examines the role of a common genetic polymorphism as a link between objective body mass index (BMI) and perceived weight. This study builds on the gene-environment interaction (GxE) literature to assess the possibility that carriers of the short allele in the 5HTT gene are more likely than those with two long alleles at this loci to report being overweight at higher levels of BMI. This hypothesis stems from work showing that the S' allele in the 5HTT gene predicts sensitivity to environmental cues[5, 6, 7, 8]. 5HTTLPR is believed to encode the serotonin transporter protein and is active in the serotonin nerve pathways that are involved in controlling mood. The S' allele in this gene is linked to decreased serotonin reuptake in cellular synapse. Carriers of the S' allele appear to be sensitive to both healthy and unhealthy environments[9] and are characterized as differentially susceptible to the same environmental cues[10].

GxE research typically emphasizes exposure to environmental risks such as stressful life events or physical abuse, but recent work has shown that sensitivity to social norms may also be affected by this same polymorphism[11]. The emphasis on social norms provides a critical component to understanding gender differences in the subjective evaluation of one's objective weight[12] because of the prevalence of differentially gendered "ideal body types"[13, 14]. As such, this study evaluates the relevance of a genetic moderation of social cues by examining the link between objective BMI and perceived weight status among adolescent boys and girls at two points in time.

Methods

The National Longitudinal Study of Adolescent to Adult Health (Add Health) is a nationally (United States) representative and longitudinal sample of adolescents originally assessed in grades 7-12 during the 1994-95 school year. The cohort was followed into young adulthood with four in-home interviews and contains detailed information on respondents' social, psychological and physical well-being with information on respondents' family, neighborhood, school, and peer groups; thus it provides a unique way to study how social environments and behaviors in young people are linked to health outcomes in adulthood. *Study Population*: After dropping pregnant women and those for whom genetic data were not available, the overall cross-sectional sample sizes were: Wave1: 13,157; Wave 2: 10,050; Wave 3: 10,585; and Wave 4: 13,345. *Perceived Weight Status (dependent variable):* Perceived weight status was assessed with the following categories: very underweight, underweight, normal weight, overweight, and very overweight. *Genetic Sensitivity*: Similar to past research on environmental sensitivity using risk allele data[15] genetic sensitivity was assessed as the presence of two S' alleles (recessive coding). *Objective BMI:* Objective body-mass index was calculated using objective measures of height and weight taken at each wave. At Wave 1, only self-reported height and weight were assessed. However, based on the high correlation between self-reported and objective heights and weights at waves 2, 3, and 4, self-reported BMI was used as a proxy for objective BMI at Wave 1. Mean objective BMI values were 22.55, 23.05, 26.27, and 29.07 for Waves 1, 2, 3, and 4, respectively. Because it does not affect the interaction effects of interest to this study, BMI remained non-centered in our models. *Background Characteristics*: All models included controls for age and race/ethnicity. Mean ages were 15.65, 16.20, 21.94, and 28.47 for Waves 1, 2, 3, and 4, respectively. Finally, race/ethnicity was a categorical, nominal variable coded where 1= white (52.48%), 2= black (22.36%), 3=Native American (0.85%), 4= Asian (7.16%), and 5=Hispanic (17.15%).

For this study, perceived weight is regressed on objective body-mass index interacted with the sensitivity genotype. Given the categorical and ordinal nature of the dependent variable, ordinal logistic regression models with the *ologit* command in STATA 13.0 were used.

Results

[Table 1 here]

Results from ordinal logit regression models are shown in first eight columns of Table 1. The hypothesis is confirmed for Waves 1 and 2 of the study but not for Waves 3 or 4. Specifically, results show that genetic sensitivity predicts a stronger association between objective BMI and self-perceived weight status for young women but not for young men. These results were first identified with a three-way interaction between gender, genotype, and BMI, but separate analyses for men and women are reported to facilitate the interpretation of the interactions. Importantly, the failure to find significant GxE associations in the later waves is in line with previous work showing that the social forces on ideal body type wane following late adolescence and early adulthood[16]. Results only confirm sensitivity at the heavier weights and not at the lower weights; that is the lightest women and men in the study were not significantly more likely to report being underweight as a function of genotype.

