Concordance Rates for Smoking among African-American Twins

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Objectives: Despite greater negative environmental influences such as lower socioeconomic status, less parental education, more single-parent households and urban dwelling, African Americans are less likely to begin smoking than European Americans. The goal of the current investigation was to examine the proportion of genetic and environmental influences on smoking in a sample of adult African-American twins.

Design: Birth records from North Carolina Register of Deeds Offices were used to identify participants for the Carolina African-American Twin Study of Aging (CAATSA). Participants completed an in-person interview that included measures of health status, cognition and psychosocial measures.

Participants: Data for the analysis come from 200 pairs of same-sex twins (97 identical pairs and 113 fraternal), with a mean age=46.9 years (SD=13.9) and 38% of the sample being men.

Results: Compared to previous research on smoking, our estimates are very similar with genetics, accounting for about 60% of the individual variance in current smoking. We did find that there was a significant amount of genetic variance in pack years but no shared environmental influences.

Conclusion: Similarity in proportions of genetic influences lead to larger questions about the genes involved in smoking among African Americans working in the same manner as in Caucasians or other groups. Additionally, this same question holds for the environmental variance. It is perhaps most likely that while the proportions of environmental variance are similar between groups that the actual source of variance (e.g., poverty, urban rural context, socioeconomic status, attitudes of family and friends) may differ when comparing ethnic groups.

Key words: twins ■ tobacco ■ genetics ■ heritability ■ environment

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BACKGROUND

Genetic susceptibility to cigarette smoking behaviors has been observed with respect to smoking initiation,[1,2] consumption,[3] dependence,[1,4-7] withdrawal and cessation.[4-8] Many candidate genes have been isolated and, in one case, functional polymorphisms of the gene encoding the cytochrome P450 2A6 enzyme have been found to influence susceptibility to habitual smoking via alterations in nicotine metabolism.[7,9-10] In addition, polymorphisms in dopaminergic receptor and transporter genes have been found to affect nicotine receptor quantity and function.[7,11-14] For example, the long (*L*) allele of the dopamine receptor D4 (DRD4) has been found to be associated with greater cravings and larger responses to smoking stimuli than receptors with the short allele (*S*).[7]

Reaffirming genetic influence, several studies[1-2,15-16] have found that concordance for smoking behaviors in monozygotic (MZ) twins as significantly higher than in dizygotic (DZ) twins. While these rates could be artificially inflated by interactive genetic x environmental effects, adoption studies,[17] which demonstrate greater concordance rates in MZ than DZ twins, appear to refute arguments associated with the significant potency of environmental factors.

On balance, smoking behavior is likely the additive effects of genetic (A), shared twin environment (C) and nonshared (E) environmental factors, however, in what proportions is not well understood. A meta-analysis of data from 12 twin studies with subjects from diverse age and geographic locations found that genetic factors

accounted for approximately 60% of the variance in smoking initiation while shared environment and nonshared environment each contributed roughly 20% of variance in initiation.[16] This study was the basis of recent studies that highlighted the importance of shared environment, especially as it relates to smoking initiation during middle-to-late adolescence, a time notably characterized by significant peer group influences.[2,18-19]

