Published in final edited form as:

Int J Eat Disord. 2015 May ; 48(4): 375–382. doi:10.1002/eat.22280.

Are There Common Familial Influences for Major Depressive Disorder and an Overeating-Binge Eating Dimension in both European-American and African-American Female Twins?

Melissa A. Munn-Chernoff, PhD^{1,2}, Julia D. Grant, PhD^{1,2}, Arpana Agrawal, PhD^{1,2}, Rachel Koren, BA³, Anne L. Glowinski, MD, MPE^{1,2}, Kathleen K. Bucholz, PhD^{1,2}, Pamela A. F. Madden, PhD^{1,2}, Andrew C. Heath, DPhil^{1,2}, and Alexis E. Duncan, PhD, MPH^{1,2,4}

¹Department of Psychiatry, Washington University School of Medicine, St. Louis, MO 63105

²Midwest Alcoholism Research Center, Washington University School of Medicine, St. Louis, MO 63105

³Genetic Alliance, Washington D.C. 20008

⁴George Warren Brown School of Social Work, Washington University, St. Louis, MO 63130

Abstract

Objective—Although prior studies have demonstrated that depression is associated with an overeating-binge eating dimension (OE-BE), phenotypically, little research has investigated whether familial factors contribute to the co-occurrence of these phenotypes, especially in community samples with multiple racial/ethnic groups. We examined the extent to which familial (i.e., genetic and shared environmental) influences overlapped between Major Depressive Disorder (MDD) and OE-BE in a population-based sample and whether these influences were similar across racial/ethnic groups

Method—Participants included 3226 European-American (EA) and 550 African-American (AA) young adult women from the Missouri Adolescent Female Twin Study. An adaptation of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) was administered to assess lifetime DSM-IV MDD and OE-BE. Quantitative genetic modeling was used to estimate familial influences between both phenotypes; all models controlled for age.

Results—The best-fitting model, which combined racial/ethnic groups, found that additive genetic influences accounted for 44% (95% CI: 34%, 53%) of the MDD variance and 40% (25%, 54%) for OE-BE, with the remaining variances due to non-shared environmental influences. Genetic overlap was substantial ($r_g = .61$ [.39, .85]); non-shared environmental influences on MDD and OE-BE overlapped weakly ($r_e = .26$ [.09, .42])

Discussion—Results suggest that common familial influences underlie MDD and OE-BE, and the magnitude of familial influences contributing to the comorbidity between MDD and OE-BE is similar between EA and AA women. If racial/ethnic differences truly exist, then larger sample

sizes may be needed to fully elucidate familial risk for comorbid MDD and OE-BE across these groups.

Keywords

Race/ethnicity; African-American; twins; major depression; overeating; binge eating

Introduction

Previous research has indicated that Major Depressive Disorder (MDD) is associated with eating disorders¹⁻³ and specific eating disorder symptoms, including binge eating (BE)⁴ -- a symptom that cuts across eating disorder diagnoses and can be present among individuals who overeat. Major Depressive Disorder and BE co-occur more often than by chance alone. Participants in the National Comorbidity Study Replication who reported any lifetime BE were nearly twice as likely to meet criteria for lifetime MDD as those who did not report lifetime BE¹. Further, higher rates of depression have been reported among individuals who meet diagnostic criteria for Binge Eating Disorder compared with individuals who do not⁵. Both traits are attributable to a combination of genetic and environmental factors among women, with a heritability estimate of roughly 40% for MDD⁶ and approximately 50% for BE⁷. Thus, given that MDD and BE often co-occur and are both heritable, it is important to consider that they could share a portion of their genetic or environmental risk.

Interestingly, few studies have attempted to identify possible genetic and environmental overlap among these or related traits, yielding mixed results. Walters et al. (1992) reported a moderate genetic correlation ($r_g = .46$) between MDD and Bulimia Nervosa⁸, an eating disorder that includes BE. In a study investigating genetic and environmental contributions to six different psychiatric disorders -- including MDD and Bulimia Nervosa -- in adult female twins, Kendler and colleagues⁹ found shared genetic factors across Bulimia Nervosa, Phobia, and Panic Disorder, but not MDD, as well as a shared environmental factor specific to Bulimia Nervosa. In contrast, others¹⁰ have found genetic influences that are common across eating problems (i.e., Bulimia Nervosa symptoms) and depression symptoms among girls in both early (i.e., 8-13 year olds) and late (i.e., 14-17 year olds) adolescence, in addition to genetic influences that are specific to eating problems in early adolescence. Overlapping shared environmental factors for depression symptoms and eating problems were also present. Finally, Slane and colleagues¹¹ reported a large genetic correlation ($r_g = .70$) between continuous measures of depressive symptoms and general disordered eating characteristics, which included BE, in a small sample of young adult women ($n = 292$ twins). Notably, there have been no twin studies investigating overlapping etiologic factors for MDD and Binge Eating Disorder. The heterogeneity in findings could be due to the age differences across samples, the use of disorder symptoms versus clinical diagnoses, differences in diagnoses examined, and relatedly, the use of continuous versus categorical variables. The specific examination of common familial factors underlying the comorbidity of categorical MDD and overeating, which may include BE, has not been previously published.