[Figure 1 here]

Figure 1b plots the results for women at Wave 2 of the study. The y-axis depicts the outcome variable, here shown as the probability of reporting to be "very overweight" on the 5-point perceived weight scale; the x-axis is BMI. As shown in Figure 1b, young women at wave 2 display differential susceptibility in their likelihood of reporting being overweight as objective BMI increases, with those young women with the sensitive genotype (two short alleles) for 5HTT more likely to report being "very overweight" compared to their relatively insensitive genotype counterparts (two long alleles or one long and one short allele). There are three important observations. First, the genetic moderation is very slight in magnitude. Next, this association is statistically significant, but genotype does not lead to differences in BMI and perceived weight for the bulk of the BMI distribution. Third, as mentioned above, it is only the heavier weights, once BMI exceeds levels approaching obesity that a true (and significant) departure in the predicted values is seen. Figure 1a shows the results for the likelihood of reporting "very underweight" on the 5-point perceived weight scale. As expected a similar but non-significant relationship is demonstrated; those young women with the sensitive genotype are more likely to report being "very underweight" as BMI decreases. These results are very much in line with the differential susceptibility hypothesis[10]. Analogous results were demonstrated for women in Wave 1. Models were further stratified by race/ethnicity, with results indicating stronger effects for the interaction between sensitivity genotype and objective BMI for young, white women than for young, black women (results not shown).

To test whether or not observations are robust across time, BMI change between Wave 1 and Wave 2 was interacted with sensitivity genotype to predict perceived weight status while controlling for age, race/ethnicity, and the objective BMI values from Wave 1 in a gender-stratified model. BMI change was calculated by subtracting the objective BMI values from Wave 1 from the objective BMI values in Wave 2. Further, to more accurately measure the likelihood of reporting being overweight, respondents who reported “overweight” or “very overweight” in Wave 1 as well as respondents whose objective BMI was clinically overweight (25 or greater) were removed from this supplemental analysis (reduced N= 2257 young and 2364 young women). The last two columns of Table 1 demonstrates that, even accounting for changes across time, genetic sensitivity continues to predict a stronger association between BMI and self-perceived weight status for young women, but not for young men.

[Figure 2 here]

Figure 2 plots predictive values for women; the y-axis depicts the outcome variable, the probability of reporting to be “very overweight” on the 5-point perceived weight scale; the x-axis is change in objective BMI from Wave 1 to Wave 2. Again, young women display differential susceptibility in their likelihood of reporting being overweight as the change in objective BMI increases between waves, with those young women with the sensitive genotype more likely to report being “very overweight” compared to those young women without the sensitivity genotype. It is again important to emphasize that results only confirm sensitivity at larger values of BMI change for girls.

Discussion

This study builds on previous work that demonstrates a genetic basis for the internalization of social norms regarding body size[17]. Importantly, this is the first paper to show a link between a specific polymorphism (5HTTLPR'S') and sensitivity to social cues about body size. Findings lay the foundation for future work to evaluate specific environmental cues and social norms about body size limited to adolescents. This is an important next step, because the social GxE framework suggests that the places in which people live, work, play, and go to school affects the relative contribution of genotype to observed health outcomes[18]. This is especially important given the gendered nature of GxE associations in general[19] and our GxE association in particular.

Speaking to the limitations of this study, a growing body of literature points toward simple sensitivity-allele, single-candidate gene studies like this one as often non-replicable and thus as producing false-positive results[20]. Furthermore, the effect sizes of the findings are relatively small and are only found amongst young women in the early waves of the Add Health dataset. Yet despite these limitations, this study opens an important potential avenue of consideration in the embodiment of social norms and body image literature. Given the links between perceived weight and gender, this study may provide the foundations for important future work that investigates the forces that lead young women in America to develop ideas about what "ideal weight" should look like.

References

1. Conley A, Boardman J. Weight overestimation as an indicator of disordered eating behaviors among young women in the United States. *International Journal of Eating Disorders* 2007;40.5:441-445.

2. Sciacca JP, Melby CL, Hyner GC, Brown AC, Femea PL. Body mass index and perceived weight status in young adults. *Journal of Community Health* 1991;16.3:159-168.

3. Farrell C, Lee M, Shafran R. Assessment of body size estimation: a review. *European Eating Disorders Review* 2005;13.2:75-88.

