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GENETIC AND ENVIRONMENTAL RISK FOR MAJOR DEPRESSION IN AFRICAN-AMERICAN AND EUROPEAN-AMERICAN WOMEN

Alexis E. Duncan[1,2,3,*], **Melissa A. Munn-Chernoff**[2,3], **Darrell L. Hudson**[1], **Michaela A. Eschenbacher**[6], **Arpana Agrawal**[2,3], **Julia D. Grant**[2,3], **Elliot C. Nelson**[2,3], **Mary Waldron**[2,4], **Anne L. Glowinski**[2,3], **Carolyn E. Sartor**[2,5], **Kathleen K. Bucholz**[2,3], **Pamela A.F. Madden**[2,3], and **Andrew C. Heath**[2,3]

[1]George Warren Brown School of Social Work, Washington University, St. Louis, MO, USA

[2]Midwest Alcoholism Research Center, Washington University School of Medicine, St. Louis, MO, USA

[3]Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA

[4]Indiana University School of Education, Bloomington, IN, USA

[5]Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA

[6]E. Kenneth Hatton Institute for Research and Education, Cincinnati, OH, USA

Abstract

It is unknown whether there are racial differences in the heritability of major depressive disorder (MDD) because most psychiatric genetic studies have been conducted in samples comprised largely of white non-Hispanics. To examine potential differences between African-American (AA) and European-American (EA) young adult women in (1) DSM-IV MDD prevalence, symptomatology and risk factors and (2) genetic and/or environmental liability to MDD, we analyzed data from a large, population representative sample of twins ascertained from birth records (n= 550 AA and n=3226 EA female twins) aged 18–28 years at the time of MDD assessment by semi-structured psychiatric interview. AA women were more likely to have MDD risk factors; however, there were no significant differences in lifetime MDD prevalence between AA and EA women after adjusting for covariates (Odds Ratio = 0.88, 95% confidence interval: 0.67–1.15). Most MDD risk factors identified among AAs were also associated with MDD at similar magnitudes among EAs. Although the MDD heritability point estimate was higher among AA than EA women in a model with paths estimated separately by race (56%, 95% CI: 29%–78% vs. 41%, 95% CI: 29%–52%), the best-fitting model was one in which additive genetic and nonshared environmental paths for AA and EA women were constrained to be equal (A = 43%,

[*]Correspondence to: Alexis E. Duncan, Ph.D., M.P.H., George Warren Brown School of Social Work, Washington University, One Brookings Drive, Campus Box 1196, St. Louis, MO 63130, USA, aduncan@wustl.edu, Phone: 314-935-6758, Fax: 314-935-8511.

CONFLICT OF INTEREST

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33%–53% and E = 57%, 47%–67%). Despite a marked elevation in the prevalence of environmental risk exposures related to MDD among AA women, there were no significant differences in lifetime prevalence or heritability of MDD between AA and EA young women.

Keywords

depression; race; African-American; women; twins; heritability

Major depression is common in women, with 17% of women aged 18 and older from a nationally representative United States sample reporting a history of one or more major depressive episodes (Hasin et al., 2005). Results from multiple population surveys have revealed that African-American (AA) women are less likely than European-American (EA) women to meet criteria for lifetime DSM-IV major depressive disorder (MDD: e.g., (Hasin et al., 2005; R. C. Kessler et al., 2003; Williams et al., 2007)) – a finding that has been noted as paradoxical in light of the considerably higher disease burden from “physical” illnesses and exposure to environmental stressors among AAs in the US (Jackson et al., 2010; C. L. M. Keyes, 2009). Studies exploring reasons for the lower lifetime prevalence of MDD among AAs have often combined data across genders and/or age categories (R. C. Kessler et al., 2003; K. M. Keyes et al., 2011; Williams et al., 2007). The few studies that have examined racial differences in MDD prevalence and risk factors specifically in women have focused on middle- and older-aged women. Since there is consistent evidence of birth cohort effects on the prevalence of MDD with individuals born more recently having greater cumulative lifetime prevalence of MDD than members of older age cohorts did at the same ages (R. C. Kessler et al., 2003; Wittchen & Uhmann, 2010), it is possible that associations between and within racial categories observed in previous studies using older samples do not generalize to young adult women.

