Published in final edited form as:

J Affect Disord. 2016 November 15; 205: 311–318. doi:10.1016/j.jad.2016.08.016.

African-American Representation in Family and Twin Studies of Mood and Anxiety Disorders: A Systematic Review

Eleanor Murphy*

New York State Psychiatric University – Columbia University

Abstract

Purpose—Mood and anxiety disorders are common and disabling psychiatric disorders with known heritable risk factors. But the extent to which their heritability and familial risks can be generalized across ethnic/racial groups is still largely unknown, but remains of considerable scientific and clinical interest. The main objective in this review was to evaluate African-American (AA) representation in family and twin studies of major mood and anxiety disorders.

Method—We conducted key word-driven computerized searches in MEDLINE and PsycINFO and manual searches from reference lists of selected articles. Search parameters included family or twin studies, mood or anxiety disorders, and familial aggregation or heritability. US-based studies published from 1980 to 2015 were included.

Results—The final selection yielded 209 studies, of which 88 did not report race/ethnicity or only reported Caucasian/white race. Of the remaining 121 studies, 66% did not include AAs, 24% included 1 – 10% AA, 8% included greater than 10% AA and 2 studies were exclusively AA. These trends were similar across study type, disorder and time periods spanning 35 years.

Limitations—Small samples, including the large number of studies without race/ethnicity reports, limited detailed analyses of change across time by disorder and study type. Adoption studies were not included in this review.

Conclusions—Underrepresentation of AAs in family and twin studies of affective disorders is substantial and can limit generalizability of established heritability and familial risk estimates across clinical and research settings. Additional twin and family studies focusing on AAs can be of benefit in closing this gap.

Introduction

Mood and anxiety disorders together account for over 50% of psychiatric illness diagnosed in the 57.7 million American adults estimated to have a diagnosable mental disorder in a given 12-month period (Kessler et al., 2005). The current and projected public health burden

*Corresponding author. New York State Psychiatric Institute, Columbia University, 1051 Riverside Drive, Unit 24, New York, NY 10032. Tel: +(646) 774-6498; emurphy@nyspi.columbia.edu, em713@cumc.columbia.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

from these psychiatric disorders is significant and has been extensively documented (Kessler et al., 2005; Murray and Lopez, 1996; Organization, 2008; van Os and Kapur).

As in many biomedical fields, current focus in psychiatry has been identification of biological – including genetic – contributors to disease. Despite increased emphasis on molecular genetics, familial risk and heritability estimates from family and twin studies continue to play a vital role in enhancing the interpretability of findings in genetic research (Hettema et al., 2001a; Kendler and Diehl, 1993; Merikangas and Low, 2005; Smoller and Finn, 2003; Tsuang et al., 2001). However, these estimates have questionable generalizability to diverse racial and ethnic groups.

In particular, in the United States, non-Hispanic Blacks or African Americans (AA), who form the second-largest racial group, and in the last three decades comprised 11-13% of the population (Bureau, 2002, 2011), have been poorly represented in much of the extant literature addressing genetic and familial risks for affective disorders. Epidemiological studies based on household surveys have suggested that AA have comparable or lower rates of mood and anxiety disorders compared to non-Hispanic Whites (Hunter and Schmidt, 2010; Williams et al., 2007). Yet for some mood disorders such as major depression, AA patients have shown greater levels of impairment and severity of disorder, with poorer treatment outcomes relative to their white counterparts (Murphy et al.; Trivedi et al., 2006). However, in part due to the poor representation of AA in family and twin studies, very little else is known about patterns of familial aggregation, and genetic influences on intergenerational transmission, disease heterogeneity, and comorbidity among affective disorders in this population.

This underrepresentation of AA in family and twin studies exists despite the recognition that neurobiological mechanisms affecting patterns of inheritance, disease liability and treatment success can vary across racial and ethnic groups (Chaudhry et al., 2008; Chiao and Blizinsky, 2013). Accordingly, racial/ethnic homogeneity of the mostly European/white study samples, which prevented generalizability across racially diverse groups, was a key limitation highlighted by Sullivan et al. (2000) in their extensively-cited review and meta-analysis of family and twin studies on major depressive disorder (Sullivan et al., 2000). This gap in knowledge can complicate conclusions drawn from molecular genetic studies that are based on racially diverse samples including AA. Although there are many excellent reviews on the genetic epidemiology of mood and anxiety disorders, we are not aware of any review that has examined AA representation in such studies.

This paper therefore reviews AA representation in family and twin studies of major mood and anxiety disorders from 1980 through 2015. The objective is to determine (1) the proportion of the selected family and twin study samples that are AA; (2) trends for these proportions across the 35-year period studied; (3a) whether there are any family or twin studies specifically focusing on African Americans, and (3b) if any, to what extent do their familial risk and heritability estimates match those of family and twin studies conducted primarily using Caucasian/white samples.

Family and Twin Studies

Family studies address the degree to which disorders aggregate in families and usually represent the first step toward assessing the genetic underpinnings of a disorder. Familial aggregation does not necessarily imply a genetic cause since it can result from either shared environmental or genetic risk factors; however, family studies can potentially identify the subtype of disease) or disorder that is most familial and therefore likely to have the strongest genetic influence (e.g., early-onset, recurrent major depression).

Twin Studies—Although family studies cannot distinguish between genetic or environmental contributions to familial aggregation, twin studies overcome this limitation. They are designed to distinguish the genetic and environmental contributions to a given disorder by comparing similarity (concordance or correlation) in monozygotic twins, who share 100% of their alleles, and dizygotic twins who share on average 50% of their alleles, as do biological full siblings. Heritability estimates from twin studies have shown a modest to substantial genetic contribution to the familial aggregation of major mood and anxiety disorders (Hettema et al., 2001b), (Sullivan, 2000).