4. Chang VW, Christakis NA. Self-perception of weight appropriateness in the United States. *American Journal of Preventive Medicine* 2003;24.4:332-339.

5. Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, Harrington HL, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science* 2003;301.5631:386-389.

6. Glatz K, Mössner R, Heils A, Lesch KP. Glucocorticoid-regulated human serotonin transporter (5-HTT) expression is modulated by the 5-HTT gene-promotor-linked polymorphic region. *Journal of Neurochemistry* 2003;86.5: 1072-1078.

7. Tsang SWY, Lai MKP, Francis PT, Wong PTH, Spence I, Esiri MM, et al. Serotonin transporters are preserved in the neocortex of anxious Alzheimer's disease patients. *Neuroreport* 2003;14.10:1297-1300.

8. Heinz A, Braus DF, Smolka MN, Wrase J, Puls I, Hermann D, et al. Amygdala-prefrontal coupling depends on a genetic variation of the serotonin transporter. *Nature*

Neuroscience 2004;8.1: 20-21.

9. Simon MS, L'Heureux J, Murray JC, Winokur P, Weiner G, Newbury E, et al. Active choice but not too active: public perspectives on biobank consent models. *Genetics in Medicine* 2011;13.9:821-831.

10. Belsky J, Jonassaint C, Pluess M, Stanton M, Brummett B, Williams R. Vulnerability genes or plasticity genes? *Molecular Psychiatry* 2009;14.8:746-754.

11. Daw J, Shanahan M, Harris KM, Smolen A, Haberstick B, Boardman JD. Genetic Sensitivity to Peer Behaviors 5HTTLPR, Smoking, and Alcohol Consumption. *Journal of Health and Social Behavior* 2013;54.1:92-108.

12. Rodin J, Silberstein L, Striegel-Moore R. Women and Weight: a Normative Discontent. In: *Nebraska Symposium on Motivation*. Lincoln, NE: University of Nebraska Press; 1984.

13. Grogan S. Body Image: Understanding Body Dissatisfaction in Men, Women and Children. London: Routledge; 2007.

14. Sands ER, Wardle J. Internalization of ideal body shapes in 9-12-year-old girls. *International Journal of Eating Disorders* 2003;33.2:193-204.

15. Morrison AC, Bare LA, Chambless LE, Ellis SG, Malloy M, Kane JP, et al. Prediction of coronary heart disease risk using a genetic risk score: the Atherosclerosis Risk in Communities Study. *American Journal of Epidemiology* 2007;166.1:28-35.

16. Kuskowska-Wolk A, Karlsson P, Stolt M, Rössner S. The predictive validity of body mass index based on self-reported weight and height. *International Journal of Obesity* 1988;13.4:441-453.

17. Boardman JD, Roettger ME, Domingue BW, McQueen MB, Haberstick BC, Harris

KM. Gene–environment interactions related to body mass: School policies and social context as environmental moderators. *Journal of Theoretical Politics* 2012;24.3:370-388.

18. Boardman JD, Daw J, Freese J. Defining the Environment in Gene–Environment Research: Lessons From Social Epidemiology. *American Journal of Public Health* 2013;103.S1:S64-S72.

19. Perry BL, Pescosolido BA, Bucholz K, Edenberg H, Kramer J, Kuperman S, et al. Gender-Specific Gene–Environment Interaction in Alcohol Dependence: The Impact of Daily Life Events and GABRA2. *Behavior Genetics* 2013;43.5:402-414.

20. Duncan LE, Keller MC. A critical review of the first 10 years of candidate gene-by-environment interaction research in psychiatry. *American Journal of Psychiatry* 2011;168.10:1041-1049.

Table and Figures Legends

Table 1. Ordered Logistic Regression Tables (Coefficients and Standard Errors) for Waves 1-4 US Men and Women and for Waves 1-2 US Men and Women Measuring BMI Change.

Figure 1. Ordered Logistic Regression Plots for Women at Wave 2 Predicting Perceived Weight Status Outcomes for Sensitivity and Non-Sensitivity Genotypes.

Figure 2. Ordered Logistic Regression Plot for BMI Change in Waves 1-2 Women Predicting Perceived Weight Status Outcomes for Sensitivity and Non-Sensitivity Genotypes.