Using data from monozygotic and dizygotic twin pairs reared together (sharing 100% or an average of 50% of segregating genes, respectively), it is possible to parse the variance in a phenotype into additive genetic sources (heritability), environmental sources shared by members of a twin pair (e.g., family socioeconomic status, neighborhood, school) and environmental influences that contribute to within-pair differences. Classical twin studies have shown that genetic, as well as environmental, factors contribute to risk of MDD. In a meta-analysis of twin studies consisting almost entirely of men and women of European ancestry (Bierut et al., 1999; Kendler, Pedersen, et al., 1995; Kendler & Prescott, 1999; Kendler, Walters, et al., 1995; Lyons et al., 1998; McGuffin et al., 1996), 37% (95% confidence interval (CI) = 31%-42%) of the variance in liability to MDD was estimated to be attributable to additive genetic effects, with the remaining variance due to nonshared environmental factors (Sullivan et al., 2000). Similar estimates were reported in a more recent study of the heritability of lifetime DSM-IV MDD using data collected at baseline from the same EA and AA female twin pairs used for the current analyses (Glowinski et al., 2003). Given the relatively low prevalence of MDD due to the young age of the sample (median age 15 years) at the baseline assessment, there was insufficient statistical power to permit contrasts of the heritability of lifetime MDD by race.

Environmental factors may affect heritability estimates through gene by shared environment interaction (G × SE); variance attributable to G × SE interactions, if present, is included in the heritability estimate, as heritability and variance due to G × SE interactions are confounded using the classical twin method (Heath & Martin, 1993). Thus, it is possible that heritability estimates from European ancestry samples do not generalize to African Americans due to differences in environmental exposures. To our knowledge, to date only one study has examined the heritability of depressive symptomatology among AA twin pairs, finding that both additive genetic (40%) and nonshared environmental (56%) effects influenced liability to past week depressive symptoms in AA male and female twin pairs aged 25–88 years (mean age 47.1 years) (Whitfield et al., 2008). While these estimates were similar to those from previous studies using European ancestry samples, conclusions regarding depression heritability differences by race cannot be drawn because the study used a non-diagnostic, state measure of past-week depressive symptoms and did not include any European ancestry twin pairs for comparison (Suthers et al., 2004).

Given the paucity of information in the literature about potential racial differences in the heritability of major depression, the objectives of the current study were to explore racial differences in (1) MDD prevalence, symptomatology and risk factors and (2) latent genetic and/or environmental liability to DSM-IV MDD in a large, representative sample of AA and EA young adult female twins.

MATERIALS AND METHODS

Sample

The Missouri Adolescent Female Twin Study (MOAFTS) is a study of female twin pairs identified from state birth records as born in Missouri between 1975 and 1985 to a mother who was a state resident. Participants included both AA (14.6%) and EA (85.4 %) individuals (as reported by the mother at the time of birth), reflecting the racial distribution in the state during this time period. A baseline interview was conducted with the twins beginning in 1995 (median age = 15 years) (Glowinski et al., 2003). When possible, interviews were also conducted with a parent (usually the mother) at the time the twins entered the study. Zygosity was assigned using an algorithm based on answers to standard questions (Nichols & Bilbro, 1966) included in the young adult follow-up assessment. This method has been shown to be 95% accurate in comparison to genotyping (Eaves et al., 1989). The first full-length 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 of age 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, unless they or their families had previously refused consent. All protocols were approved by the institutional review board at Washington University School of Medicine. Additional details regarding the sample are available elsewhere (Glowinski et al., 2003; Heath et al., 2002; Heath et al., 1999; Waldron et al., 2013). There were 550 AA (254 complete pairs, 43.7% monozygotic (MZ)) and 3226 EA (1514 complete pairs, 56.3% MZ) respondents with complete depression assessments at

follow-up, out of a total of 370 AA and 1999 EA pairs originally identified from birth records.

Assessment

Twins were interviewed at baseline and follow-up by telephone using an adaptation of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA), a comprehensive structured psychiatric diagnostic instrument that has been shown to be a reliable and valid diagnostic assessment of lifetime DSM-IV psychiatric disorders, including MDD (Bucholz et al., 1994; Hesselbrock et al., 1999). For the current analyses, information on lifetime MDD symptoms was obtained from the follow-up interview, with lifetime diagnosis coded by computer algorithm. In the depression section of the follow-up interview, 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 fewer than five symptoms were endorsed or if five or more 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 and routed through the full depression section again for this other episode. Those who reported experiencing five or more symptoms 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.

Demographic and environmental variables identified from the literature as being associated with MDD that were assessed in one or more waves of MOAFTS data collection were included as covariates in logistic regression models. Age at interview was modeled as a binary variable using the median age at interview of 22 years as the cutoff. Age at menarche was dichotomized into early (<12 years) vs. average/late (≥12 years) (Black & Klein, 2012; Joinson et al., 2011). Twin marital status (e.g., (Hasin et al., 2005; R. C. Kessler et al., 2003) at the time of follow-up interview was coded as married or living with someone as though married vs. not married or living with someone as though married.

