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GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO BMI IN ADOLESCENT AND YOUNG ADULT WOMEN

A.E. Duncan, **A. Agrawal**, **J.D. Grant**, **K.K. Bucholz**, **P.A.F. Madden**, and **A.C. Heath**
Midwest Alcoholism Research Center, Department of Psychiatry, Washington University School of Medicine, St. Louis, MO

Abstract

The objective of this study was to determine the genetic and environmental contributions to variation in BMI over time in European-American (EA) and African-American (AA) adolescent and young adult women. Self-reported BMI (kg/m^2) data from 2816 EA (1306 twin pairs, 56.5% monozygotic [MZ]) and 404 AA (178 twin pairs, 42.7% MZ) women at baseline (T1; median age 15 years) and 3225 EA (1511 twin pairs, 55.3% MZ) and 539 AA (252 pairs, 43.3% MZ) women at follow-up (T2; median age 22 years) from a Midwestern US, population-based twin registry were used to construct biometrical genetic models. For EA women, the majority of the variance in BMI was attributable to additive genetic effects at both time points (82% for each), with the remaining variance attributable to non-shared environment. Genetic and non-shared environment correlations between adolescent and young adult BMI were 0.87 and 0.23, respectively. Among AA women, non-additive genetic effects comprised 68% of the variance at T1 and 73% at T2, and were highly correlated (r_D= 0.94). The proportions of variance attributable to non-shared environment at T1 (29%) and T2 (25%) were more modestly correlated (r_E=0.31). The remaining variance in AA women could be attributed to additive genetic effects. Additive versus non-additive genetic effects contribute differentially to BMI in AA versus EA adolescent and young adult women. Additional research is needed to better characterize the environmental and genetic factors related to BMI in persons of different races to aid understanding of the complex determinants of body weight in individuals.

Keywords

Body mass index; twins; MOAFTS

INTRODUCTION

Overweight and obesity in adolescent and young adult women are highly prevalent, with approximately a third of female adolescents and slightly more than half of young adult women meeting criteria for overweight or obesity (1). African-American (AA) adolescent and young adult women have higher rates of overweight and obesity than their European-American (EA) peers (1). Relative body weight, as measured by body mass index (BMI), has been shown to be highly heritable in twin studies (2;3). Since the prevalence of overweight and obesity increases with increasing age until later adulthood (1;4), examining the relative contributions of genetics and environment to BMI over time could provide valuable insight into the causes of the obesity epidemic. While several studies examining the heritability of obesity and/or BMI

*Correspondence to: Alexis E. Duncan, Ph.D., Department of Psychiatry, Washington University School of Medicine, 660 S. Euclid, Box 8134, St. Louis, MO 63110, 314-286-2210 (phone), 314-286-2213 (fax), E-mail: aduncan@wustl.edu.

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over time have been conducted in samples of adolescent, young adult and middle aged male twins (5–7), few have been conducted in adolescent and young adult female twin samples. Since heritability estimates have been found to differ between male and female adolescents and young adults, and there is evidence that different genes may influence variation in BMI for men and women (3;8), results from longitudinal studies conducted on male samples may not be generalizable to women. Furthermore, the majority of previous studies have been conducted on twins of European descent. Those studies that have used AA twin pairs have been conducted on relatively small samples that included individuals of both sexes and over a broad age range and have focused on BMI at a single time point (9;10). Therefore, we sought to determine the genetic and environmental contributions to BMI over time in a sample of adolescent and young adult female twins and to determine whether these contributions differed by race.

