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Concordance Rates for Cognitive Impairment among Older African American Twins

Keith E. Whitfield[1], **Jared Kiddoe**[2], **Alyssa Gamaldo**[3], **Ross Andel**[4], and **Christopher L. Edwards**[5]

1 *Department of Psychology and Neuroscience, Duke University*

2 *Duke University School of Medicine*

3 *Department of Psychology, North Carolina State University*

4 *School of Aging Studies, University of South Florida*

5 *Department of Psychiatry, Duke University Medical Center*

Abstract

We calculated concordance rates and heritability for cognitive impairment in 95 same-sexed pairs of African American twins from the Carolina African American Twin Study on Aging (CAATSA). The average age of the sample was 59.6 yrs (*SD* = 8.6 years, range 50–88 years) and 60% of the sample was female. The Telephone Interview for Cognitive Status (TICS) was used in the assessment of cognitive impairment. We lowered the cutoff for cognitive impairment based on our previous research with African American twins. Thirteen of the monozygotic (MZ) twins (30.2%) and 9 of the dizygotic (DZ) twins (17.3%) were cognitively impaired. The concordance rate was 72% for MZ and 45% for DZ. We found the heritability for cognitive impairment to be 54%. The study findings indicate that cognitive impairment is highly heritable, suggesting that genetics may play a relatively large role in the development of cognitive impairment in African American twins.

1. Introduction

The African American elderly population in the US is projected to increase by 131% by year 2030 [1]. There is growing interest in estimating who and how many within this population will be affected by cognitive impairment. The etiology of cognitive impairment has not been well studied in African Americans due, in part, to their lack of willingness to participate in research studies as well as the lack of ascertainment efforts to have them represented [2]. Previous research on European Americans suggests that there is a strong genetic influence on Alzheimer's Disease (AD) [3]. AD and other types of dementia are usually preceded by cognitive impairment. Therefore, the assessment of cognitive impairment is central to timely dementia diagnosis.

Several popular measures designed to assess cognitive impairment in dementia, including the Orientation-Memory-Concentration test [5], Storandt Battery [6], Iowa Battery [7], Mini-

Send Correspondence To: Keith E. Whitfield, Department of Psychology and Neuroscience, P.O. Box 90086, Duke University, Durham, NC 27708.

Mental State Examination (MMSE) [8], and the Kahn-Goldfarb Mental Status Questionnaire [9], have been found to have higher false positive rates in comparison to more in depth clinical diagnostic criteria such as the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) guidelines [10]. One of the major sources of inaccuracy stemmed from not taking race and educational levels into account [10]. There has been an effort to establish revised cutoffs to make more accurate assessments using established cognitive screeners. For example, Kiddoe et al. [11] compared prevalence of cognitive impairment in a sample of African American twin pairs when using the Telephone Interview of Cognitive Status (TICS; 12) as opposed to the Short Portable Mental Status Questionnaire (SPMSQ; 13), which has been found to be less biased toward African Americans than other cognitive tests [14], and found that reducing the cutoff from 30 to 27 may improve the specificity of the instrument in this population. The TICS has been used in a prior study to estimate concordance rates in community dwelling female twin pairs [15]. However, results showed very low incidence rates of cognitive impairment in this group and in addition, none of the pairs were found to have both twins affected.

In the present study, we examine the genetic and environmental proportions of variability in cognitive impairment by examining the concordance rates and heritability among older African American twins.

2. Methods

2.1. Sample

The participants were selected from the Carolina African American Twin Study of Aging (CAATSA) [16]. The CAATSA sample includes twin pairs, siblings and surviving members of non-intact twin pairs. The analysis was performed on 95 same-sexed pairs of African American twins who were 50 years of age and older. The participants were 43 monozygotic (MZ) and 52 dizygotic (DZ) male and female twin pairs. Birth records from North Carolina Register of Deeds Offices were used to identify participants for the CAATSA study. Details on the registry, sample ascertainment and variables can be found elsewhere [16].

Zygosity was established using a physical similarity questionnaire developed by Nichols and Bilbro [17]. This questionnaire uses physical similarity criteria to predict zygosity and has been found to be 93 percent accurate in diagnosing zygosity compared to genetic markers from blood [17].

2.2. Measures

Demographic variables included age (in years), gender, and education (in years). The average age of the population was 59.6 yrs (*SD*=8.6) and range of 50 – 88 yrs. Forty percent of the sample was male and the participants had completed an average of 12.9 years of education (*SD*=3.92).