Much of what is known about genetic and environmental influences on psychopathology, including the sources of covariation between MDD and BE, comes from samples of primarily European ancestry, which is in part due to the low number of non-Caucasian individuals in most major twin studies. A notable exception is a study by Whitfield and colleagues¹² which reported that additive genetic effects accounted for 40% of the overall liability to past week depressive symptoms, with non-shared environmental effects accounting for the remaining variance among African-American (AA) male and female twin pairs in middle adulthood (mean age = 47.1 years). Unfortunately, studies that have investigated genetic and environmental effects on overeating/BE, or the extent to which its genetic and environmental risk is shared with MDD, have not examined AA individuals separately. Therefore, it is unknown whether the magnitude of overlapping genetic and environmental effects for MDD and overeating/BE is similar in European-American (EA) and AA women. This is important to consider given that in non-twin populations, prior studies have reported lower rates of MDD in AA compared with EA individuals¹³⁻¹⁵, lower¹⁶, similar¹⁷, or higher^{18;19} rates of BE for AA compared with EA women, and lower²⁰ or higher¹⁹ rates of Binge Eating Disorder in AA than EA women. Differences in the prevalence of MDD and overeating/BE between racial/ethnic groups could result from differences in environmental factors known to be associated with these phenotypes. Any differences in etiologic underpinnings may affect the relative contribution of genetic and environmental risk, as well as the correlations, for MDD and overeating/BE. Thus, examining genetic and environmental risks on these phenotypes could yield important information to guide the tailoring of prevention and treatment of MDD, overeating/BE, and their co-occurrence in individuals across racial/ethnic groups.

The current study uses a population-based sample of EA and AA young adult female twins to investigate: 1) genetic and environmental influences on MDD and an overeating-binge eating dimension (OE-BE); 2) whether there are overlapping genetic and environmental influences for MDD and OB-BE within each racial/ethnic group; and 3) whether the magnitude of these specific and overlapping influences are the same in EA and AA women. Examining specific eating disorder symptoms, such as overeating/BE, in addition to clinical eating disorders, will help determine whether these symptoms that can cut across diagnoses and predict the later development of eating disorders²¹ show the same magnitude of genetic and environmental correlations as previous studies examining MDD and eating disorders.

Method

Participants

Participants were part of the Missouri Adolescent Female Twin Study (MOAFTS)^{22;23}, a population-based longitudinal twin study of female twins identified from state birth records and born between July 1st 1975 and June 30th 1985 in Missouri to a mother who was a state resident. Twins were recruited using a cohort sequential sampling design. Importantly, the MOAFTS sample is demographically representative of the Missouri population at the time the twins were born, with nearly 15% of twins being AA and the remainder being of European descent (as reported by the mother at the time of birth). A baseline interview was conducted with the twins beginning in 1995 (median age = 15 years). When possible,

interviews were also conducted with at least one parent (usually the mother) at the time the twins entered the study. Zygosity was determined by standard questions²⁴ that have shown approximately 95% agreement with genotyping methods²⁵. The Wave 4 young adult follow-up interview was conducted an average of six years after the baseline assessment (median age = 22 years). Since all members of the target cohort were 18 years old or older and study participation was no longer contingent upon parental consent, all individuals from the original sampling frame were invited to participate, even if they had not participated at baseline. The only twins who were excluded from being recontacted were those individuals who had either themselves refused future contact or whose parents had refused all future contact with family members. Analyses were conducted on 3226 EA twins (1514 complete pairs, 56.3% monozygotic (MZ)) and 550 AA twins (254 complete pairs, 43.7% MZ) who completed the Wave 4 assessment, out of a total of 3998 EA twins (1999 pairs) and 740 AA twins (370 pairs) originally identified from birth records. Thus, 81% of EA and 74% of AA respondents from the original sampling frame were included in the current analyses. A summary of response rates is provided elsewhere²⁶. The protocol was approved by the Washington University School of Medicine Institutional Review Board, and all twins gave informed consent before study participation.