Trauma history (e.g., child abuse (Molnar et al., 2001; Nelson et al., 2002; Widom et al., 2007)) was assessed at baseline (twins age 16 and older only) and follow-up using a checklist of traumatic events adapted from the National Comorbidity Survey (see Table 2 for list of traumas assessed) (R. C. Kessler et al., 1995). Information on physical abuse from the checklist was combined with responses to additional questions regarding harsh physical punishment from the childhood rearing environment section to form a single physical abuse variable. Similarly, checklist responses regarding rape and sexual molestation were combined with responses to questions on forced sex and incest from other interview sections to form a single childhood sexual abuse variable. Child abuse variables were coded positive

if a respondent reported having experienced the event at either baseline or follow-up and the event first happened before age 16 years. This age cutoff was chosen because we were specifically interested in events occurring in childhood and early adolescence (Sartor et al., 2013).

Maternal and paternal education level (used as an indicator of family socioeconomic status, e.g., (Hasin et al., 2005; R. C. Kessler et al., 2003)) were obtained from parental self-report or, if only one parent completed an interview, from the co-parent's report. If data were not available from either parent, twin report of parental education from Wave 5, the only twin interview to query all respondents in the cohort regarding parental education, was substituted for parent report if available. Parental education was categorized into < high school, ≥ high school, and a third category for women with missing maternal (n=93) or paternal (n= 159) education data and included in multivariable models as a set of indicator variables with parental education ≥ high school as the referent. History of parental separation (Amato & Keith, 1991) for reasons of relationship dissolution before the twins reached age 18 was coded from items included in the parent and twin interviews, with twin interviews only used when parental interviews were not available. (Due to limitations of the interview data it was not possible to date the separation more precisely than < 18 years for a portion of the sample; see (Waldron et al., 2013) for details.) Maternal and paternal alcohol use disorder (Anda et al., 2002) was coded as a three-level variable. A parent was considered “definite” for alcohol use disorder if (1) he or she met criteria for DSM-IV alcohol dependence through self-report, or (2) two or more informants indicated that the parent had ≥ three alcohol dependence symptoms (asked of the co-parent) or that drinking had ever caused the parent “problems with health, family job or police, or other problems” and that the parent was an “excessive drinker” (asked of the twins) (Waldron et al., 2013). Parents with only one positive informant report were grouped into a second, “probable” category. Thus, maternal and paternal alcohol use disorder were each included in logistic regression models as a set of indicator variables (definite, probable, and no alcohol use disorder [referent]).

Phenotypic analyses

Phenotypic statistical analyses were conducted using Stata Version 9 (StataCorp, 2005). Survey commands were used for the analysis of bivariate associations. Under the survey command, the Pearson χ^2 statistic is corrected for the twin sampling design using the Rao and Scott (1984) second order correction, converting the Pearson χ^2 into an F statistic (Rao & Scott, 1984). Racial differences in continuous and ordinal variables were evaluated with t-tests and Mann-Whitney U Tests, respectively. For logistic regression models, Huber-White robust variance estimation was used to adjust standard errors for the non-independence of observations inherent in twin data (StataCorp, 2005).

Phenotypic analyses proceeded in several steps. First, we assessed bivariate associations between race and the prevalence of lifetime DSM-IV MDD, as well as endorsement of specific MDD symptoms during the most severe depressive episode among women with a lifetime MDD diagnosis history (see Table 1). Second, we compared AA and EA women on MDD risk factors, initially including all women in the analysis and then limiting analyses to

women with a lifetime MDD diagnosis (see Table 2). Variables with *p*-values < 0.20 for contrasts in the entire sample were then used as covariates in a logistic regression model for the association between race and MDD. Third, we compared women with and without MDD on MDD risk factors separately by race (see Table 3). To identify independent risk factors for MDD in AA and EA women, variables with *p*-values < 0.20 in the stratified analyses were then entered into stratified logistic regression models. In the interest of parsimony, variables that were not statistically significant after adjusting for the other variables in the full model were then removed, and a log-likelihood ratio test was performed to ensure that the reduced and full models were comparable in fit. Final stratified models included any independent variable that was retained in the reduced model for either AA or EA women to allow for comparability between groups.