Method

Literature Search and Screening Strategy

Search & Import—We utilized an iterative multi-step process to select studies to include in this review. We performed a computerized key word-driven search from PUBMED/MEDLINE and PSYCHINFO databases, with the consultation of a library systems information analyst. This was conducted for each group of disorders (i.e., mood or anxiety disorders) separately. Our basic keyword search parameters included major mood, or anxiety disorders AND *family study* or *twin study*,¹ AND *heritability* or *familial aggregation* or *genetic* (see Figure 1a for key-word search details). Duplicates were removed using the existing automated library duplicate removal feature. Articles were then imported into Endnote, Version X7 where any outstanding duplicates not captured by the automated library feature were removed before further screening.

Initial Screening—For each group of disorders, we eliminated articles that were published before 1980. We then screened out articles that were obviously not relevant to the subject matter based on their titles and/or abstracts. Our broad inclusion criteria at this point were family studies examining rates of major mood and anxiety disorders in probands and first-degree relatives, and twin studies examining concordance rates and/or heritability of major mood and anxiety disorders.

The remaining articles were then separated into twin studies and family studies. We then performed hand searches from reference lists of selected reviews that featured family and twin studies of mood disorders (Smoller and Finn, 2003; Sullivan et al., 2000; Taylor et al., 2002; Wilde et al., 2014), anxiety disorders (Chapman et al., 2012; Hettema et al., 2001a; Merikangas and Low, 2005), or both (Kendler, 2001; Rasic et al., 2013; Shih et al., 2004).

¹Through the last week in December 2015.

We added any articles from those lists determined to be relevant. This concluded the first step of our article selection process (See Figure 1a).

Final screening, review and selection

Upon completion of step 1, we were left with 159 family studies of mood disorders, 110 twin studies of mood disorders, 109 family studies of anxiety disorders, and 98 twin studies of anxiety disorders (Figure 1b). We performed a closer review of these articles and removed those that did not meet our inclusion criteria. We further eliminated studies in which the samples were derived from non-US populations. The final selection process yielded a total of 58 family studies of anxiety disorders, 76 family studies of mood disorders, 33 twin studies of anxiety disorders, and 42 twin studies of mood disorders (Figure 1b). The remaining studies were examined for reporting of race/ethnicity and AA representation.

Results

A total of 209 studies were reviewed for AA representation. Many studies did not report the racial/ethnic composition of their samples. Some studies reported just the proportion of Caucasians (Non-Hispanic whites) – who comprised the majority but not the totality – with no indication of the proportion of AA (or other races/ethnicities), if any. Together, these 88 non-reporters or partial reporters (*NR/PR*) accounted for 42% of the total number of studies reviewed. We characterized studies with full reports on race/ethnicity by the % of AA representation in their samples in four discrete categories: 0%, 1-10%, > 10% (10-99%), and 100% AA. Eighty studies reported no AA participants in their samples, 29 studies reported 1-10% AA; 10 studies reported >10% AA, and only two studies focused exclusively on AA.

Trends in Representation Across a 35-year Period

Based on publication year, articles were grouped into three chronological categories across a 35-year period: 1980-1994 (Period 1), 1995-2004 (Period 2), and 2005-2015 (Period 3) (Figure 2). There were 74 studies in Period 1, 70 studies in Period 2 and 65 studies in period 3. Across all periods, the *NR/PR* and 0% AA categories were most prevalent. The *NR/PR* category showed a non-significant increasing trend from periods 1 to 3. However, the 0% AA category showed a significant decline from period 1 to period 2, $\chi^2(1, N=144) = 7.24, p = .007$; and from period 2 to period 3, $\chi^2(1, N=135) = 5.04, p = .025$. The 1-10% AA category increased significantly from period 1 to 2, $\chi^2(1, N=100) = 8.79, p = .003$. The > 10% AA and the 100% AA categories both showed non-significant increases in period 3. As shown in Table 1, when the studies were separated according to study type (family, twin) and disorder (anxiety, mood), the trends of AA representation across the three periods were similar to the trends shown in Figure 2 for all the studies.

Studies with Significant AA representation (exceeding 10%)

There were 12 studies in which AA representation exceeded 10% of the sample – including two studies focusing exclusively on AA (Chapman et al., 2012; Whitfield et al., 2008) (Table 2). Ten of the 12 studies shown in Table 2, had AA proportions ranging from 11% to 24% of their samples. They included three family studies of anxiety disorders (Beidel and Turner,

1997; Brown, 1994; Capps et al., 1996), two family studies of mood disorders (Gershon et al., 2011; Taylor et al., 1993), one twin study of anxiety disorder (Sartor et al., 2011) and four twin studies of mood disorders (Duncan et al., 2014; Munn-Chernoff et al., 2015; Slane et al., 2011; Tackett et al., 2011). Only two of these studies – which were both twin studies using the same sample - reported specifically on findings pertinent to race/ethnicity (Duncan et al., 2014; Munn-Chernoff et al., 2015). The first examined the heritability of depression and found racial group differences in heritability point estimates, which were 0.56 (0.29-0.78) for AA and 0.41 (0.29-0.52) for non-Hispanic whites (Duncan et al., 2014). The second found no racial group differences in heritability for the comorbid depression-binge eating disorder (Munn-Chernoff et al., 2015).