Measures

At the Wave 4 follow-up, a telephone interview using an adaptation of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA)²⁷ assessed DSM-IV lifetime criteria of psychopathology, including MDD and OE-BE. In the depression section, respondents who reported ever experiencing dysphoria, anhedonia, and/or irritability (if <18 years at the time the symptom was experienced) for two weeks were asked to identify the most severe period of having such symptoms. A series of questions probing functional impairment during that period followed, including receipt of treatment, substantial work or educational difficulties, and serious relationship disturbances. Respondents indicating functional impairment were then asked about specific DSM-IV Major Depression symptoms during their most severe depressive episode, and asked whether they had experienced five symptoms together during the same two week period. If < five symptoms were endorsed or five symptoms did not occur together in a two week period, respondents were asked to nominate another two week period of time when they experienced dysphoria, anhedonia, and/or irritability, assessed for functional impairment, and if impaired, evaluated with the full depression section for this other episode. Respondents who endorsed clustering during a depressive episode were coded positive for lifetime MDD. At the end of the section, respondents were also asked if and when they had experienced other depressive episodes, and if so, brief characterizations of these were obtained.

Lifetime OE-BE was based on the endorsement of two questions: "Has there ever been a time in your life when you went on eating binges- eating a large amount of food in a short period of time, usually less than 2 hours?" and "During these binges, were you afraid you could not stop eating or that your eating was out of control?". Responses to these questions were combined into a three-level variable: no OE-BE (coded 0), overeating (i.e., eating a large amount of food but no loss of control; coded 1), and BE (i.e., eating a large amount of food and having a loss of control; coded 2). Of note, individuals who reported lifetime OE-

BE may have also reported lifetime use of compensatory behaviors. Although it has been shown that MDD is associated with Binge Eating Disorder^{1,28}, only four individuals in our sample met diagnostic criteria for this disorder, thus preventing us from examining it with MDD. Additional information regarding the assessment of MDD and OE-BE in the MOAFTS sample is provided elsewhere^{29,30}.

Statistical Analyses

Descriptive phenotypic analyses were conducted in STATA³¹ using Huber-White robust variance estimators to adjust the standard errors for the non-independence of observations inherent in twin data. Using raw data, bivariate twin models were employed to examine three sources of variance/covariance influencing liability to MDD and OE-BE: additive genetic (sum of the genes that combine additively to influence the trait, A), shared environmental (environmental factors that are shared by family members reared together, C), and non-shared environmental (environmental factors that are unique to each family member for a trait, E) effects. The proportion of variance attributable to genetic effects is often referred to as heritability, and non-shared environmental effects include measurement error as well as individual-specific influences. We began by evaluating the full ACE models for each phenotype within the EA and AA groups. Multiple submodels in which the parameter estimate (i.e., A, C, or E) was set to zero were then compared to the full models to determine whether it could be dropped. All model-fitting analyses were conducted in Mx³². Minus two log-likelihood (-2LL) and standard chi-square difference tests (χ^2)³³ were used to compare the fit of nested models under the full ACE models. In addition, Akaike's Information Criterion (AIC; calculated as -2LL minus twice the degrees of freedom (df))³⁴ was used to determine model fit. Models with lower (or more negative) AIC values are more parsimonious and provide a better fit of the model. We controlled for age by modeling probit regressions on age (i.e., allowing for prevalence rates of MDD and BE to differ by age).

Because OE-BE was defined as a polychotomous measure, a test of multivariate normality was conducted. The model provided a non-significant *p*-value (*p* = .31) separately in EA and AA twins, supporting the assumption of multivariate normality.

Results

European-American women were significantly younger than AA women (EA women: median age = 21 years, range = 19-24 years; AA women: median age = 22 years, range 19-24 years; Wald F statistic = 4.51 (1, 2010), *p* = .03). There were 3208 EA women and 547 AA women with complete data on MDD and OE-BE. European-American women had significantly lower rates of MDD than AA women (EA: 18.80%; AA: 24.86%; *p* = .003). For lifetime OE-BE, 7.39% of EA and 10.23% of AA women reported any overeating or BE. Of those individuals, 64.50% (4.77% of the population) of EA and 58.50% (6.03% of the population) of AA women endorsed overeating and the remainder indicated BE. Differences in rates of OE-BE were not significantly different between EA and AA groups (*p* = .07). Forty-two (41.83) percent of the EA women who reported overeating and 77.38% of women who reported BE also reported compensatory behaviors. Among AA women,

42.42% and 52.17% who endorsed overeating and BE, respectively, also reported compensatory behaviors.

In EA twins, 1.50% of the overall population had co-occurring MDD and BE and 1.68% had cooccurring MDD and overeating. Among AA women, 2.74% of the overall population had both MDD and BE, whereas 2.56% reported MDD and overeating. These differences between EA and AA women were statistically significant ($p < .0001$). The phenotypic correlation between MDD and OE-BE was .40 (95% confidence interval (CI): .32, .48) in EA women, .43 (.26, .59) in AA women, and .41 (.33, .48) in the combined sample of EA and AA women.