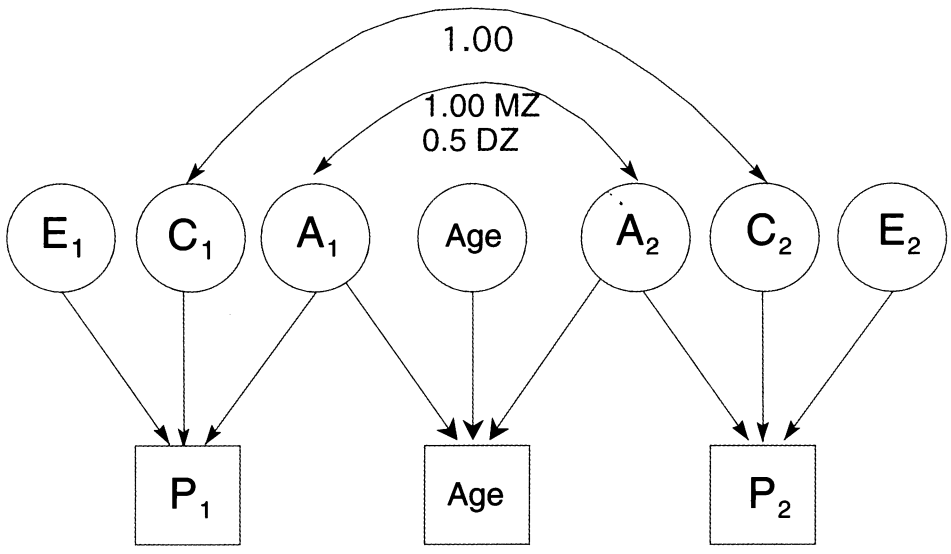
Both persistence of smoking and the development of nicotine dependence are also strongly influenced by genetic factors (~86%), with shared twin environment having nearly negligible effects.[6,16] However, and in consideration of the persistence of smoking behaviors, the degree of genetic susceptibility is known to be mediated by age.[1,19] Among younger-aged adolescents (12–15 years old) the relative risk of smoking for MZ and DZ twins was not found to differ significantly, suggesting that genetic factors may not have a major influence on smoking in this age group.[1,19] However, with older adolescents (16–20 years old), the relative risk of smoking when a cotwin smoked was much higher for MZ twins (mean: 12.1) than for DZ twins (mean: 3.0).[19] These findings indicate that additive genetic effects on smoking may increase with age during adolescence. In adult populations, the average concordance rates for smoking initiation is higher for MZ adult twins than for DZ adult twins (0.84 and 0.73, respectively).[1,16]

The severity of withdrawal symptoms has also been found to contribute to rates of failed smoking cessation.[4,8,20] In a study of Vietnam veteran male twins, the correlations for MZ twins for failed smoking cessation (0.52) and nicotine withdrawal (0.30) were that of DZ twin cessation (0.18) and withdrawal (0.16), suggesting an influence of additive genetics.[4] The best-fitting model for both failed cessation and severity of withdrawal symptoms included influences from additive genetic (A) and nonshared environmental effects (E). Under this model, genes (A) contributed to 29.7%, and nonshared environment (E) contributed to 70.3% of the variance in severity of withdrawal symptoms.[4] Similarly, the model for failed smoking cessation showed that genes contributed to 51%, and nonshared environment contributed to 49% of the variance in failed cessation.[4]

The previous studies involved samples of European Americans. Few if any studies have evaluated these genetic and environmental proportions of variability in African Americans. Although population prevalence data suggest that among adults ≥18 years of age the prevalence of smoking is almost identical for European Americans (men 25.8% and women 21.6%) and African Americans (men 26.1% and women 20.8%)[21], the sources of variability in African Americans have not been thoroughly evaluated. To our knowledge, only one unreplicated study has evaluated smoking patterns in African-American twins.[15] Adolescent African-American twins were found to smoke considerably less than twins of European and other ancestry (EOA). Despite greater negative environmental influences such as lower socioeconomic status, less parental education, more single-parent households and urban dwelling, African American females were less likely to begin smoking-than EOA twins.

Although comparative analyses across racially or ethnically classified social groups are valuable, the goal of the present analyses was to establish the influence of genetic factors on smoking among an adult African-American sample of twins. We examine the strength of genetic and environmental influences on smoking behavior in African Americans.

Figure 1. Structural equation model of twin analysis



METHODS

Sample

Analyses described in this study are based on the pairwise responses from 200 same-sex African-American twin pairs who participated in the Carolina African American Twins Study of Aging (CAATSA).[22] The sample consists of 97 MZ and 113 DZ twin pairs. Briefly, birth records from North Carolina Register of Deeds Offices were used to identify participants for the CAATSA study. Potential subjects were contacted by phone and asked to participate. Those who agreed participated in a personal interview that included measures of health status, cognition and psychosocial measures. Details on the registry and sample ascertainment can be found elsewhere.[22]

Zygosity was established using a physical similarity questionnaire. This questionnaire was derived from research that used physical similarity criteria to predict with 93% accuracy diagnoses and zygosity compared to genetic markers from blood.[23]

Measures

Smoking status. Cigarette smoking was assessed as part of a general health questionnaire. Subjects were asked if they smoked currently or if they had smoked in the past. If they currently smoked, they were also asked how long they had smoked and how much they smoked per day.