The studies focusing exclusively on AA were a family study of anxiety and a twin study of depression. The family study examined the rates of anxiety disorders in a community-based sample of 97 offspring (age 6-17) of AA parents with or without ($n=42$) anxiety disorders (Chapman et al., 2012). Because this study had a high-risk design with parent-child dyads, siblings and parents of probands were not assessed. There were six anxiety disorders represented among the 55 parent cases – agoraphobia, panic disorder, generalized anxiety disorder, social phobia, simple phobia, and obsessive-compulsive disorder. The familial risk estimate obtained in this study (Odds Ratio= 4.39) was within the range of estimates (O.R. = 2-8) from comparable high-risk studies of anxiety disorders with majority or all Caucasian samples (Biederman et al., 1991; Black et al., 2003; Johnson et al., 2006; Merikangas et al., 1998; Turner et al., 1987).

The second study focusing exclusively on AA was a twin study on the heritability of depressive symptoms as measured by the Center for Epidemiologic Studies-Depression Scale (CES-D), using a sample of 212 twins (Whitfield et al., 2008). The study used cutoff points to dichotomize the CES-D scores into “depressed” vs. “non-depressed” to obtain heritability estimates. In this study, the heritability estimates were greater for men (0.42) than for women (0.16), and greater for younger participants (0.28) than for participants aged 50+ (0.06), which contrasted the findings of an earlier population-based twin study of depression with among Caucasians (Kendler and Prescott, 1999), in which no age or gender differences were found.

Like the majority of studies reviewed, the 12 studies in Table 2 had some limitations, in that they each failed to meet one or more of the following methodological criteria met only by a small minority of family and twin studies in our selection. The criteria for the family studies were (1) systematic recruitment and ascertainment of probands, (2) explicit diagnostic criteria for the disorder of interest (i.e., not symptoms or syndromes), (3) controlled, (4) blinded, and (5) direct interviews to at least 75% of first degree relatives. The criteria for twin studies were (1) Population- or hospital-based twin registry, (2) explicit diagnostic criteria for disorder(s) of interest, (3) zygosity of twins established through standardized methods, and (4) independence of co-twin interviews. There were 28 family and twin studies (not shown in table 2), meeting these criteria. Eight of the studies were *NR/PR* (Black et al., 1992; Crowe et al., 1983; Fyer et al., 1993; Merikangas et al., 2003; Noyes et al., 1987; Noyes et al., 1986; Pauls et al., 1995; Stein et al., 1998), 18 were *0 % AA* (Fyer et al., 2005; Fyer et al., 1995; Fyer et al., 1990; Gershon et al., 1982; Hettema et al., 2001c; Kendler et

al., 2001; Kendler et al., 1992a, b, 1993; Kendler and Prescott, 1999; Klein et al., 1995; Lipsitz et al., 2005; Merikangas et al., 2014; Neale et al., 1994; Nestadt et al., 2000; Tsuang et al., 1980; Weissman et al., 1984; Weissman et al., 1993), and two were *1-10% AA* (Lyons et al., 1998; Scherrer et al., 2000). The two studies featuring AA participants did not report any race-based statistical controls, stratification of analyses or results.

Discussion

This paper reviewed a selection of family and twin studies of mood and anxiety disorders in order to investigate AA representation. We wanted to determine the proportion of studies with varying degrees of AA representation, and the change in those proportions over time. To our knowledge, this is the first systematic review to highlight the extent and long-term trends of AA representation in this particular area of psychiatric research. We reviewed 134 family studies and 75 twin studies and over a 35-year period, and found only one twin study of depression and one family study of anxiety focusing exclusively on AA, which means that as of 2015, there were no published family studies of mood disorders or twin studies of anxiety disorders among AA. We also found that a substantial number of the studies had no AA participants in their samples, despite a significant 35-year decline in the proportion of such studies. Moreover, we found that the significant decline in the proportion of studies with no AA was accompanied by non-significant increases in studies which did not report or only partially reported race/ethnicity of the sample, or studies in which AA comprised only 1-10 percent of the sample.

The decline in the proportion of studies that report 0% AA appears to be consistent with the timeline of the National Institutes of Health (NIH), which in 1987, established and implemented a policy for the inclusion of women and minorities in clinical research (Health, 2015). This policy became congressionally mandated through the NIH Revitalization Act of 1993, and was updated by the NIH to reflect this change in 1994 (Health, 2015). Under this law, all studies had to include minorities and women in research unless there was appropriate justification for non-inclusion. By 2001, the NIH inclusion mandate was well-established with an update of 15 racial/ethnic categories for reporting on samples. Although this mandate covers research protocols first submitted to the NIH funding and in subsequent annual reporting, it does not cover reporting for future manuscripts published from the initial study. So this could explain the persistence in the significant proportion of *NR/PR* studies, despite the decline in *0% AA* category.

We did not find a consistent trend in the *1-10% AA* categories or the *>10% AA* categories, but there was some improvement in the numbers, particularly in twin studies of mood disorders in period 3. This increase was driven by a number of twin studies published between 2008 and 2015, including the one study that focused exclusively on AA (Whitfield et al., 2008), and a second study in which AA represented 15% of the sample (Duncan et al., 2014). Despite some methodological limitations in the first study, such as assessing depressive symptoms in recent weeks (as opposed to lifetime DSM-diagnosed disorder), and not establishing independence of co-twin interviews, we consider noteworthy the findings of age and gender differences in heritability, contrasting findings from the earlier-published twin studies that found no age/gender differences. The second study used a sample of young

adult female twin pairs. The restricted age-range and gender of the study sample underscores the need for additional studies with AA that include participants of diverse age and gender groups.