METHODS AND PROCEDURE

The Missouri Adolescent Female Twin Study (MOAFTS) is a study of female twin pairs identified from state birth records as being born between 1975 and 1985 in the state of Missouri to a mother residing in that state. Participants reflect statewide demographics, coming from both rural and urban areas, and include individuals of both African-American (AA) and European-American (EA) ancestry. A baseline interview was conducted in 1995 (median age 15); the first full-length young adult follow-up interview was conducted on average 5 years after the baseline assessment (median age 22), with individuals from the target cohort who had not participated at baseline invited to participate in the young adult assessment. Self-reported height and weight, elicited in the zygosity section of the baseline and follow-up interviews, were used to calculate body mass index at each time point (BMI: weight in kg/height in m^2). New participants at the young adult follow-up assessment (n=934) had a slightly higher mean BMI (24.57 [SD=5.73] vs. 24.06 [SD=5.45]; p=.02) and were significantly more likely to be obese (BMI≥30; 15.77% vs. 12.25%; p=.01). There were 2816 EA (1306 twin pairs, 56.5% monozygotic [MZ]) and 404 AA (178 twin pairs, 42.7% MZ) respondents at baseline and 3225 EA (1511 twin pairs, 55.3% MZ) and 539 AA (252 pairs, 43.3% MZ) respondents at follow-up with height and weight data; 2491 EA (1110 pairs, 57.7% MZ) and 327 AA (137 pairs, 46.7% MZ) women had data at both time points. Zygosity was assigned based on standard questions included in the young adult follow-up assessment (11). All protocols were approved by the institutional IRB at Washington University School of Medicine. Additional details regarding the sample are available elsewhere (12;13).

Biometrical analyses were conducted using log-transformed BMI. Individual differences in liability to BMI in adolescence and young adulthood was estimated from three sources, additive genetic effects (a^2), either shared environment effects (c^2) or non-additive genetic effects (dominance: d^2) and unique environmental effects (e^2), and correlations between a^2, c^2/d^2 and e^2 at each time point were also calculated. In the classical twin design (i.e. utilizing data from monozygotic (MZ) and dizygotic (DZ) twins alone), additive genetic factors are shared 100% and 50%, between members of MZ and DZ pairs respectively. Shared environmental factors (or those environmental factors that make twins similar to each other) are shared 100% across members of MZ and DZ pairs (under the equal environments assumption) while unique environmental influences, which encompass effects of measurement error, are uncorrelated across twins (i.e., not shared by co-twins). In some instances, non-additive genetic effects (dominance or epistasis) may come into play. Non-additive genetic factors are correlated 100% and 25% in MZ and DZ twin pairs respectively. It is not possible to estimate shared environment and non-additive genetic effects in the same model with data from twin pairs only. Bivariate genetic models were fitted to raw data, using full information maximum likelihood, in the software package Mx (14). The most parsimonious model was selected using the likelihood ratio test to compare nested submodels to the full model and Akaike's Information Criterion

(AIC) to compare non-nested models, with the model with the lowest AIC considered to be the most parsimonious (15). Analyses were adjusted for age and for known pregnant or post-partum (≤6 mos.) status at baseline and follow-up interviews. Data from all individuals participating at both timepoints was used rather than using only data from pairs in which both co-twins had participated at both time points to improve the precision of the variance component estimates as well as to reduce the potential bias associated with excluding women who participated only at follow-up, who were more likely to have higher BMIs.

RESULTS

The mean BMI (SD) among EA twins was 21.16 (4.02) at baseline and 23.61 (5.28) at follow-up. AA twins had a mean BMI of 23.86 (5.60) at baseline and 27.58 (6.80) at follow-up. AA twins had a significantly higher mean BMI at both time points ($p<.001$ for both). Baseline, follow-up, and cross-twin, cross-occasion MZ and DZ twin pair correlations for EA and AA participants are presented in Table 1. Among the EA twins, the MZ correlation was less than twice that of the DZ correlation at both time points and cross-twin, cross-occasion, suggesting an ACE model. For AA twins, however, the MZ correlation was greater than twice that of the DZ correlation at baseline and the MZ follow-up and cross-twin, cross-occasion correlations were nearly four times those of the DZ correlations, indicating that an ADE model was most appropriate. Additional analyses with an ACE model confirmed that the shared environmental component could be dropped in AA women without a significant deterioration in fit; however, the non-additive component could not be dropped from the ADE model. Therefore, results are presented separately for EA and AA women.