Twin correlations for EA and AA women for MDD, OE-BE, and their co-occurrence, are summarized in **Table 1**. In all instances, the r_{MZ} was less than one, confirming that nonshared environmental effects contributed to the variance and covariance of MDD and OE-BE in both ethnic/racial groups. In EA women, the r_{MZ} was greater than the r_{DZ} for MDD and OE-BE, indicating that genetic factors were likely influencing both traits. The r_{DZ} was greater than half the r_{MZ} in all three instances, suggesting that shared environmental effects were also influencing MDD, OE-BE, and their covariance. In AA individuals, the r_{MZ} was greater than the r_{DZ} for MDD, as well as the covariance between MDD and OE-BE, indicating that genetic factors were likely influencing both traits. The r_{DZ} was less than half the r_{MZ} in two instances, suggesting that dominant genetic effects were influencing the variance in MDD and the covariance of MDD and OE-BE. For BE in AA women, although the r_{DZ} was somewhat greater than the r_{MZ} , the correlations were not significantly different because the point estimate in one correlation fell within the 95% confidence interval of the other correlation. This suggests that any familial influences for OE-BE were attributable to C.

For the bivariate twin analyses, we first estimated genetic and environmental risk for the liability to MDD and OE-BE, as well as the covariance between the traits, separately in EA and AA women (**Table 2**). In EA women, a model that included only additive genetic and non-shared environmental effects on the variance in, and the covariance between, MDD and OE-BE (i.e., Model 3) provided the best fit to these data ($AIC = -7501.75$, $\chi^2 = 2.13$, $df = 3$, $p = .55$). Alternative models, such as those allowing for shared and non-shared environmental (but not genetic) effects, also provided an adequate fit to the data (Model 2: $AIC = -7499.69$, $\chi^2 = 4.19$, $df = 3$, $p = .24$). However, a model allowing only for non-shared environmental effects (i.e., Model 4) provided a poor fit to the data ($AIC = -7434.89$, $\chi^2 = 74.99$, $df = 6$, $p < .001$). In the best-fitting model, as indicated by the lowest AIC, additive genetic effects accounted for 42% of the variance in MDD and 39% of the variance in OE-BE; non-shared environmental effects accounted for the remaining variance in MDD and OE-BE. Furthermore, there were significant additive genetic ($r_g = .66$) and non-shared environmental ($r_e = .22$) correlations.

In AA women, of the three submodels tested, only Model 8 (dropping all genetic and shared environmental parameters) yielded a significant decrement in model fit ($AIC = -1062.01$, $\chi^2 = 20.41$, $df = 6$, $p = .002$), indicating that there were significant familial influences on MDD, OE-BE, and the covariance between MDD and OE-BE. Still, by AIC, the best-fitting model

indicated that additive genetic effects accounted for 57% of the variance in MDD and 35% of the variance in OE-BE, with the remaining variances due to non-shared environmental effects. There was a significant non-shared environmental ($r_e = .46$), but not additive genetic ($r_g = .42$) correlation.

As can be seen in Table 2, despite the genetic correlation between MDD and OE-BE being nearly twice as large in the EA versus AA twins (and conversely, the non-shared environmental correlation between MDD and OE-BE half as small), the confidence limits surrounding these estimates were broad. Therefore, we then evaluated whether we could equate the genetic and environmental effects across the EA and AA groups. A model that equated both additive genetic and non-shared environmental effects in EA and AA women provided a better fit to the data (AIC = -8585.40, -2LL = 5480.60, $\chi^2 = 2.42$, df = 6, $p = .88$) than a model allowing for different path coefficients across groups (AIC = -8575.82, -2LL = 5478.18). We also examined a model that allowed for additive genetic and non-shared environmental effects for MDD, OE-BE, and their covariance, as well as shared environmental effects specific to OE-BE that were constrained across racial/ethnic groups. This model yielded an AIC = -8583.52 (-2LL = 5480.48) and thus gave a worse fit to the data. Taken together, results from these analyses indicated that best-fitting model was one in which the magnitude of the additive genetic and non-shared environmental factors that influenced the variance and covariance of MDD and OE-BE did not differ across racial/ethnic groups.

In the overall best-fitting model, the heritability estimate was 44% for MDD and 39% for OE-BE, with the remaining phenotypic variance due to non-shared environmental effects (56% and 61%, respectively). The genetic correlation was .62 and the non-shared environmental correlation was .26. The estimates indicated that 38% ($[(.62)^2]$) and 7% ($[(.26)^2]$) of the genetic and non-shared environmental variance, respectively, between MDD and OE-BE was overlapping. Thus, these data suggest that while there are independent effects of genetic and non-shared environmental factors influencing MDD and OE-BE, there are also overlapping genetic and non-shared environmental effects influencing the liability to both traits.