Genetic analyses

Data from monozygotic (MZ) and dizygotic (DZ) twin pairs can be used to estimate the liability to MDD that is due to additive genetic effects (A), shared environmental effects (C) or dominant genetic effects (D), and non-shared environmental effects (E), where: A is the sum of the individual effects of multiple genes on a given trait, C represents factors that make family members similar, D represents non-additive or genetic interaction effects, and E comprises factors that make family members dissimilar as well as measurement error. In the classical twin design, members of MZ and DZ pairs are assumed to share 100% and 50% of additive genetic factors, respectively. Shared environmental factors are assumed to be shared 100% across members of MZ and DZ pairs, and unique environmental influences are uncorrelated across twins (i.e., not shared by co-twins). Notably, in a classical twin design, the statistical power to detect dominant genetic effects is low, and it is not possible to examine these effects simultaneously with shared environmental effects due to confounding (Sham, 1998).

Twin correlations and biometrical model-fitting were conducted in Mx (Neale et al., 2006; Neale & Cardon, 1992). Lifetime MDD was modeled as a binary variable and variance components were adjusted for age at interview by controlling for the probit regression on age, which was included as a set of dummy variables reflecting age quartiles (ages 18–19, 20–22 and 23–24, with ≥25 years as the referent category). To determine the best-fitting model, we first estimated the full univariate twin model separately among AA and EA women. Next, multiple submodels of the full ACE or ADE model that constrained A, C, or D to zero were fitted to the data. Once the best-fitting models for each racial group were selected, we then tested whether the specific parameter estimates could be equated across EA and AA groups. For all analyses, standard chi-square (χ^2) difference tests were used to compare the fit of nested models, with *p*-values < 0.05 an indication that the parameter(s) could not be dropped from the model without a significant decrement in model fit (Neale et al., 2006). Akaike's Information Criterion (AIC) was used to compare non-nested models, with lower AIC values indicating better-fitting and more parsimonious models.

RESULTS

Phenotypic analyses

The prevalence of lifetime MDD among AA women was significantly greater than that among EA women (24.73% vs. 18.78%, p=0.003). As shown in Table 1, AA women with MDD were more likely to report recurrent episodes (41.79% vs. 32.23%; $p < 0.001$) but were less likely to have ever been treated for depression (20.59% vs. 37.62%, $p < 0.001$) compared to their EA counterparts. Rates of symptom endorsement for the most severe depressive episode were broadly comparable across groups, with the notable exception being the lower endorsement of feelings of guilt/worthlessness by AA women (65.44% vs. 79.70%, $p < 0.001$).

Risk factors for MDD were more commonly endorsed by AA women (Table 2, **left half**), with the most substantial differences observed for childhood sexual abuse (20.11% vs. 11.23%), childhood physical abuse (41.48% vs. 14.96%), parental separation (75.14% vs. 37.41%) and witnessing injury or death (12.82% vs. 4.19%). Similar differences in rates were seen even when comparisons were limited to MDD cases (Table 2, **right half**). Despite a higher overall prevalence of lifetime MDD, AA women had lower, but not statistically significant, odds of lifetime MDD than EA women after adjusting for risk factors that differed between AA and EA women (OR =0.88, 95% CI = 0.67–1.15).

Although many associations between MDD risk factors and diagnosis were similar for AA and EA women in bivariate analyses stratified by race, there were several risk factors that were only associated with MDD among EA women, such as parental separation and maternal and paternal education and alcohol use disorder (Table 3). ORs in the final logistic regression models predicting MDD for AA and EA women tended to be similar; however, some ORs were only statistically significant among EA women (see Table 4). The only variables with substantial differences in effect size were definite maternal alcohol use disorder, which was positively associated with MDD solely in EA women (1.82 (1.25–2.64) vs. 0.90 (0.28–2.88) in AA women), and missing paternal education data (a function of paternal non-participation or lack of maternal or twin knowledge regarding paternal education level), which was associated with MDD only among AA women (2.29 (1.14–4.63) vs. 0.91 (0.54–1.54) in EA women.