Results from the best-fitting bivariate genetic model are presented in Table 2. For EA women, the common environmental paths could be dropped without a significant deterioration of fit. The best fitting model included additive genetic and non-shared environmental paths to BMI at both time points as well as correlations between the additive genetic and non-shared environmental paths at each time point. The heritability of BMI was high at both time points (81.65% and 81.86% for baseline and follow-up, respectively), with the remaining variance attributable to non-shared environment. Genetic and non-shared environment correlations between baseline and follow-up were .87 (95% CI: .85–.89) and .24 (95% CI: .17–.31), respectively. The majority of the genetic variance at young adult follow-up (76.32%) was shared with baseline, with 23.68% of the variance unique to the follow-up. Conversely, only 5.70% of the variance in non-shared environment at follow-up was shared with baseline, with the remaining 94.30% of the variance unique to follow-up.

A large proportion of the total variance for BMI was also attributable to genetic factors (additive and non-additive) at both time points among AA women (71.33% and 75.29% for baseline and follow-up, respectively), with the vast majority of the genetic variance ascribed to non-additive genetic effects at both adolescent baseline (95.78%) and young adult follow-up (97.16%). Non-additive genetic and non-shared environment correlations between baseline and follow-up were .94 (95% CI: .77–1.00) and .31 (95% CI: .10–.50), respectively. The majority of the non-additive genetic variance at young adult follow-up was shared with baseline (88.70%), with only 11.30% of the non-additive genetic variance unique to follow-up. Conversely, 9.74% of the variance in non-shared environment at follow-up was shared with baseline, with the remaining 90.26% of the variance unique to follow-up. Post hoc analyses comparing the ratios of additive to non-additive variance in EA and AA women indicated that these ratios differed significantly ($p>0.0001$), providing additional evidence in favor of the ADE model in AA women in this sample.

DISCUSSION

We found that different factors contributed to individual differences in BMI in AA and EA adolescent and young adult women in this Midwestern twin sample. For EA women, the majority of the variance in BMI was attributable to additive genetic effects at both time points, with the remaining variance attributable to non-shared environment. The genetic correlation, although very high, was significantly different from unity, while the non-shared environment correlation was much more modest. In contrast, among AA women, non-additive genetic effects comprised the majority of the variance at both time points, with very little variance attributable to additive genetic effects. Non-additive genetic effects at both time points were almost completely correlated, while the non-shared environmental correlation was much lower.

The variance component estimates in EA young adult women are similar to many previously published univariate analyses of data from adolescent and young adult twin pairs of European descent (e.g., (3;8). Also of relevance to results presented here, Jacobson and Rowe (1998) found that a substantial proportion of the variance in BMI at a single time point was attributable to additive genetic effects in AA, but not in EA, female adolescents participating in wave 1 of the Add Health study. The best fitting model for EA female adolescents consisted of additive genetic, shared and non-shared environmental components (16). Other studies conducted with AA samples have not found a significant non-additive genetic effect, but these samples were smaller than that in the current study and would not have had the statistical power to detect non-additive genetic effects (9;10). Power analyses for the univariate case (estimated using standard asymptotic methods using the non-central chi-square distribution, assuming negligible shared environmental contributions to variations in AA pairs) demonstrated sufficient statistical power in the current AA sample (293 pairs with either wave 1 or wave 4 data –including 121 MZ pairs) to detect a significant non-additive genetic effect for a trait as strongly familial as BMI (rMZ=.65 at baseline and r MZ=.78 at follow-up). Assuming dominance ratios of 0, 0.25, 0.5 0.75 or 1, power to detect significant heritability ranged from 81% to 96% assuming heritability of BMI of 65%, increasing with the proportion of the genetic variance that is due to non-additive genetic effects. Power is further increased in a bivariate analysis that includes cross-temporal data (i.e., baseline combined with follow-up) as presented here. To our knowledge the current study is the first to examine the relative contributions of genetic and environmental factors in adolescent versus young adult women of European and African descent.