	MEN				WOMEN				BMI CHANGE	
Wave or Gender	1	2	3	4	1	2	3	4	Men	Women
Age (Years)	-.30***	-.24***	-0.01	-0.01	-.07***	-.01***	0.02	.05***	-.24***	-.05***
	(.02)	(.08)	(.08)	(.07)	(.06)	(.07)	(.07)	(.06)	(.03)	(.03)
Race (non-Hispanic White)										
Black	-.45*	-.32***	-.31***	-.79***	-.88***	-.63***	-.75***	-.82***	-0.29*	-0.64***
	(.07)	(.08)	(.08)	(.07)	(.06)	(.07)	(.07)	(.06)	(.16)	(.14)
Native American	-.59*	-0.61	-0.59	-0.18	-0.18	-0.25	0.002	-0.35	-0.81	0.17
	(.31)	(.38)	(.35)	(.32)	(.3)	(.35)	(.34)	(.32)	(.63)	(.7)
Asian	-0.08	-0.06	0.16	.29**	-0.12	-0.26	-0.03	-0.02	-0.03	-0.28
	(.11)	(.13)	(.12)	(.11)	(.11)	(.13)	(.12)	(.11)	(.23)	(.25)
Hispanic	0.02	0.04	.27***	-0.11	-.30***	-.27***	.25**	-0.09	-0.24	-0.51***
	(.08)	(.09)	(.09)	(.08)	(.07)	(.08)	(.08)	(.07)	(.03)	(.16)
Objective BMI	.44*	.40***	.41***	.36***	.42***	.35***	.33***	.30***		
	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)		
Wave 1 Objective BMI									0.42***	0.52***
									(.03)	(.03)
BMI Change (Wave 1 to 2)									0.40***	0.32***
									(.04)	(.32)
Sensitivity Genotype	-0.19	-0.13	-0.44	-0.04	-.66*	-.72*	0.2	-0.1	0.07	-0.13*
	(.32)	(.34)	(.35)	(.29)	(.31)	(.32)	(.27)	(.25)	(.13)	(.13)
Interaction (GxE)	0.01	0.01	0.02	-0.05	.03***	.03***	-0.01	0.01	-0.1	0.19**
	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.06)	(.07)
N	6333	4814	4951	6352	6824	5236	5634	6993	2257	2364

*p < .05. **p < .01. ***p < .001. Standard Error Values in Parentheses.

Table 1. Ordered Logistic Regression Tables (Coefficients and Standard Errors) for Waves 1-4 US Men and Women and for Waves 1-2 US Men and Women Measuring BMI Change.

Figure 1a. Wave 2 Women: Probability of Reporting Very Underweight.