Discussion

This study investigated genetic and environmental effects on liability to MDD and an overeating-binge eating dimension (OE-BE), as well as the covariance between them, both separately for EA and AA young adult female twins and in combined models which allowed for the assessment of comparability across race/ethnicity. Our results showed that the heritability estimates for both MDD and OE-BE could be statistically equated across the two racial/ethnic groups. The heritability of MDD was 44% and of OE-BE was 39%. Importantly, there was a significant genetic correlation ($r_g = .62$) and non-shared environmental correlation ($r_e = .26$) between MDD and OE-BE, suggesting that some of the genetic and non-shared environmental factors that influence liability to MDD also influence vulnerability to OE-BE.

In contrast to prior studies¹³⁻¹⁵, we found higher lifetime rates of MDD in AA compared with EA women (24.73% vs. 18.78%). When compared with the previous study in this sample that combined EA and AA girls³⁰ and a study of past week depression in an entirely AA sample of adult men and women¹², our heritability estimates were comparable. That these estimates were similar across studies, even in light of differences in assessment age, sample demographics (e.g., men versus women), and classification of MDD (symptoms versus clinical diagnoses), highlight the significant impact MDD has on individuals from multiple racial/ethnic groups.

In this epidemiologic sample of young adult female twins, there were higher rates of overeating or BE in AA compared with EA women. The lifetime prevalence of any overeating or BE was 10.23% in AA women and 7.39% in EA women. These rates are higher than those from other epidemiologic samples where lifetime rates of BE were approximately 5% in women¹. In addition, our rates were slightly higher than those reported in other studies that included AA women (5.30% to 5.82%)^{19;35}, which could be due to the difference in defining OE-BE across studies. Nevertheless, our pattern of results was similar to prior research that reported higher rates of recurrent BE in the past three months¹⁸ and any lifetime BE¹⁹ in AA than EA women.

Furthermore, this study found that the heritability of OE-BE was similar in EA and AA women (39% and 35%, respectively). Indeed, the best-fitting model indicated that the heritability estimates could be constrained across groups, yielding an overall heritability of 39%, with the remaining variance due to non-shared environmental effects. These estimates, both for EA and AA women separately and together, corroborate prior research by suggesting that additive genetic and non-shared environmental factors influence liability to BE, with a heritability estimate of ~50%⁷. Larger sample sizes, especially of AA women, are needed to further explore the role genetic and environmental effects play in the etiology of overeating, including BE specifically.

In addition to additive genetic and non-shared environmental influences contributing to the liability of MDD and OE-BE, there was a substantial genetic and weak non-shared environmental correlation between MDD and OE-BE in the EA and AA women. These significant correlations suggest that some of the genetic and non-shared environmental risk factors that influence liability to MDD also influence liability to OE-BE for both racial/ethnic groups. Further, although the difference was not statistically different, this genetic correlation was larger in EA compared with AA women (see Table 2); however, our pooled genetic correlation was similar to other studies^{8;11}. Cross-disorder association studies, which examine genetic variants that influence multiple traits simultaneously, are needed to better elucidate whether specific polymorphisms may increase the risk for comorbid MDD and OE-BE and how they may interact with environmental risk factors, such as trauma (which has been shown to be a risk factor for MDD and eating disorders³⁶⁻³⁸). Understanding genetic and environmental risk factors -- and how they may interact with each other -- will be crucial in identifying those who are at high risk for MDD, OE-BE, and their comorbidity, as well as providing adequate treatment for individuals with these behaviors.

This study makes a unique contribution as the first twin study to examine genetic and environmental effects on OE-BE in AA women. As previous twin studies have primarily focused on samples of European-ancestry, these results highlight the importance of including individuals of other racial/ethnic groups because genetic and environmental effects on these traits may differ between groups. Despite these strengths, there are some limitations. First, the small number of AA women ($n = 550$ twins) limited our statistical power to detect possible differences in the variance and covariance of MDD and OE-BE. In addition, over half of the AA women ($n = 23$) in the OE-BE group did not report BE as defined in the DSM (i.e., eating a large amount of food in a short period of time *and* having loss of control during the episode), which may have affected our results. Nevertheless, this is one of the largest twin samples of AA women currently available. Second, the OE-BE questions in the interview were asked immediately after a question about whether the respondent had ever been treated for an eating disorder. This could have affected the overall endorsement rate of overeating and BE in this sample. Third, these women may not have been through the period of risk for MDD, overeating, or BE at the time of the interview, when participants had a median age of 22 years. Given that MDD can develop at any age³⁹, it is possible that some women in the sample who did not meet criteria for MDD will develop MDD in the future. Studies have shown that the peak onset for BE in EA women is 16-18 years old⁴⁰ and the median age of onset for BE in AA women has been reported to be 20 years³⁵. For Binge Eating Disorder, the median age of onset is approximately 21 years old¹, which is slightly younger than the median age of our sample (median age = 22 years). Although it is possible that some women who did not report overeating, BE, or Binge Eating Disorder in this study may do so in the future, it is not likely that age unduly influenced our results. Finally, as with most other questionnaires and diagnostic interviews, the MDD and OE-BE questions asked in the SSAGA were tested in EA women. The extent to which these questions are interpreted the same across other racial/ethnic groups is unknown.

