Genetic and Environmental Influences on Forced Expiratory Volume in African Americans: The Carolina African-American Twin Study of Aging

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Objectives: Previous research found measures of pulmonary functioning to be strong predictors of cognitive functioning and mortality; however, there is considerable individual variability in performance on these measures. In the present analyses, the relative contribution of genetic and environmental influences to variability in average peak expiratory flow rate (APEFR) are examined 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, which 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 with 39% of the sample being men.

Results: Phenotypic correlations between APEFR, age, gender, height, and cigarette consumption (measured in pack years), were all significant, ranging from −.63 to .43. After the affects of age, gender, height, and pack years were partialled out of APEFR, quantitative genetic analyses were conducted on the residuals. Model fitting demonstrated that variance in APEFR was accounted for by shared environmental effects (30%), genetic effects (14%), and non-shared environmental effects (56%).

Conclusion: These results are discussed in relation to previous research conducted in other countries, and the importance of a complex systems approach to explanations of the impact of genes on central indices of health, such as APEFR. (*Ethn Dis*. 2004;14:206–211.)

Key Words: African Americans, Average Peak Expiratory Flow Rate, Pulmonary Function, Quantitative Genetics, Twins

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Introduction

Epidemiological studies have investigated the decline in spirometry measures as an indicator of lung function,[1] chronic airways obstructive disease,[2] the presence and course of asthma,[3] and as a measure of the effects of air pollution.[4] Spirometry measures have been used in various forms to assess changes in pulmonary functioning related to chronic obstructive pulmonary disease (COPD). Chronic obstructive pulmonary disease (COPD) is the only indicator among the top 10 age-adjusted causes of mortality that has been increasing over the past 30 years.[5] There is still a great dearth in our understanding of why some, and not others, are predisposed to COPD. Previous research has also demonstrated that measures of pulmonary function are useful predictors of remaining life in older adults.[6,7]

Racial differences in lung function as measured by spirometry have been well demonstrated in the literature. Even accounting for differences in height between African Americans and Caucasians does not eliminate the differences observed between these 2 ethnic groups.[8] While there are racial differences in spirometry levels favoring Caucasians, there is also evidence that the rate of spirometry level decline with age is less among African Americans.[9]

Decline in forced expiratory volume has been observed during the middle part of the third decade of life.[7] While population-based studies provide insight into the "normal" rate of decline in forced expiratory volume, there is considerable individual variability in these rates. To better understand the risk factors for poor expiratory volume in late life, it is important to understand the biological, as well as environmental, contributions to individual variation in lung function.

Relatively few studies have focused on sources of individual differences in forced expiratory volume. Quantitative genetics is a useful approach for understanding sources of individual differences. Utilizing this approach, sources of variation are decomposed into genetic and environmental components.[10,11] Although there is considerable inter-individual variability in level,[1] and rate of change in pulmonary functioning,[9] very few studies have assessed the genetic and environmental sources of this variability. In an analysis of the influence of genetic and environmental factors on pulmonary functioning in Swedish twins, McClearn et al[12] found substantial influence of genetic factors in middle and late adulthood, using average peak expiratory flow rate (APEFR) as the dependent variable. Average peak expiratory flow rate is a common and simple to use assessment of pulmonary functioning, which is calculated from the mean of 3 blows on a flow rate meter. Researchers found that 57% of the individual variation (in the middle adulthood group) was due to genetic factors, and the remainder of the variance was due to non-shared environmental factors. Whitfield et al[13] found that after the effects of age, gender, height, and smoking were partialled out of APEFR, shared environmental effects accounted for 47% of the variance in APEFR, and genetic effects were responsible for about 28% of the variance. Whitfield et al[13] discuss the differences between the Russian and Swedish studies, concluding that these were likely due to environmental differences between the countries. The comparison demon-

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strates that the genetic and environmental estimates generated from twin studies are population-specific.

Twin studies of American Caucasians have found relatively consistent and significant genetic influence on APEFR,[14–16] with heritabilities as high as .77. There are no previous studies that have produced heritability estimates for African-American adults.

The purpose of this article is to examine the genetic and environmental influences on average peak expiratory flow rate by analyzing data from a sample of adult African Americans. The data come from The Carolina African American Twin Study of Aging (CAATSA), one of the only studies of adult African-American twins, which provides a unique opportunity to examine how genetic and environmental influences work in concert to create individual variability in a relatively unstudied population. It also provides an opportunity to examine potential areas of discovery of environmental influences on health.

One could argue that the environment for African Americans consists of stressors and social influences that are not observed at the same level as among Caucasian populations. One could further argue that the health disparities observed for African Americans arises from inequities in the environment of African Americans. Cultural influences from these unique perspectives represent a force with the potential force to produce group differences in the proportions of sources variation identified in quantitative genetic studies.[17] The variation in environment influences on APEFR is hypothesized to result in lower heritability estimates for African Americans, as compared to those found in previous studies of Caucasians.

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 CAATSA. The sample consisted of 97 monozygotic and 113 dizygotic twin pairs, with a mean age=46.9 years (SD=13.9), with 38% of the sample being men. Details on the registry and sample ascertainment can be found elsewhere.[18] 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 an in-person interview, which included measures of health status, cognition, and psychosocial measures.

Zygosity was established using a physical similarity questionnaire. This questionnaire was derived from Nichols and Bilbro's[19] research, which used physical similarity criteria to predict with 93% accuracy diagnoses and zygosity compared to genetic markers from blood.