Pack years. Using responses from the smoking questionnaire, pack years were calculated by first multiplying the number of packs smoked per day multiplied by the number of years the subject had smoked, divided by 20 (number of cigarettes in a pack). The result is a variable that standardizes consumption.

Procedures

Participants were contacted from the CAATSA twin registry. Once they agreed to participate, they were scheduled a time for the interview. Participants read and signed an informed consent form that was approved by the Pennsylvania State University institutional review board and then completed a 2.5-hour interview in their home. Upon completion of the interview, participants received $40.

Analyses

The contribution of genetic and environmental influences was assessed by calculating concordance rates in the sample of twins. The concordance rates were calculated using the following formula:

$$\text{Concordance rate} = \frac{a}{a+b+c}$$

To establish heritability from the data, the following formula was employed:

$$2\,(\text{cMZ} - \text{cDZ})$$

where cMZ represents the concordance rate for the MZ twin pairs, and cDZ is the concordance rate for the DZ twin pairs.[24,25]

It is assumed in the basic quantitative genetic model that differences among 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 VP, such that the phenotypic variance now equals unity, the following expression results:

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

where h^2 is heritability, or the proportion of the phenotypic variance attributable to additive genetic variance, c^2 is the proportion of variance attributable to shared environmental influences, and e^2 is the proportion of variance attributable to nonshared environmental influences. Figure 1 depicts a structural equation model that consists of genetic, shared environmental and nonshared environmental influences for a pair of twins. P_1 and P_2 are the phenotypic scores for twin 1 and twin 2, and A_1 and A_2 are the latent additive genotypic values for the pair of twins. S_1 and S_2 represent the environment shared by a twin pair, and NS_1 and NS_2 represent environmental influences specific to each twin. Designation of twins as twin 1 or twin 2 was based on random assignment.

Although the components of variance are unobserved or latent variables in quantitative genetic analyses, they nonetheless can be estimated from MZ and DZ twin correlations and variances. The correlation between genotypes in MZ twin pairs is 1.0, since they are genetically identical, while the correlation between genotypic values in DZ twins is 0.5, since they share, on average, half of the segregating alleles. By definition, both MZ and DZ pairs are assumed to be influenced by their shared envi-

Table 1. Descriptive statistics

	Men	Women
Current smokers	58 (24.4%)	63 (18.9%)
Past smokers	80 (35.1%)	79 (23.7%)
Nonsmokers	90 (39.5%)	191 (57.1%)

Note: % are for within gender

ronments to the same extent, thus the correlation between S_1 and S_2 is constrained to equal 1.0. Although MZ twins may have been treated more alike than DZ twins, the model assumes that, on average, this differential treatment will not significantly affect estimates of shared environmental influences.[26] The expected correlation between twin 1 and twin 2 on a single phenotype is then a function of the genes and environment that they share and can be derived by aid of the path diagram. So, the expected correlations are $h^2 + c^2$ for MZ twin pairs and $1/2\ h^2 + c^2$ for DZ twin pairs.

Comparisons of the full model to reduced models, which have elements of the full model constrained to equal 0, are reported and represented as a χ^2 ($\chi^2_{Reduced} - \chi^2_{Full} = \chi^2_{\Delta}$), whose degree of freedom are calculated as $df_{Reduced} - df_{Full} = df_{\Delta}$).[27] Models were fit using Lisrel VII statistical modeling package.[28]

RESULTS

Descriptive Analysis

In the sample, twins had a mean age of 46.9 years (SD =13.9), and 38% (39% is reported in the abstract) of the sample were men. About 22% of the sample smoked cigarettes, 28.3% reported they were former smokers but were not smokers at the current time, and 50.1% were not smokers. As can be seen in Table 1, nonsmokers are in greater proportion among women (57%) compared to men (39.5%). The mean number of years of smoking was 23.7 years. The average age participants initiated smoking was 22.9 years (SD=8.4). The mean number of pack years was 0.67 (SD=0.82) for those who were current smokers. We also conducted a linear regression to assess the impact of age and gender on pack years and found that age (ß=0.135, $p<0.005$) but not gender (ß=-0.085, $p>0.06$).