In summary, this study found that additive genetic effects accounted for 44% and 39% of the overall liability to MDD and OE-BE, respectively, under the best-fitting model, with the remaining variance due to non-shared environmental effects. There were also significant genetic and non-shared environmental correlations between MDD and OE-BE, indicating that some -- but not all -- of the genetic and non-shared environmental factors that influence liability to MDD also influence vulnerability to OE-BE. Importantly, the additive genetic and non-shared environmental estimates were the same in EA and AA young adult women. Although we did not find significant differences in these estimates, there may still be potential racial/ethnic differences in the magnitude of these effects that our study did not have enough power to detect. Our findings highlight the importance of including multiple racial/ethnic groups in twin research, as there may be potential differences that can inform the tailoring of prevention and treatment of psychiatric disorders, including MDD and eating disorder symptoms such as OE-BE. Additional studies with larger sample sizes are needed to fully elucidate familial risk for comorbid MDD and OE-BE within different racial/ethnic groups.

Acknowledgements

This work was supported by grants from the National Institute of Alcohol Abuse and Alcoholism (AA09022, AA07728, AA11998, AA12640, AA17688, and AA17915), the National Institute of Drug Abuse (DA019951, DA14363), and the National Institute of Child Health and Human Development (HD49024). Dr. Munn-Chernoff was supported by training grant T32 AA07580 (Dr. Heath) and Dr. Agrawal received funding from ABMRF/The Foundation for Alcohol Research. Dr. Glowinski is on the advisory board for the Klingenstein Third Generation Foundation.

References

1. Hudson JI, Hiripi E, Pope HG Jr, Kessler RC. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry*. 2007; 61:348–358. [PubMed: 16815322]
2. Braun DL, Sunday SR, Halmi KA. Psychiatric comorbidity in patients with eating disorders. *Psychol Med*. 1994; 24:859–867. [PubMed: 7892354]
3. Herzog DB, Keller MB, Sacks NR, Yeh CJ, Lavori PW. Psychiatric comorbidity in treatment-seeking anorexics and bulimics. *J Am Acad Child Adolesc Psychiatry*. 1992; 31:810–818. [PubMed: 1400111]
4. Reichborn-Kjennerud T, Bulik CM, Sullivan PF, Tambs K, Harris JR. Psychiatric and medical symptoms in binge eating in the absence of compensatory behaviors. *Obes Res*. 2004; 12:1445–1454. [PubMed: 15483209]
5. Araujo DM, Santos GF, Nardi AE. Binge eating disorder and depression: A systematic review. *World J Biol Psychiatry*. 2010; 11:199–207. [PubMed: 20218783]
6. Kendler KS, Gatz M, Gardner CO, Pedersen NL. A Swedish national twin study of lifetime major depression. *Am J Psychiatry*. 2006; 163:109–114. [PubMed: 16390897]
7. Thornton LM, Mazzeo SE, Bulik CM. The heritability of eating disorders: Methods and current findings. *Curr Top Behav Neurosci*. 2011; 6:141–156. [PubMed: 21243474]
8. Walters EE, Neale MC, Eaves LJ, Heath AC, Kessler RC, Kendler KS. Bulimia nervosa and major depression: A study of common genetic and environmental factors. *Psychol Med*. 1992; 22:617–622. [PubMed: 1410087]
9. Kendler KS, Walters EE, Neale MC, Kessler RC, Heath AC, Eaves LJ. The structure of the genetic and environmental risk factors for six major psychiatric disorders in women. Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. *Arch Gen Psychiatry*. 1995; 52:374–383. [PubMed: 7726718]
10. Silberg JL, Bulik CM. The developmental association between eating disorders symptoms and symptoms of depression and anxiety in juvenile twin girls. *J Child Psychol Psychiatry*. 2005; 46:1317–1326. [PubMed: 16313432]
11. Slane JD, Burt SA, Klump KL. Genetic and environmental influences on disordered eating and depressive symptoms. *Int J Eat Disord*. 2011; 44:605–611. [PubMed: 21997423]
12. Whitfield KE, Edwards CL, Brandon D, McDougald C. Genetic and environmental influences on depressive symptoms by age and gender in African American twins. *Aging Ment Health*. 2008; 12:221–227. [PubMed: 18389402]
13. Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of major depressive disorder: Results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Arch Gen Psychiatry*. 2005; 62:1097–1106. [PubMed: 16203955]
14. Williams DR, Gonzalez HM, Neighbors H, et al. Prevalence and distribution of major depressive disorder in African Americans, Caribbean blacks, and non-Hispanic whites: Results from the National Survey of American Life. *Arch Gen Psychiatry*. 2007; 64:305–315. [PubMed: 17339519]
15. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: Results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003; 289:3095–3105. [PubMed: 12813115]
16. Neumark-Sztainer D, Croll J, Story M, Hannan PJ, French SA, Perry C. Ethnic/racial differences in weight-related concerns and behaviors among adolescent girls and boys: Findings from Project EAT. *J Psychosom Res*. 2002; 53:963–974. [PubMed: 12445586]