The Telephone Interview of Cognitive Status (TICS) is a cognitive screening test that can be administered over the telephone [12]. It is highly related to the Mini Mental Status Examination (MMSE) (*r*=.94) which is the most commonly used measure of mental status. It is scored on a scale of 0 to 41, with individuals scoring below 30 considered to have cognitive impairment [12]. TICS has been shown to have high test-retest reliability (0.97) and inter-rater reliability (0.97), as well as sensitivity (92%) and specificity (100%) [12,20]. Using the SPMSQ, a test previously reported as having relatively good specificity for cognitive impairment in African Americans (9) as our gold standard, we found that applying a cut-off point of 27 points on the TICS provided a preferable balance between sensitivity (90%) and specificity (84%) than the

cut point of 30 [11]. This is likely due to unique characteristics of our sample such as African American ethnicity and relatively low education.

2.3. Procedures

Participants were contacted by the CAATSA twin registry team and an appointment was scheduled upon agreement to participate. Participants read and signed an informed consent form that was approved by both the Pennsylvania State University and the University of North Carolina institutional review boards. Participants completed a 2.5 hour interview in their home and received 40-dollars incentive for participation.

2.4. Analyses

The contribution of genetic and environmental influences was assessed by calculating concordance rates using the following formula:

According to established assumptions about genetic modeling [18,19], differences between people on a trait of interest, or phenotype, can be attributed to three sources of variation: (1) additive genetic variance (V_A), (2) variance due to common experiences shared by family members living together (V_C)(e.g., parental socioeconomic status), and (3) variance due to unique experiences specific to the individual and not shared by the family members (V_E)(e.g., work history in adulthood). More explicitly, the phenotypic variance (V_P) can be expressed as:

$$V_P = V_A + V_C + V_E$$

If each term in the above equation is divided by V_P, such that the phenotypic variance now equals unity, the following expression results:

$$1 = h^2 + c^2 + e^2,$$

where h^2 is heritability (proportion of variance in cognitive impairment across individuals attributable to genetic influences), c^2 is the proportion of variance attributable to shared environmental influences, and e^2 is the proportion of variance attributable to non-shared environmental influences. To establish the proportions of variance from the data, the following formulas were employed:

$$h^2 = 2(\text{cMZ} = \text{cDZ})$$
$$c^2 = (2 * \text{cDZ}) - \text{cMZ}$$
$$e^2 = 1.00 - (h^2 + c^2)$$

where cMZ represents the concordance rate for the monozygotic twin pairs and cDZ is the concordance rate for the dizygotic twin pairs. [18,19]

3. Results

Using a 27-point cut-off on TICS, we found a 37.2% (32/86) prevalence of cognitive impairment among individuals in the MZ group and 17.2% (30/104) in the DZ group. There was a significant difference in rates of prevalence between the groups ($\chi^2 = 4.842$, $p < .05$). The concordance rate for cognitive impairment between twin pairs was 72% for MZ (13 pairs/43 pairs) and 45% (9 pairs/52 pairs) for DZ pairs. Using the formulas described above, we found heritability for cognitive impairment to be 54% and the proportion of shared and non-shared environmental influences 18% and 28%, respectively.

4. Discussion

The goal of the study was to examine genetic and environmental influences on cognitive impairment in African American adults. We found high genetic contribution to cognitive impairment (54%) and individual variability in cognitive status. This is considerably more than the 30% heritability reported by Brandt et al. [20] or the 35% heritability reported by Reynolds et al. [21]. One possible explanation of these differences is that both previous studies had populations predominantly comprised of Caucasians while our sample was comprised entirely of African Americans. It may be that genetic influences play a greater role in cognitive impairment among African Americans compared to Caucasians. Alternatively, racial differences in education and literacy [22], which are a known to disadvantage African Americans on cognitive tests, may have led to a disproportionate number of false positives. However, our loosening of the cut-off score most likely accounted for this possibility.

Brandt et al. found that education accounted for most of the contribution of shared environmental influences on cognitive functioning, raising an interesting question regarding the possible role of education in heritability of cognitive impairment. Unfortunately, we were unable to properly test the possible impact of education on our results due to a limited sample size. The examination of identical twin pairs discordant for education would be useful in examining cognitive impairment in this population. Future research needs to be performed to elucidate the differences in our findings from those of others especially since research in this area is still growing.

Our sample was somewhat younger than samples used in previous similar studies. We included younger twins in our sample due to the possibility of accelerated cognitive aging among African Americans [23]. In addition, as only cross-sectional data were available, we were unable to control for previous levels of cognitive performance. Finally, we cannot be sure that cognitive impairment was correctly represented in all participants. We based the cutoff for cognitive impairment on our own research where we compared the TICS to a measure found to have relatively low racial bias, the SPMSQ [24]. However, more research is needed to establish criteria for cognitive impairment in this population. Regardless of these limitations, our results underscore the need for further research in factors underlying genetic contribution to cognitive impairment in African Americans.

In conclusion, we found high heritability for cognitive impairment in a sample of complete twin pairs from the Carolina African American Twin Study of Aging. Research is needed to assess whether genetic factors contribute disproportionately to cognitive impairment in African Americans compared to other ethnic groups.

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