Quantitative Genetic Analyses

We calculated the concordance rates for identical or MZ twins pairs, and for fraternal or DZ twin pairs separately and then calculated the ratio of MZ concordance rates to DZ rates to examine the relative genetic risk. We calculated the concordance rates and ratios for two comparisons: nonsmokers compared to current smoker,s and nonsmokers compared to subjects who ever reported smoking (current smokers and quitters).

The comparison of nonsmokers to current smokers resulted in concordance rates of 65% for MZ twins and 25% for DZ twins. This resulted in a 2.50 ratio of MZ-to-DZ concordance, and a heritability of 80%. The comparison of nonsmokers to subjects who ever reported smoking resulted in concordance rates of 43% for MZ twins and 15% for DZ twins with a concordance ratio of 2.88 and a heritability of 56%. These results suggest that there is a statistically significant genetic influence for smoking among African-American twins.

Pack Years

The variance decomposition estimate of pack years resulted in a significant amount of additive genetic variance (A) (43%). As can be seen in Table 2, there was a significant change in the fit of the model when A was removed. There were no shared environmental influences (C) found, but 57% of the variance was due to nonshared environmental influences (E) (Table 3). Age was also found to be a significant predictor in the model, accounting for roughly 3% of the variance.

DISCUSSION

The goal of the present study was to examine genetic and environmental influences on smoking behavior in African-American adults. Most respondents began smoking in adolescence and young adulthood, but more than a quarter of persons interviewed had quit smoking

Table 2. Model fitting results

Model	χ^2_{Full}	df_{Full}	p	GFI	RMR	χ^2_{Δ}	df_{Δ}	p	GFI	RMR
Full	1.90	7	0.965	0.993	0.039					
Drop age	1.90	7	0.965	0.993	0.039	9.95	2	0.05	0.956	0.117
Drop C	1.90	7	0.965	0.993	0.039	1.90	1	NS	0.993	0.039
Drop A	1.90	7	0.965	0.993	0.039	5.90	1	0.05	0.981	0.061

GFI: Goodness of Fit Index; RMR: Root Mean Square Residual

Table 3. Parameter estimates and proportions of variance

Variance Components	Parameter Estimates	Proportions of Variance
Age	0.16	0.03
Additive genetic	0.64	0.41
Shared environment	0.00	0.00
Nonshared environment	0.75	0.56

by the time of evaluation. Although the sample was limited to twins born in North Carolina, rates of smoking and general tobacco use behaviors were quite similar to national studies of African Americans.[29,30] We found that genetics accounted for about 60% of the individual variance in current smoking behavior. We also found that there was a statistically significant amount of genetic variance in pack years and also failed to demonstrate significance in shared environmental influences.

Consistent with previous research on smoking and genetic influences, our results demonstrate that for "ever having smoked" the heritability was 43% and the nonshared environmental influences were 57%. Our findings with African Americans did not differ from the results of similar studies in Caucasians.[16] However, we minimize comparison because of potential differences in ascertainment of the sample as well as potential differences in relevant environment factors not controlled in making such comparisons.[31]

Some studies have alluded to genetic differences in the likelihood of racially classified social groups to quit smoking. While the results from this study suggest that the proportions of environmental variance may be similar between groups, we recognize that the actual source of variance (e.g., friends, neighborhood, socioeconomic status) may differ.[32] While there may be very few meaningful differences in the genes that determine or influence smoking behavior between racially classified social groups—and particularly coding regions of genes—there is a significant value in understanding phenotypic sequelae before making effective comparisons between populations.

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