The family study of anxiety disorders focusing exclusively on AA participants (Chapman et al., 2012), is to our knowledge, the first and only such family study among African Americans and represents an important step in addressing the need for more within-group family studies of anxiety in this population. A limitation of this study was that parental probands with different anxiety disorders were all grouped together so that the specificity of parent-offspring transmission based on anxiety disorder of the parent could not be assessed. In addition, the study sample was limited to parent-child dyads, so morbidity risks among other relatives (e.g., siblings) could not be assessed.

The results from the two exclusively-AA studies point to broad similarities between AA and non-Hispanic Whites on overall heritability estimates and morbidity risks, but more nuanced differences when it comes to within-group variation along factors such as gender, age, and disorder subtypes. It is often these subtle variations that tend to provide the most important clues as the etiological and development drivers of disease and genetic transmission, given different environmental pressures. Additional research, including further replication of these within-group family and twin studies, is necessary before any definitive conclusions can be drawn.

Some unique features of family and twin studies may present additional challenges for the recruitment and retention of ethnic and racial minorities, including AA. We consider the possibility that researchers may be dissuaded from pursuing diverse samples for fear of not being able to meet certain methodological standards, but that concern may be illusory. As noted earlier, only 28 out of the 209 twin and family articles reviewed featured studies meeting the most rigorous methodological criteria. The majority of the studies reviewed, regardless of sample ethnic or racial composition, had one or more methodological limitations. As shown in Table 2, the studies with significant AA representation, like the majority of studies reviewed, had some limitations. However, these limitations did not appear to significantly impact the heritability and morbidity risks, which fell within the range of those obtained in the most-rigorously conducted studies. This suggests that the benefits of inclusion versus the disadvantages of failing to meet one or more methodological criteria must be systematically weighed and applied to individual studies, instead of serving as a uniform deterrent to inclusion of racially diverse groups.

Study Limitations—Having discussed the findings and their implications, it is important to consider some limitations of this study. First, the small group of studies selected for review restricted our ability to systematically evaluate changes in representation by disorder type, within study type across the three time periods. However, we were able to provide descriptive trends, which were consistent with the overall patterns across the three periods. A second limitation is that while a significant number of the studies did not report or only reported Caucasian/white race in their samples, we cannot assume that they did not have AA. Theoretically, AA could comprise 1-100% in these studies. Still, with AA being the second largest racial minority group in the US, it is extremely unlikely that a published

scientific study with a sample that is majority AA or has a significant proportion of AA would fail to report the racial/ethnic composition of its sample. So there is no basis for assuming that studies in which race/ethnicity are not reported have a *higher* proportion of AA than studies in which race/ethnicity are reported. A third limitation was that the three time periods are unevenly divided, at 14, 10 and 11 years respectively. These cutoffs may seem arbitrary, but were so selected to track the progression vis-à-vis the NIH's timeline for inclusion of minorities in research policies and congressional mandates. Furthermore, key findings, such as a lack of family studies of mood disorders or twin studies of anxiety disorders among AA, are not influenced by these cutoff points. And the substantive point of little positive change in AA representation in these studies over a 35 year-span remains the same. A fourth limitation is that we did not cover adoption studies, which can be a valuable complement to family and twin studies in sorting out the genetic influences on disorders. However, few US-based adoption studies focus on affective disorders, prohibiting any meaningful analysis of changes in AA representation within and across time periods. As adoption resources and databases in the US continue to be developed and expanded, they may eventually be more easily accessed for research of psychiatric disorders and other conditions, with adequate ethnic/racial group representation.

Conclusion and Future Directions

The findings from this review clearly demonstrate a persistent gap in adequate African-American representation in family and twin studies of mood and anxiety disorders. This is a significant drawback in the field which currently relies on established heritability and familial risk estimates for contemporary studies in molecular genetics, as well as clinically-relevant symptom and disorder manifestation, intergenerational transmission, and treatment outcomes in diverse populations. Although proportionally more studies now include AA in their samples compared to 35 years ago, it is unclear what is driving this result, be it a tendency for more studies to simply not report race/ethnicity, or an actual increase in studies with AA participants, or a combination of both. Even with small increases in AA representation in study samples, the lack of family studies of mood disorders or twin studies of anxiety disorders among AA continues to be of concern, and the rare studies focusing exclusively on AA stress the need for additional studies and replication of findings. This underrepresentation in traditional family and twin studies may persist in contemporary molecular genomic studies with various family- and twin-based designs. Understanding the reasons for the persistent underrepresentation of AA in family and twin studies of mood and anxiety disorders and taking measures to address them would be a logical step in the direction towards rectifying this research gap.

Acknowledgments

The author wishes to thank Nighat A. Ispahany, library informationist (Columbia University Medical Center Libraries) for consultative advice during the article search process. The author also wishes to thank Ruth Ottman, PhD, and Myrna Weissman, PhD, for their valuable insights and feedback in the preparation of this manuscript.

Funding Sources and Disclosures

This manuscript was made possible with funding support from the National Institutes of Health, National Institute for Minority Health and Health Disparities, 1K22MD006140-01 (P.I. Murphy, E).