Latent Genetic and Environmental Risk for Lifetime MDD

The MZ twin pair correlation was greater than the DZ twin pair correlation among AA (rMZ=0.61, 95% CI=0.31–0.82; rDZ=0.16, 95% CI=0.00–0.45) and EA (rMZ=0.40, 95% CI=0.27=0.51; rDZ=0.19, 95% CI=0.02–0.34) twins. In both AA and EA pairs, the best-fitting model allowed for additive genetic and nonshared environmental, but not shared environmental, contributions to variation in MDD liability (See Table 5). Among AA women, 56% (95% CI: 29%–78%) of the variance in MDD liability was attributable to additive genetic effects, with the remainder due to nonshared environment (44%, 95% CI = 22%–72%; AIC = −464.29). In contrast, additive genetic and nonshared environmental effects accounted for 41% (29%–52%) and 59% (48%–71%) of the overall phenotypic variance in MDD, respectively (AIC = −3228.87) among EA women. A model in which

estimates were constrained to be equal across racial category, however, did not provide a statistically significantly worse fit to the data, and was thus chosen as the final model. In this model, additive genetic variance explained 43% (33% –53%) of the variance in MDD, with the remainder attributable to nonshared environment (57%, 47%–67%).

DISCUSSION

This study examined racial differences in MDD prevalence, symptomatology and risk factors in a large, representative sample of African- and European-American young adult female twins. Although the lifetime prevalence of MDD was higher in AA women, most of the assessed risk factors were more likely to be endorsed by AA than by EA women, and after adjusting for these factors AA women had lower, but not statistically significant, odds of meeting criteria for MDD than EA women. This finding is consistent with previous studies reporting no significant differences or lower prevalence of depression in AAs compared to EAs (Dunlop et al., 2003; Hasin et al., 2005; R. C. Kessler et al., 2003; Riolo et al., 2004; Williams et al., 2007). Results from latent genetic analyses provided some evidence for heterogeneity of effects by race, with higher heritability among AA women; however, the best fitting model was one in which additive genetic and nonshared environmental effects were constrained to be equal for AA and EA women. We obtained zero estimates for shared environmental contributions to variation in MDD risk, a pattern seen consistently in twin studies of MDD (c.f. Sullivan et al., 2000). This pattern of consistent zero estimates across studies strongly implies negative confounding, i.e. non-additive genetic contributions to risk are masking any shared environmental influences, so that we are unable to precisely quantify the magnitude of the latter influences. It is sometimes misinterpreted as implying the absence of shared environmental effects (Sullivan et al., 2000): if the true value of a variance component were zero, in the absence of negative confounding, we would expect to observe some studies reporting positive point estimates.

To our knowledge, this was the first study to examine racial differences in the heritability of MDD among AA and EA young women. Our combined heritability estimate was comparable to that reported in a previous meta-analysis of twin studies of the heritability of major depression conducted with predominantly European ancestry samples (37%, 31%-42%)(Sullivan et al., 2000); as well as more recent studies (Glowinski et al., 2003; Kendler et al., 2006),including that from a previously published study that estimated the heritability of MDD to be 40.4% (23.9–55.1) in the same cohort using combined data (i.e., no stratification by race) collected at the baseline interview, which was conducted a median of six years prior to the data used for the current analyses (Glowinski et al., 2003). Although the heritability estimate calculated separately among AA women in our study was greater than that reported in the only other published study of the heritability of depression in AA twins, that study used a state depression phenotype (CES-D score, which is a measure of past 7-day depressive symptoms), an older sample that included men and women, and did not include non-AA twins(Whitfield et al., 2008). Thus, one cannot draw meaningful comparisons to the results presented here.

It was possible to constrain the MDD heritability estimates to be equivalent between AA and EA women; however, it should be noted that the heritability estimate among AA women

was 1.36 times higher than that among EA women and that, given the relatively small number of AA twin pairs, we were underpowered to detect a difference of this magnitude. Thus, further research with larger samples of AA female twin pairs is needed to more definitively answer the question of whether or not there are differences between AA and EA women in the heritability of MDD, particularly since there are multiple reasons why such differences in heritability might be observed. For example, a plausible explanation for the higher heritability of MDD among AA compared with EA women is that there is a stronger contribution of genotype by shared environment interaction effects in AA women, with increased opportunity for the realization of genetic risk in this group because of the high prevalence and familiality of adverse environmental experiences.. Since the effects of G × SE interaction cannot be estimated separately in the classical twin study, variance attributable to G × SE interaction is included in the total heritability estimate (Heath & Martin, 1993). Of note, multiple previous studies have reported evidence of specific gene-by-measured environment interaction in MDD (Caspi et al., 2003; Karg et al., 2011; Munafo, 2012; Risch et al., 2009). Given racial discrimination, residential segregation and lower availability of socioeconomic resources, AA women on average are more likely to be exposed to many stressors than are EA women (Gee et al., 2012; Shuey & Willson, 2008; Walsemann et al., 2009; Walsemann et al., 2008). In the current study, many of the risk factors significantly associated with MDD in multivariable models among AA women were also associated with MDD at similar magnitudes among EA women, but these risk factors were significantly more likely to be endorsed by AA than by EA women. Another potential explanation is that heritability differences could be due to true or artifactual differences in the MDD phenotype between AA and EA women, though similar symptom endorsement probabilities by AA versus EA women with MDD histories make this explanation less likely.