One limitation of the classical twin method is that it is not possible to detect gene by shared environment interactions (G×E; (17). Variance attributable to G×E, if present, would be included in the estimate of additive or non-additive genetic variance. Therefore, it is possible that although the shared environmental component for both time points could be dropped from the model without a significant decrease in fit, shared environment still contributes to the variability in BMI through a gene by environment interaction. The fact that the additive genetic correlation between adolescent and young adult BMI in EA women is significantly less than unity suggests that the genes associated with BMI at each time point may not be entirely the same, or if a G×E interaction is present at one or both time points, it could indicate that different aspects of the shared environment are interacting with genes at each time point. Given the age range at baseline, imperfect genetic correlation over time may also reflect (genetically influenced) differences in pubertal timing associated with differences in BMI in younger members of the cohort.

In this study, BMI was computed using self-reported height and weight. Although self-report of height and weight has been found to correspond highly with actual height and weight in young women (18;19), a bias toward underreporting weight has been observed in adolescents (19;20). In the MOAFTS interviews, respondents were asked their cotwins' heights and

weights as part of the zygosity interview, and questions were sequenced (self height; cotwin height; self weight; cotwin weight) so that at the time respondents were asked about their own weight, they could anticipate that their weight would also be reported by their twin sister. Respondents' BMI based on self-reported height and weight was highly correlated with that calculated based on their co-twins' reports at both time points (baseline r=.86 and follow-up r=.90). In the models presented here, measurement error is included in the estimates of nonshared environmental effects. The relatively low unique environmental correlation between time points indicates that the non-shared environmental variance, as well as potential measurement error, is largely unique to each time point.

The rapid increase in rates of overweight and obesity in the past quarter century (21) suggests a strong role for environmental factors acting either alone or together with genetic factors in gene by environment interactions in the development of excess adiposity. In particular, environmental factors shared by individuals of the same family are likely to interact with genetic differences to account for a significant portion of the variance in BMI. Future research is needed to better characterize both the environmental (including changing dietary practices and levels of physical activity) and, particularly, the genetic factors related to BMI in persons of different races and to facilitate testing of measured gene by measured environment interactions to aid understanding of the complex determinants of body weight in individuals.

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Table 1

Twin-pair correlations for BMI at baseline and follow-up for European- and African-American participants in the Missouri Adolescent Female Twin Study

	r_{MZ} (95% CI)	r_{DZ} (95% CI)
European-Americans		
Baseline	0.82 (0.79–0.84)	0.49 (0.43–0.55)
Follow-up	0.81 (0.79–0.83)	0.46 (0.40–0.52)
Cross twin – cross occasion	0.78 (0.75–0.79)	0.46 (0.40–0.50)
African-Americans		
Baseline	0.65 (0.51–0.77)	0.28 (0.11–0.45)
Follow-up	0.78 (0.69–0.84)	0.21 (0.05–0.35)
Cross twin – cross occasion	0.71 (0.62–0.78)	0.23 (0.09–0.36)

Table 2

Variance Components from the best-fitting bivariate models for European- and African-American women participating in the Missouri Adolescent Female Twin Study

	A^2	D^2	E^2	r_A	r_D	r_E
European-Americans						
Baseline	81.65 (79.54–83.54)	--	18.35 (16.46–20.46)	0.87 (0.85–0.89)	--	0.24 (0.17–0.31)
Follow-up	81.86 (79.83–83.67)	--	18.14 (16.33–20.17)			
African-Americans						
Baseline	3.01 (0.00–61.34)	68.32 (9.16– 79.28)	28.67 (20.72–40.14)	1.00 (−1.00–1.00)	0.94 (0.77–1.00)	0.31 (0.10–0.50)
Follow-up	2.14 (0.00–53.83)	73.15 (20.98–81.11)	24.71 (18.88–32.53)			

A^2: proportion of variance due to additive genetic factors; D^2: proportion of variance due to non-additive genetic factors; E^2: proportion of the variance due to non-shared environmental factors; r_A: correlation between additive genetic components at baseline and follow-up; r_D: correlation between non-additive genetic components at baseline and follow-up; r_E: correlation between non-shared environmental components at baseline and follow-up. C^2 and D^2 variance components are confounded in twin data and therefore were not fit simultaneously in the same model.