17. Crago M, Shisslak CM, Estes LS. Eating disturbances among American minority groups: A review. *Int J Eat Disord.* 1996; 19:239–248. [PubMed: 8704722]
18. Striegel-Moore RH, Wilfley DE, Pike KM, Dohm FA, Fairburn CG. Recurrent binge eating in black American women. *Arch Fam Med.* 2000; 9:83–87. [PubMed: 10664648]
19. Marques L, Alegria M, Becker AE, et al. Comparative prevalence, correlates of impairment, and service utilization for eating disorders across US ethnic groups: Implications for reducing ethnic disparities in health care access for eating disorders. *Int J Eat Disord.* 2011; 44:412–420. [PubMed: 20665700]
20. Striegel-Moore RH, Dohm FA, Kraemer HC, et al. Eating disorders in white and black women. *Am J Psychiatry.* 2003; 160:1326–1331. [PubMed: 12832249]
21. Striegel-Moore RH, Silberstein LR, Rodin J. Toward an understanding of risk factors for bulimia. *Am Psychol.* 1986; 41:246–263. [PubMed: 3457546]
22. Heath AC, Madden PA, Grant JD, McLaughlin TL, Todorov AA, Bucholz KK. Resiliency factors protecting against teenage alcohol use and smoking: Influences of religion, religious involvement and values, and ethnicity in the Missouri Adolescent Female Twin Study. *Twin Res.* 1999; 2:145–155. [PubMed: 10480749]
23. Heath AC, Howells W, Bucholz KK, Glowinski AL, Nelson EC, Madden PA. Ascertainment of a midwestern US female adolescent twin cohort for alcohol studies: Assessment of sample representativeness using birth record data. *Twin Res.* 2002; 5:107–112. [PubMed: 11931688]
24. Nichols RC, Bilbro WC Jr. The diagnosis of twin zygosity. *Acta Genet Stat Med.* 1966; 16:265–275. [PubMed: 4959152]
25. Eaves, LJ.; Eysenck, HJ.; Martin, NG. Genes, culture and personality: An empirical approach. Academic Press; London: 1989.
26. Waldron M, Bucholz KK, Lynskey MT, Madden PA, Heath AC. Alcoholism and timing of separation in parents: Findings in a midwestern birth cohort. *J Stud Alcohol Drugs.* 2013; 74:337–348. [PubMed: 23384382]
27. Bucholz KK, Cadoret R, Cloninger CR, et al. A new, semistructured psychiatric interview for use in genetic-linkage studies: A report on the reliability of the SSAGA. *J Stud Alcohol.* 1994; 55:149–158. [PubMed: 8189735]
28. Kessler RC, Berglund PA, Chiu WT, et al. The prevalence and correlates of binge eating disorder in the World Health Organization World Mental Health Surveys. *Biol Psychiatry.* 2013
29. Duncan AE, Bucholz KK, Neuman RJ, Agrawal A, Madden PA, Heath AC. Clustering of eating disorder symptoms in a general population female twin sample: A latent class analysis. *Psychol Med.* 2007; 37:1097–1107. [PubMed: 17472759]
30. Glowinski AL, Madden PA, Bucholz KK, Lynskey MT, Heath AC. Genetic epidemiology of self-reported lifetime DSM-IV major depressive disorder in a population-based twin sample of female adolescents. *J Child Psychol Psychiatry.* 2003; 44:988–996. [PubMed: 14531581]
31. Stata Statistical Software: Release 9. StataCorp LP; College Station, TX: 2005.
32. Neale, MC.; Boxer, SM.; Xie, G.; Maes, HH. Mx: Statistical modeling. 7th ed.. Department of Psychiatry; Richmond, VA 23298: 2006. VCU Box 900126
33. Neale, MC.; Cardon, LR. Methodology for genetic studies of twins and families. Kluwer Academic; Boston: 1992.
34. Akaike H. Factor analysis and the AIC. *Psychometrika.* 1987; 52:317–332.
35. Taylor, JY.; Caldwell, CH.; Baser, RE.; Faison, N.; Jackson, JS. *Int J Eat Disord.* Vol. 40. Suppl: 2007. Prevalence of eating disorders among Blacks in the National Survey of American Life.; p. S10-S14.
36. Caspi A, Sugden K, Moffitt TE, et al. Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science.* 2003; 301:386–389. [PubMed: 12869766]
37. Karg K, Burmeister M, Shedden K, Sen S. The serotonin transporter promoter variant (5-HTTLPR), stress, and depression meta-analysis revisited: Evidence of genetic moderation. *Arch Gen Psychiatry.* 2011; 68:444–454. [PubMed: 21199959]
38. Jacobi C, Hayward C, de ZM, Kraemer HC, Agras WS. Coming to terms with risk factors for eating disorders: Application of risk terminology and suggestions for a general taxonomy. *Psychol Bull.* 2004; 130:19–65. [PubMed: 14717649]

39. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005; 62:593–602. [PubMed: 15939837]
40. Stice E, Killen JD, Hayward C, Taylor CB. Age of onset for binge eating and purging during late adolescence: A 4-year survival analysis. *J Abnorm Psychol*. 1998; 107:671–675. [PubMed: 9830254]

Table 1

Polychoric twin correlations for Major Depressive Disorder (MDD) and an overeating-binge eating dimension (OE-BE)

	<i>r</i> _{MZ}	<i>r</i> _{DZ}
<i>European-Americans</i>		
MDD	.42 (.30, .53)	.21 (.08, .35)
OE-BE	.40 (.22, .55)	.26 (.08, .46)
MDD and OE-BE	.24 (.12, .35)	.23 (.12, .34)
<i>African-Americans</i>		
MDD	.61 (.33, .77)	.17 (.00, .45)
OE-BE	.13 (.00, .60)	.40 (.04, .68)
MDD and OE-BE	.29 (-.02, .54)	-.04 (-.28, .23)

Note: *r*_{MZ} = monozygotic twin correlation; *r*_{DZ} = dizygotic twin correlation. 95% confidence intervals are presented in parentheses.

Proportions of variance due to genetic and environmental factors for bivariate twin models

Model Number	Model	AIC	a ²	c ²	e ²	a ²	c ²	OE-BE	e ²	r _g	r _c	r _e
<i>European-Americans</i>												
1	ACE-ACE r_g, r_e	-7497.88	.24 (.00, .48)	.16 (.00, .40)	.60 (.53, .72)	.16 (.00, .50)	.21 (.01, .45)	.63 (.47, .79)	.33 (-1.00, 1.00)	.33 (-1.00, 1.00)	1.00 (-1.00, 1.00)	.25 (.07, .42)
2	CE-CE r_c, r_e	-7499.69	---	.34 (.25, .43)	.66 (.57, .76)	---	.33 (.19, .46)	.67 (.54, .81)	---	---	.76 (.51, 1.00)	.22 (.07, .36)
3	AE-AE r_g, r_e	-7501.75	.42 (.30, .50)	---	.58 (.48, .70)	.39 (.23, .51)	---	---	.61 (.46, .76)	.66 (.42, .95)	---	.22 (.04, .39)
4	E-E r_e	-7434.89	---	---	1.00	---	---	1.00	---	---	---	.39
<i>African-Americans</i>												
5	ACE-ACE r_g, r_e	-1070.42	.55 (.02, .77)	.02 (.00, .41)	.43 (.23, .70)	.12 (.00, .57)	.25 (.00, .55)	.63 (.35, .94)	1.00 (-1.00, 1.00)	1.00 (-1.00, 1.00)	-1.00 (-1.00, 1.00)	.48 (.05, .81)
6	CE-CE r_c, r_e	-1072.37	---	.39 (.17, .57)	.61 (.43, .83)	---	.33 (.03, .58)	.67 (.42, .97)	---	---	.26 (-.44, .84)	.54 (.21, .80)
7	AE-AE r_g, r_e	-1074.06	.57 (.30, .77)	---	.43 (.23, .53)	.35 (.00, .67)	---	---	.65 (.33, 1.00)	.42 (-.20, 1.00)	---	.46 (.01, .81)
8	E-E r_e	-1062.01	---	---	1.00	---	---	1.00	---	---	---	.44
<i>Combined Samples</i>												
9	AE-AE r_g, r_e	-8585.40	.44 (.34, .53)	---	.56 (.47, .66)	.39 (.24, .52)	---	---	.61 (.47, .76)	.62 (.40, .87)	---	.26 (.09, .42)

Note: MDD = Major Depressive Disorder; OE-BE = overeating-binge eating dimension; AIC = Akaike's Information Criterion; a² = additive genetic influences; c² = shared environmental influences; e² = non-shared environmental influences; r_g = correlation between MDD and OE-BE that is due to additive genetic influences; r_c = correlation between MDD and OE-BE that is due to shared environmental influences; r_e = correlation between MDD and OE-BE that is due to non-shared environmental influences. 95% confidence intervals are presented in parentheses.

^a Compared to the same, unconstrained model with AIC = -8575.82 (additive genetic and non-shared environmental estimates in Models 3 and 7). The best-fitting model is in bold-type.