References

- Beidel DC, Turner SM. At risk for anxiety: I. Psychopathology in the offspring of anxious parents. *J Am Acad Child Adolesc Psychiatry*. 1997; 36:918–924. [PubMed: 9204669]
- Biederman J, Rosenbaum JF, Bolduc EA, Faraone SV, Hirshfeld DR. A high risk study of young children of parents with panic disorder and agoraphobia with and without comorbid major depression. *Psychiatry research*. 1991; 37:333–348. [PubMed: 1891513]
- Black DW, Gaffney GR, Schlosser S, Gabel J. Children of parents with obsessive-compulsive disorder -- a 2-year follow-up study. *Acta psychiatrica Scandinavica*. 2003; 107:305–313. [PubMed: 12662254]
- Black DW, Noyes R Jr, Goldstein RB, Blum N. A family study of obsessive-compulsive disorder. *Archives of general psychiatry*. 1992; 49:362–368. [PubMed: 1586271]
- Brown TA. Familial aggregation of panic in nonclinical panickers. *Behaviour research and therapy*. 1994; 32:233–235. [PubMed: 8155061]
- Bureau, U.S.C.. Historical Census Statistics on Population Totals By Race, 1790 to 1990, and By Hispanic Origin, 1970 to 1990, For The United States, Regions, Divisions, and States. G., C.; J., K., editors. Washington D.C.: 2002. Working Paper Series No 56
- Bureau, U.S.C.. The Black Population: 2010. 2010 Census Briefs; 2011.
- Capps L, Sigman M, Sena R, Henker B, Whalen C. Fear, anxiety and perceived control in children of agoraphobic parents. *J Child Psychol Psychiatry*. 1996; 37:445–452. [PubMed: 8735444]
- Chapman LK, Petrie J, Vines L, Durrett E. The co-occurrence of anxiety disorders in African American parents and their children. *J Anxiety Disord*. 2012; 26:65–70. [PubMed: 21963233]
- Chaudhry I, Neelam K, Duddu V, Husain N. Ethnicity and psychopharmacology. *Journal of psychopharmacology (Oxford, England)*. 2008; 22:673–680.
- Chiao JY, Blizinsky KD. Population disparities in mental health: insights from cultural neuroscience. *American journal of public health*. 2013; 103(Suppl 1):S122–132. [PubMed: 23927543]
- Crowe RR, Noyes R, Pauls DL, Slymen D. A family study of panic disorder. *Archives of general psychiatry*. 1983; 40:1065–1069. [PubMed: 6625855]
- Duncan AE, Munn-Chernoff MA, Hudson DL, Eschenbacher MA, Agrawal A, Grant JD, Nelson EC, Waldron M, Glowinski AL, Sartor CE, Bucholz KK, Madden PAF, Heath AC. Genetic and environmental risk for major depression in African-American and European-American women. *Twin Research and Human Genetics*. 2014; 17:244–253. [PubMed: 24910290]
- Fyer AJ, Lipsitz JD, Mannuzza S, Aronowitz B, Chapman TF. A direct interview family study of obsessive-compulsive disorder. I. Psychological medicine. 2005; 35:1611–1621. [PubMed: 16219119]
- Fyer AJ, Mannuzza S, Chapman TF, Liebowitz MR, Klein DF. A direct interview family study of social phobia. *Archives of general psychiatry*. 1993; 50:286–293. [PubMed: 8466390]
- Fyer AJ, Mannuzza S, Chapman TF, Martin LY, Klein DF. Specificity in familial aggregation of phobic disorders. *Arch Gen Psychiatry*. 1995; 52:564–573. [PubMed: 7598633]
- Fyer AJ, Mannuzza S, Gallops MS, Martin LY, Aaronson C, Gorman JM, Liebowitz MR, Klein DF. Familial transmission of simple phobias and fears. A preliminary report. *Archives of general psychiatry*. 1990; 47:252–256. [PubMed: 2306167]
- Gershon A, Hayward C, Schraedley-Desmond P, Rudolph KD, Booster GD, Gotlib IH. Life stress and first onset of psychiatric disorders in daughters of depressed mothers. *J Psychiatr Res*. 2011; 45:855–862. [PubMed: 21524424]
- Gershon ES, Hamovit J, Guroff JJ, Dibble E, Leckman JF, Sceery W, Targum SD, Nurnberger JI Jr, Goldin LR, Bunney WE Jr. A family study of schizoaffective, bipolar I, bipolar II, unipolar, and normal control probands. *Archives of General Psychiatry*. 1982; 39:1157–1167. [PubMed: 7125846]
- Health, N.I.o. Background - Inclusion of Women and Minorities in Clinical Research. 2015
- Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. *The American journal of psychiatry*. 2001a; 158:1568–1578. [PubMed: 11578982]

- Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. *The American Journal of Psychiatry*. 2001b; 158:1568–1578. [PubMed: 11578982]
- Hettema JM, Prescott CA, Kendler KS. A population-based twin study of generalized anxiety disorder in men and women. *The Journal of nervous and mental disease*. 2001c; 189:413–420. [PubMed: 11504317]
- Hunter LR, Schmidt NB. Anxiety psychopathology in African American adults: literature review and development of an empirically informed sociocultural model. *Psychological Bulletin*. 2010; 136:211–235. [PubMed: 20192561]
- Johnson JG, Cohen P, Kasen S, Brook JS. A multiwave multi-informant study of the specificity of the association between parental and offspring psychiatric disorders. *Comprehensive psychiatry*. 2006; 47:169–177. [PubMed: 16635644]
- Kendler KS. Twin studies of psychiatric illness: an update. *Archives of general psychiatry*. 2001; 58:1005–1014. [PubMed: 11695946]
- Kendler KS, Diehl SR. The genetics of schizophrenia: a current, genetic-epidemiologic perspective. *Schizophr Bull*. 1993; 19:261–285. [PubMed: 8322035]
- Kendler KS, Myers J, Prescott CA, Neale MC. The genetic epidemiology of irrational fears and phobias in men. *Arch Gen Psychiatry*. 2001; 58:257–265. [PubMed: 11231833]
- Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. Generalized anxiety disorder in women. A population-based twin study. *Archives of general psychiatry*. 1992a; 49:267–272. [PubMed: 1558460]
- Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. The genetic epidemiology of phobias in women. The interrelationship of agoraphobia, social phobia, situational phobia, and simple phobia. *Arch Gen Psychiatry*. 1992b; 49:273–281. [PubMed: 1558461]
- Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. Panic disorder in women: a population-based twin study. *Psychol Med*. 1993; 23:397–406. [PubMed: 8332656]
- Kendler KS, Prescott CA. A population-based twin study of lifetime major depression in men and women. *Archives of General Psychiatry*. 1999; 56:39–44. Erratum appears in *Arch Gen Psychiatry*. 2000 Jan;57(1):94-5; PMID: 10632241. [PubMed: 9892254]
- Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of general psychiatry*. 2005; 62:617–627. [PubMed: 15939839]
- Klein DN, Riso LP, Donaldson SK, Schwartz JE, Anderson RL, Ouimette PC, Lizardi H, Aronson TA. Family study of early-onset dysthymia. Mood and personality disorders in relatives of outpatients with dysthymia and episodic major depression and normal controls. *Archives of General Psychiatry*. 1995; 52:487–496. [PubMed: 7771919]
- Lipsitz JD, Mannuzza S, Chapman TF, Foa EB, Franklin ME, Goodwin RD, Fyer AJ. A direct interview family study of obsessive-compulsive disorder. II. Contribution of proband informant information. *Psychological medicine*. 2005; 35:1623–1631. [PubMed: 16219120]
- Lyons MJ, Eisen SA, Goldberg J, True W, Lin N, Meyer JM, Toomey R, Faraone SV, Merla-Ramos M, Tsuang MT. A registry-based twin study of depression in men. *Archives of General Psychiatry*. 1998; 55:468–472. [PubMed: 9596050]
- Merikangas K, Cui L, Heaton L, Nakamura E, Roca C, Ding J, Qin H, Guo W, Yao-Shugart Y, Zarate C, Angst J. Independence of familial transmission of mania and depression: Results of the NIMH family study of affective spectrum disorders. *Molecular Psychiatry*. 2014; 19:214–219. [PubMed: 24126930]
- Merikangas KR, Dierker LC, Szatmari P. Psychopathology among offspring of parents with substance abuse and/or anxiety disorders: a high-risk study. *Journal of child psychology and psychiatry, and allied disciplines*. 1998; 39:711–720.
- Merikangas KR, Lieb R, Wittchen HU, Avenevoli S. Family and high-risk studies of social anxiety disorder. *Acta psychiatrica Scandinavica*. 2003; (Supplementum):28–37. [PubMed: 12950434]
- Merikangas KR, Low NC. Genetic epidemiology of anxiety disorders. *Handbook of experimental pharmacology*. 2005:163–179. [PubMed: 16594258]

- Munn-Chernoff MA, Grant JD, Agrawal A, Koren R, Glowinski AL, Bucholz KK, Madden PAF, Heath AC, Duncan AE. Are there common familial influences for major depressive disorder and an overeating-binge eating dimension in both European American and African American female twins? *International Journal of Eating Disorders*. 2015; 48:375–382. [PubMed: 24659561]
- Murphy E, Hou L, Maher BS, Woldehawariat G, Kassem L, Akula N, Laje G, McMahon FJ. Race, genetic ancestry and response to antidepressant treatment for major depression. *Neuropsychopharmacology*. 38:2598–2606. [PubMed: 23827886]
- Murray CJ, Lopez AD. Evidence-based health policy--lessons from the Global Burden of Disease Study. *Science (New York, N.Y.)*. 1996; 274:740–743.
- Neale MC, Walters EE, Eaves LJ, Kessler RC, Heath AC, Kendler KS. Genetics of blood-injury fears and phobias: a population-based twin study. *American journal of medical genetics*. 1994; 54:326–334. [PubMed: 7726205]
- Nestadt G, Samuels J, Riddle M, Bienvenu OJ 3rd, Liang KY, LaBuda M, Walkup J, Grados M, Hoehn-Saric R. A family study of obsessive-compulsive disorder. *Archives of general psychiatry*. 2000; 57:358–363. [PubMed: 10768697]
- Noyes R Jr, Clarkson C, Crowe RR, Yates WR, McChesney CM. A family study of generalized anxiety disorder. *The American journal of psychiatry*. 1987; 144:1019–1024. [PubMed: 3605423]
- Noyes R Jr, Crowe RR, Harris EL, Hamra BJ, McChesney CM, Chaudhry DR. Relationship between panic disorder and agoraphobia. A family study. *Archives of general psychiatry*. 1986; 43:227–232. [PubMed: 3954542]
- Organization, T.W.H. The Global Burden of Disease: 2004 Update. 2008:40–51.
- Pauls DL, Alsobrook JP 2nd, Goodman W, Rasmussen S, Leckman JF. A family study of obsessive-compulsive disorder. *The American journal of psychiatry*. 1995; 152:76–84. [PubMed: 7802125]
- Rasic D, Hajek T, Alda M, Uher R. Risk of Mental Illness in Offspring of Parents With Schizophrenia, Bipolar Disorder, and Major Depressive Disorder: A Meta-Analysis of Family High-Risk Studies. *Schizophrenia Bulletin*. 2013
- Sartor CE, McCutcheon VV, Pommer NE, Nelson EC, Grant JD, Duncan AE, Waldron M, Bucholz KK, Madden PAF, Heath AC. Common genetic and environmental contributions to post-traumatic stress disorder and alcohol dependence in young women. *Psychological Medicine*. 2011; 41:1497–1505. [PubMed: 21054919]
- Scherrer JF, True WR, Xian H, Lyons MJ, Eisen SA, Goldberg J, Lin N, Tsuang MT. Evidence for genetic influences common and specific to symptoms of generalized anxiety and panic. *Journal of affective disorders*. 2000; 57:25–35. [PubMed: 10708813]
- Shih RA, Belmonte PL, Zandi PP. A review of the evidence from family, twin and adoption studies for a genetic contribution to adult psychiatric disorders. *International review of psychiatry (Abingdon, England)*. 2004; 16:260–283.
- Slane JD, Burt SA, Klump KL. Genetic and environmental influences on disordered eating and depressive symptoms. *The International journal of eating disorders*. 2011; 44:605–611. [PubMed: 21997423]
- Smoller JW, Finn CT. Family, twin, and adoption studies of bipolar disorder. *American journal of medical genetics. Part C, Seminars in medical genetics*. 2003; 123c:48–58.
- Stein MB, Chartier MJ, Hazen AL, Kozak MV, Tancer ME, Lander S, Furer P, Chubaty D, Walker JR. A direct-interview family study of generalized social phobia. *Am J Psychiatry*. 1998; 155:90–97. [PubMed: 9433344]
- Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. *The American journal of psychiatry*. 2000; 157:1552–1562. [PubMed: 11007705]
- Sullivan PFN, Michael C, Kendler Kenneth S. Genetic epidemiology of major depression: Review and meta-analysis. *The American Journal of Psychiatry*. 2000; 157:1552–1562. [PubMed: 11007705]
- Tackett JL, Waldman ID, Van Hulle CA, Lahey BB. Shared genetic influences on negative emotionality and major depression/conduct disorder comorbidity. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2011; 50:818–827. [PubMed: 21784301]
- Taylor L, Faraone SV, Tsuang MT. Family, twin, and adoption studies of bipolar disease. *Current psychiatry reports*. 2002; 4:130–133. [PubMed: 11914174]