Limitations

This study is subject to certain limitations. First, in addition to low power to detect differences in heritability by race/ethnicity, sample sizes also were not sufficiently large to permit disaggregation of the contributions of genotype by environmental risk factor associations for individual environmental risk-exposures, such as those suggested above. Second, onset of MDD in women occurs throughout the lifespan; (Ronald C. Kessler et al., 2005) thus, it is likely that some women in the sample who were considered unaffected in these analyses will develop MDD in the future, particularly given the relatively young age of the sample (median age 22 years). As such, it is possible that these results may not be generalizable to older cohorts. Third, some environmental risk factors and correlates of MDD that have been shown to differ between AA and EA women, such as neighborhood characteristics and availability of coping resources, were not assessed in this study. Further, we decided not to include parental depression in the phenotypic analyses because it was assessed only through parental self-report (report from the twins about parental depression was not elicited) and parental participation in this study was much less common in AA than in EA families (64.65% of AA families vs. 81.69% of EA families had maternal interviews and 28.75% of AA families vs. 61.08% of EA families had paternal interviews). Fourth, there may have been cultural differences in behavior or interpretation of interview questions that could have affected the results. Although it is possible that such cultural differences

could explain the large difference between AA and EA women in prevalence of childhood physical abuse (41.87% vs. 15.06%), the fact that the association between childhood physical abuse and MDD was stronger in AA than in EA women suggests that the higher prevalence of childhood physical abuse among AA women may not be due to over-reporting. Fifth, due to the large difference in sample size between the AA and EA groups, there was substantially more statistical power to detect variables associated with MDD among EA women than among AA women. Finally, we employed a large number of statistical tests. Since these tests were not independent of one another, there remains an increased possibility of type I error. Therefore, we have given the *p*-values for bivariate statistical tests out to the thousandth decimal place so that the reader may adopt a more stringent alpha level when considering the results.

Conclusions

Although African-American young women had higher heritability of MDD than their European-American counterparts, this difference was not statistically significant. The observed difference may be explained by the higher likelihood of environmental risk exposures among African-Americans. Environmental risk exposures associated with major depressive disorder were similar for African- and European-American women; however, the prevalence of these exposures was greater among African-Americans. These findings underscore the necessity of conducting genetic research on samples that include enough participants of non-European Ancestry to detect differential effects by race, as well as the need for comprehensive assessments of individual, family and contextual environmental factors that have been shown to differ by race. More broadly, our results point to the need to develop more comprehensive etiologic models for psychiatric disorders that take minority subgroups into account, rather than continued reliance on etiologic models developed on samples that consist largely or exclusively of white non-Hispanics, as findings may not generalize to members of other racial and ethnic groups.

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Table 1

Depression symptoms among European-American (n = 606) and African-American (n = 136) female twins meeting DSM-IV MDD.

	African-American (%)	European-American (%)	*p*-value
Most severe major depressive episode			
Symptoms endorsed			
Felt depressed	97.79	99.83	0.003
Loss of interest	98.53	94.55	0.047
Appetite/weight changes[*]	87.50	79.37	0.030
Sleep disturbance	83.09	85.31	0.512
Psychomotor agitation/retardation	55.15	48.18	0.167
Tiredness/lack of energy	86.76	90.26	0.263
Feelings of guilt/worthlessness	65.44	79.70	<0.001
Difficulty concentrating	81.62	76.24	0.211
Thoughts of death/suicide or suicide attempt	51.47	50.33	0.804
Median number of symptoms	7	7	0.790
Median duration of episode (weeks)	8.66	4.33	0.245
Lifetime			
Ever treated for depression	20.59	37.62	< 0.001
Median age onset first episode (years)	18	18	0.142
More than one episode lifetime	41.79	32.28	0.045

Note: MDD = major depressive disorder.

[*] increase or decrease. *P*-values are from chi-square tests (dichotomous variables) or Mann-Whitney tests (ordinal variables).

Table 2

Sample characteristics among the entire sample and among women meeting criteria for DSM-IV lifetime major depression (MDD).