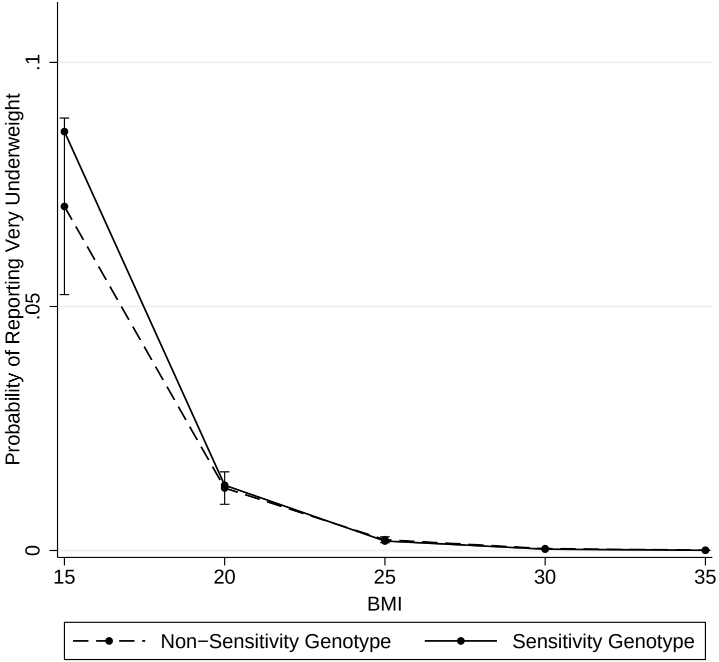
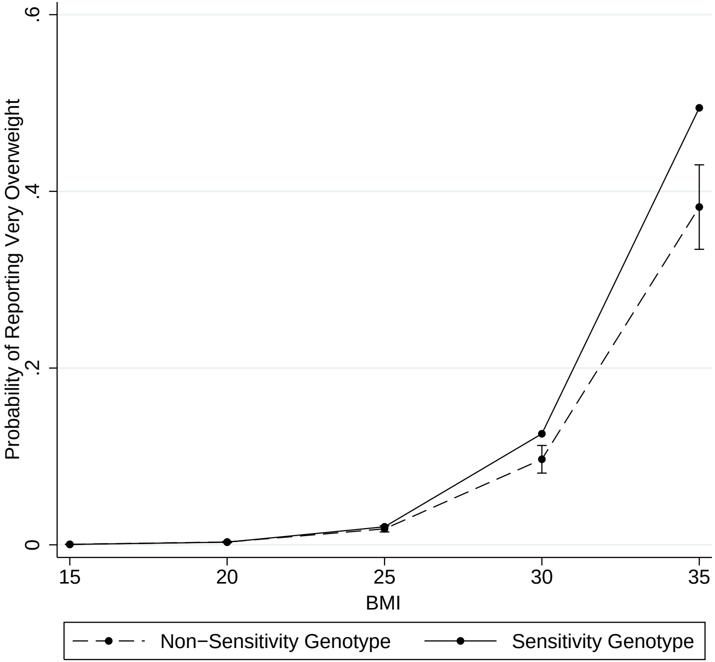
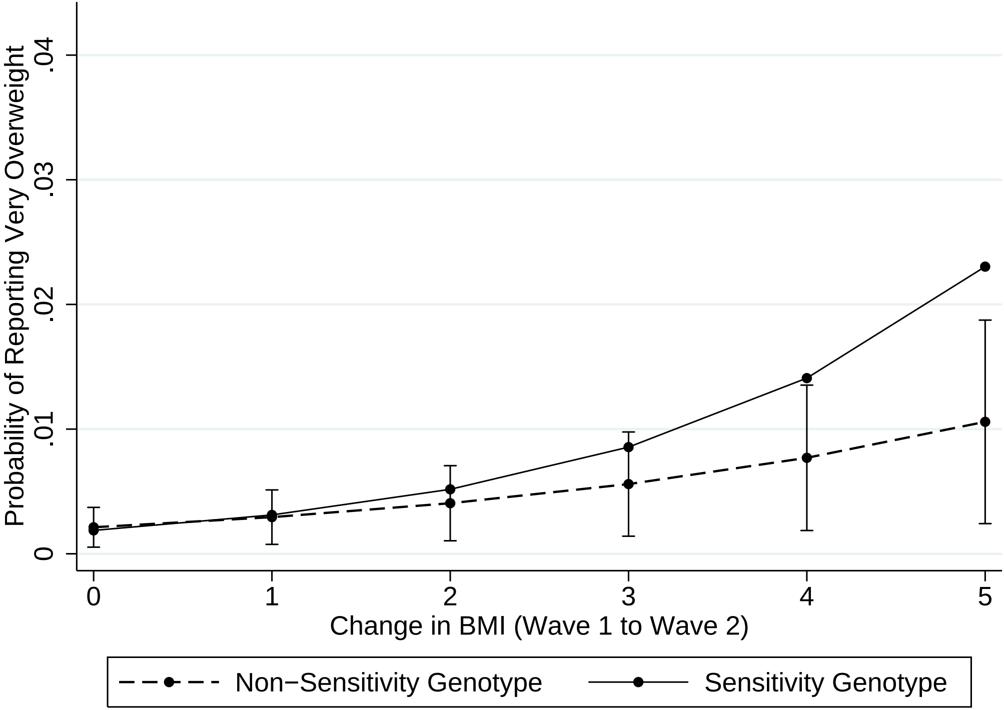


Figure 1b. Wave 2 Women: Probability of Reporting Very Overweight.





Probability of Reporting Very Overweight
0
.01
.02
.03
.04
0
1
2
3
4
5
Change in BMI (Wave 1 to Wave 2)
Non−Sensitivity Genotype
Sensitivity Genotype