- Taylor MA, Berenbaum SA, Jampala VC, Cloninger CR. Are schizophrenia and affective disorder related? Preliminary data from a family study. *The American Journal of Psychiatry*. 1993; 150:278–285. [PubMed: 8304989]
- Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, Norquist G, Howland RH, Lebowitz B, McGrath PJ, Shores-Wilson K, Biggs MM, Balasubramani GK, Fava M, Team, S.D.S. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR D: implications for clinical practice. *American Journal of Psychiatry*. 2006; 163:28–40. [PubMed: 16390886]
- Tsuang MT, Stone WS, Faraone SV. Genes, environment and schizophrenia. *The British journal of psychiatry*. 2001; (Supplement 40):s18–24. [PubMed: 11315219]
- Tsuang MT, Winokur G, Crowe RR. Morbidity risks of schizophrenia and affective disorders among first degree relatives of patients with schizophrenia, mania, depression and surgical conditions. *The British journal of psychiatry: the journal of mental science*. 1980; 137:497–504. [PubMed: 7214104]
- Turner SM, Beidel DC, Costello A. Psychopathology in the offspring of anxiety disorders patients. *Journal of Consulting and Clinical Psychology*. 1987; 55:229–235. [PubMed: 3571678]
- van Os J, Kapur S. Schizophrenia. *The Lancet*. 374:635–645.
- Weissman MM, Gershon ES, Kidd KK, Prusoff BA, Leckman JF, Dibble E, Hamovit J, Thompson WD, Pauls DL, Guroff JJ. Psychiatric disorders in the relatives of probands with affective disorders. The Yale University--National Institute of Mental Health Collaborative Study. *Archives of General Psychiatry*. 1984; 41:13–21. [PubMed: 6691780]
- Weissman MM, Wickramaratne P, Adams PB, Lish JD, Horwath E, Charney D, Woods SW, Leeman E, Frosch E. The relationship between panic disorder and major depression. A new family study. *Archives of General Psychiatry*. 1993; 50:767–780. [PubMed: 8215801]
- Whitfield KE, Edwards CL, Brandon D, McDougald C. Genetic and environmental influences on depressive symptoms by age and gender in African American twins. *Aging & Mental Health*. 2008; 12:221–227. [PubMed: 18389402]
- Wilde A, Chan HN, Rahman B, Meiser B, Mitchell PB, Schofield PR, Green MJ. A meta-analysis of the risk of major affective disorder in relatives of individuals affected by major depressive disorder or bipolar disorder. *Journal of affective disorders*. 2014; 158:37–47. [PubMed: 24655763]
- Williams DR, Gonzalez HM, Neighbors H, Nesse R, Abelson JM, Sweetman J, Jackson JS. Prevalence and distribution of major depressive disorder in African Americans, Caribbean blacks, and non-Hispanic whites: results from the National Survey of American Life. *Archives of General Psychiatry*. 2007; 64:305–315. [PubMed: 17339519]

Highlights

- African Americans (AA) underrepresented in family & twin studies of affective disorders.
- Despite some improvement over a 35-year period, this underrepresentation persists.
- To date, there are no family studies of mood disorders in AA.
- To date, there are no twin studies of anxiety disorders in AA.