	Entire sample			MDD cases		
	African-American (%)	**European–American (%)**	***p*-value**	**African-American (%)**	**European–American (%)**	***p*-value**
n	550	3226		136	606	
Age greater than 22 years	44.36	37.57	0.027	52.94	47.52	0.321
Mean age (se)	22.00 (0.17)	21.63 (0.07)	0.040	22.32 (0.27)	22.21 (0.12)	0.709
Married or cohabiting	21.68	33.61	<0.001	21.32	38.68	<0.001
Menarche before age 12 years	31.39	18.01	<0.001	38.52	23.10	<0.001
Maternal education*			<0.001			0.028
Less than high school	17.45	9.52		18.38	13.86	
High school or greater	77.09	88.53		75.00	83.83	
Missing	5.45	1.95		6.62	2.31	
Paternal education*			<0.001			<0.001
Less than high school	14.91	9.86		16.91	12.05	
High school or greater	75.45	86.86		69.12	83.83	
Missing	9.64	3.29		13.97	4.13	
Parental separation before age 18 years	75.14	37.41	<0.001	76.47	46.78	<0.001
Maternal alcohol use disorder			<0.001			0.030
Definite**	5.65	6.02		7.35	11.06	
Probable***	9.65	4.03		14.71	6.77	
No	84.70	89.95		77.94	82.18	
Paternal alcohol use disorder			<0.014			0.379
Definite**	17.77	19.65		21.80	22.15	
Probable***	16.30	10.38		20.30	14.71	
No	65.93	69.97		57.89	63.14	
Traumatic events before age 16 years						
Sexual abuse	20.11	11.23	<0.001	37.31	26.41	0.014
Physical abuse	41.48	14.96	<0.001	57.36	26.71	<0.001

	Entire sample			MDD cases		
	African-American (%)	European–American (%)	*p*-value	African-American (%)	European–American (%)	*p*-value
Natural disaster	9.72	10.81	0.575	10.45	16.14	0.093
Life threatening accident	5.31	3.26	0.019	8.15	4.79	0.113
Witnessed injury or death	12.82	4.19	<0.001	22.22	8.91	<0.001
Physically assaulted	2.75	1.06	0.002	7.41	3.80	0.079
Threatened with a weapon	2.75	1.68	0.120	5.19	4.62	0.777

* Note: self-, coparent- or twin-report;

** self-report or positive report from 2 or more informants;

*** positive report from one informant

Table 3

Sample characteristics by race and lifetime DSM-IV major depressive disorder (MDD) diagnosis.

	African-American			European-American		
	MDD (%)	**No MDD (%)**	***p*-value**	**MDD (%)**	**No MDD (%)**	***p*-value**
n	136	414		606	2628	
Age greater than 22 years	52.94	41.55	0.033	47.52	35.27	<0.001
Married or cohabiting	21.32	21.79	0.911	38.68	32.44	0.005
Menarche before age 12 years	38.52	9.06	0.043	23.10	16.83	<0.001
Maternal education*			0.737			0.001
Less than high school	18.38	17.15		13.86	8.51	
High school or greater	75.00	77.78		83.83	89.62	
Missing	6.62	5.07		2.31	1.87	
Paternal education*			0.105			0.075
Less than high school	16.91	14.25		12.05	9.36	
High school or greater	69.12	77.54		83.83	87.52	
Missing	13.97	8.21		4.13	3.09	
Parental separation before age 18	76.47	74.70	0.702	46.78	35.24	<0.001
Maternal alcohol use disorder			0.528			<0.001
Definite**	7.35	5.08		11.06	4.85	
Probable***	34.56	31.72		6.77	3.40	
No	58.09	63.20		82.18	91.75	
Paternal alcohol use disorder			0.429			<0.001
Definite**	21.80	16.46		22.15	19.07	
Probable***	30.83	32.93		14.71	9.38	
No	47.37	50.61		63.14	71.55	
Traumatic events before age 16						
Sexual abuse	37.31	14.46	<0.001	26.41	7.72	<0.001
Physical abuse	57.36	36.34	<0.001	26.71	12.26	<0.001
Natural disaster	10.45	9.49	0.731	16.83	9.58	<0.001
Life threatening accident	8.15	4.38	0.092	4.79	2.91	0.018

	African-American			European-American		
	MDD (%)	**No MDD (%)**	***p*-value**	**MDD (%)**	**No MDD (%)**	***p*-value**
Witnessed injury or death	22.22	9.73	<0.001	8.91	3.10	<0.001
Physically assaulted	7.41	1.22	<0.001	3.80	0.42	<0.001
Threatened with a weapon	5.19	1.95	<0.018	4.62	0.99	<0.001

* Note: self-, coparent- or twin-report;

** self-report or positive report from two or more informants;

*** positive report from one informant

Table 4

Odds ratios and 95% confidence intervals for variables included in the final logistic regression models predicting DSM-IV major depressive disorder among African-American and European-American women.