Figure 1 a.

Article Search and Initial Screening Strategy

Note: Keyword search:

ANXIETY DISORDERS: 1. (Family study* or Twin study*) 2. (heritability* or familial aggregation* or genetic*) 3. (anxiety disorder* or affective disorder* or panic disorder* or phobia* or agoraphobia* or obsessive-compulsive disorder* or generalized anxiety disorder* or post-traumatic stress disorder* 4. 3 and (1 or 2). 5. Remove duplicates from 4

MOOD DISORDERS: 1. (mood disorder* or affective disorder* or major depressive disorder* or major depression* or depression* or mania* or bipolar disorder* or dysthymia) 2. (Family study* or Twin study*). 3. (heritability* or familial aggregation* or genetic*) 4. 1 and (2 or 3). 5. Remove duplicates from 4

DETAILS FOR FIGURE 1a – Initial Search & Screening:

a. For mood disorders, the initial screening **eliminated articles** that were (1) Prior to 1980 – $N=26$; obviously irrelevant based on title and/or abstract – $N=1302$, (2) review papers/ commentaries – $N=67$, (3) methodological papers – $N=104$, (4) focused on molecular genetics – $N=35$, and (5)

Figure 1b.
Final Screening, Review & Selection Strategy

Figure 2.

African-American representation in family and twin studies of mood and anxiety disorders.

Note. NR/PR = Studies in which race and ethnicity were not reported or only partially reported. $N(\text{period 1}) = 74$; $n(\text{period 2}) = 70$; $n(\text{period 3}) = 65$.

Period differences in AA representation categories tested with Pearson Chi-Square test of difference in proportions, two-tailed significance:

a. significant difference between period 1 and 2;

b. significant difference between period 2 and 3. ** $p < .01$; * $p < .05$

Table 1

African-American Representation in Selected Twin and Family Studies of Mood and Anxiety Disorders.

		All	Anxiety		Mood	
		Studies	Family	Twin	Family	Twin
	Categories of AA Rep ^a	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
Period 1 (1980-1994)	NR/PR	26 (35)	9 (45)	1 (2)	15 (35)	1 (17)
	AA=0 %	43 (58)	9 (45)	4 (80)	25 (58)	5 (83)
	AA=1-10 %	3 (4)	1 (5)	0 (0)	2 (5)	0 (0)
	AA>10 %	2 (3)	1 (5)	0 (0)	1 (2)	0 (0)
	AA=100 %	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Period 2 (1995-2004)	NR/PR	29 (41)	13 (48)	3 (20)	10 (67)	3 (23)
	AA=0 %	25 (36)	9 (33)	6 (40)	3 (20)	7 (54)
	AA=1-10 %	14 (20)	3 (11)	6 (40)	2 (13)	3 (23)
	AA>10 %	2 (3)	2 (7)	0 (0)	0 (0)	0 (0)
	AA=100 %	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Period 3 (2005-2015)	NR/PR	33 (51)	7 (64)	5 (39)	12 (67)	9 (39)
	AA=0 %	12 (19)	3 (27)	3 (23)	3 (17)	3 (13)
	AA=1-10 %	12 (19)	0 (0)	4 (31)	2 (11)	6 (26)
	AA>10 %	6 (9)	0 (0)	1 (8)	1 (6)	4 (17)
	AA=100 %	2 (3)	1 (9)	0 (0)	0 (0)	1 (4)

Note. Number (n) and percentage (%) figures are for a given period.

^aCategories of African-American Representation are NR/PR (race/ethnicity not reported or partially reported); AA=0%, (no African-American participants); AA=1-10%, AA>10% (proportion of African-American participants exceeds 10%, but less than 100%); AA=100%

Table 2

Selected Family and Twin studies with African-American Representation over 10%.

Author (Year)	Disorder (s) Assessed	African American Representation
FAMILY STUDIES		
Taylor, Michael A., et al. (1993)	Unipolar and bipolar depression	22% of 237 psychiatric probands; 8% of 85 control probands (all-male proband sample)
Brown, T. A. (1994)	Panic Disorder	14.7% of 184 male and female college students.
Capps, L., et al. (1996)	Agoraphobia	12.5% of 32 children of parents with/without AGO ²
Beidel, D. C. & Turner, S. M. (1997)	Anxiety disorders	15% of 129 children of parents with/without ANX ³
Gershon, A., et al. (2011)	Unipolar depression	11% of 44 depressed/non-depressed mothers (all female proband-offspring sample)
Chapman, L. K., et al. (2012)	Anxiety disorders	100% of 97 parent-child dyads
TWIN STUDIES		
Whitfield, Keith E., et al. (2008)	Unipolar Depression (symptoms)	100% of 212 twin-pairs
Sartor, C. E., et al. (2011)	Comorbid Post-traumatic Stress disorder and alcoholism	15% of 1772 twin-pairs, and 243 singletons (all female)
Slane, Jennifer D., et al. (2011)	Comorbid depression and disordered eating (symptoms)	11% of 292 female twin-pairs (young adult)
Tackett, Jennifer L., et al. (2011)	Comorbid depression	24% of 2,022 twin-pairs (age 6-17)
Duncan, Alexis E., et al. (2014)	depression	18% of 3,776 female twin-pairs (young adult)
Munn-Chernoff, Melissa A., et al. (2015)	Comorbid depression and binge-eating disorder	18% of 3,776 female twin-pairs (young adult)

Note. Studies are listed in order of year published within each category of family and twin studies.

² Agoraphobia

³ Any anxiety disorder