	African-Americans OR (95% CI)	European-Americans OR (95% CI)
Age greater than 22 years	**1.59 (1.02–2.50)**	**1.52 (1.25–1.86)**
Menarche before age 12 years	1.17 (0.73–1.87)	**1.31 (1.03–1.66)**
Maternal alcohol use disorder		
Definite*	0.90 (0.28–2.88)	**1.82 (1.25–2.64)**
Probable**	1.39 (0.64–3.03)	1.37 (0.89–2.09)
No	1.00 (referent)	1.00 (referent)
Paternal education		
Less than high school	1.21 (0.64–2.26)	1.01 (0.74–1.39)
High school or greater	1.00 (referent)	1.00 (referent)
Missing	**2.29 (1.14–4.63)**	0.91 (0.54–1.54)
Traumatic experiences before age 16		
Sexual abuse	**2.55 (1.48–4.40)**	**2.86 (2.21–3.72)**
Physical abuse	**2.00 (1.25–3.19)**	**1.59 (1.23–2.04)**
Natural disaster	1.19 (0.53–2.63)	**1.48 (1.13–1.95)**
Witnessed injury/death	1.76 (0.98–3.17)	**2.17 (1.47–3.21)**
Assault	3.62 (0.95–13.76)	**2.74 (1.16–6.44)**

* self-report or positive report from two or more informants;

** positive report from one informant

Table 5

Model-fitting results for MDD.

	Model	a^2	c^2	d^2	e^2	−2LL	df	AIC	Δ χ^2	Δdf	Δ *p*
	African-American Women										
1	ACE	.56 (.00–.78)	.00 (.00–.42)	---	.44 (.22–.72)	533.71	498	−462.29	---	---	---
2	ADE	.10 (.00–.76)	---	.51 (.00–.81)	.39 (.19–.69)	533.11	498	−462.89	---	---	---
3	CE	---	.37	---	.63	537.40	499	−460.60	3.69(#1)	1	.05
4	**AE**	**.56 (.29–.78)**	---	---	**.44 (.22–.72)**	**533.71**	**499**	**−464.29**	**.00(#1) .60(#2)**	**1 1**	--- **.44**
5	E	---	---	---	1.00	548.03	500	−451.97	14.32(#1) 14.92(#2)	2 2	<.001 <.001
	European-American Women										
6	ACE	.41 (.02–.52)	.00 (.00–.33)	---	.59 (.48–.72)	2807.13	3017	−3226.87	---	---	---
7	ADE	.41 (.00–.52)	---	.00 (.00–.51)	.59 (.48–.71)	2807.13	3017	−3278.87	---	---	---
8	CE	---	.32	---	.68	2811.36	3018	−3222.64	4.23(#6)	1	.04
9	**AE**	**.41 (.29–.52)**	---	---	**.59 (.48–.71)**	**2807.13**	**3018**	**−3228.87**	**.00(#6) .00(#7)**	**1 1**	--- ---
10	E	---	---	---	1.00	2851.25	3019	−3186.75	44.12(#6) 44.12(#7)	2 2	<.001 <.001
	Constraining Groups										
11	AE	.56 (AA) .41 (EA)	--- ---	--- ---	.44 (AA) .59 (EA)	3340.83	3517	−3693.17	---	---	---
	Unconstrained										
12	***AE Constrain A,E**	**.43 (.33–.53)**	---	---	**.57 (.47–.67)**	**3341.93**	**3519**	**−3696.07**	**1.10**	**1**	**.29**

Note: MDD = major depressive disorder. A = additive genetic effects; C = shared environmental effects; D = dominant genetic effects; E = nonshared environmental effects; a^2 = proportion of variance in MDD due to additive genetic effects; c^2 = proportion of variance in MDD due to shared environmental effects; d^2 = proportion of variance in MDD due to dominant genetic effects; e^2 = proportion of variance in MDD due to nonshared environmental effects; −2LL = −2 log likelihood; df = degrees of freedom; AIC = Akaike's Information Criterion; $\Delta\chi^2$= chi-square difference test statistic; Δdf = change in degrees of freedom; Δ*p*= *p*-value associated with $\Delta\chi^2$. The best-fitting models are indicated by bold-type.

*This is a 1 df test because with 2 parameters, the second parameter by definition becomes fixed when the 1st parameter is equated across ethnicities.