Apparatus and Measures

Average Peak Expiratory Flow Rate (APEFR)

Pulmonary function was measured using the Mini-Wright peak flow meter, which assessed peak expiratory flow rate.[20] Subjects covered the end of the tube of the peak flow meter with their lips and blew as hard as possible, after taking a deep breath. This process was completed while standing. The variable APEFR was the average of 3 trials using the peak flow meter. There was a 30-second interval between blows.

Covariates

In addition to demographic variables like gender and age, there are 2 covariates that have been included in most of the estimates of APEFR: height and cigarette consumption, as measured by pack years.

Height

Height was ascertained with the subject barefoot and standing straight with heels against a wall in the subject's home. The interviewer placed a pencil or ruler flat on top of the subject's head with one end touching the wall. Using a tape measure, the interviewer then measured the distance from that point to the floor. Height was recorded to the nearest 8th of an inch.

Pack Year

Smoking was assessed as part of the questionnaire. Subjects were asked if they smoked, how long they had smoked, and how much they smoked per day. Using these responses, pack years was calculated by first multiplying the number of packs smoked per day by the number of days in a year (365).This product was then multiplied by the number of years the subject had smoked. The result is a variable that standardizes consumption.

Procedures

Participants were contacted from the CAATSA twin registry. Once they agreed to participate, an interview time was scheduled. Participants read and signed an informed consent, then completed a 2.5 hour interview in their homes. The respondents received $40.00 for their participation.

Analyses

First, an examination of the contribution of age, height, pack years, and gender to variation in APEFR was con-

ducted. Then, the impact of variables was residualized from the APEFR score. These particular measures were used because they have been shown to be significantly related to APEFR performance, or have been residualized in previous studies.[12]

Next we assessed the genetic and environmental influences on APEFR. It is assumed in the basic quantitative genetic model that differences among people on a trait of interest, or phenotype, can be attributed to 3 sources of variation: 1) additive genetic variance (V_A); 2) variance due to common experiences shared by family members living together (V_C) (eg, parental socioeconomic status); and 3) variance due to unique experiences specific to the individual and not shared by the family members (V_E) (eg, 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, 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 non-shared environmental influences. Figure 1 depicts a structural model that consists of genetic, shared environmental, and non-shared environmental influences for a pair of twins. P_1 and P_2 are the phenotypic scores for Twin 1 and Twin 2, and G_1 and G_2 are the latent additive genotypic values for the pair of twins. C_1 and C_2 represent the environment shared by a twin pair, and E_1 and E_2 represent environmental influences specific to each twin. Designation of twins as Twin 1 or 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 monozygotic (MZ) and dizygotic (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 .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 environments to the same extent; therefore, the correlation between C_1 and C_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.[21] 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. The expected correlations are $h^2 + c^2$ for MZ twin pairs, and $1/2h^2 + c^2$ for DZ twin pairs.

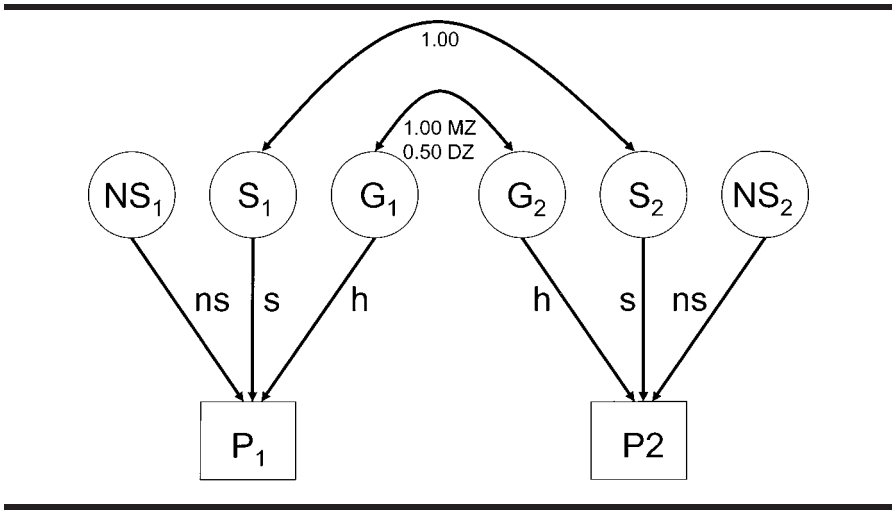

Fig 1. Structural Equation Model of Genetic and Environmental Influences. G represents the additive genetic influences, C represents the shared environmental influences and E represents the non-shared environmental influences

Comparisons of the full model to reduced models, which have elements of the full model constrained to equal zero, are reported and represented as a χ^2_Δ ($\chi^2_{Reduced} - \chi^2_{Full} = \chi^2_\Delta$ whose degree of freedom are calculated as; $df_{Reduced} - df_{Full} = df_\Delta$) (for a review of these procedures, see Neale & Cardon[22]).

Models were fitted using Lisrel VII statistical modeling package (Jöreskog & Sörbom[23]). Prior to performing the modeling, we calculated the phenotypic correlation between twins on the measure, and the interclass correlations for MZ and DZ twin, separately.

RESULTS

All covariates were related to APEFR (see Table 1). The correlations between APEFR and age, gender, height, and pack years, were all significant and in the expected direction. Height was positively related to APEFR, suggesting that taller subjects had greater APEFR. All the other variables were negatively associated, suggesting that APEFR decreased with increased age, cigarette consumption, and was lower for women than men. Figure 2 shows the mean APEFR by 10-year age groups. As demonstrated, there is a consistent and steady decline in mean APEFR after the age of 39 years.

Linear Regression

To examine the predictive ability of the covariates on mean APEFR, linear

Table 1. Phenotypic correlations

	APEFR	Age	Gender	Height	Pack Years
APEFR	1.00				
Age	−0.42	1.00			
Gender	−0.34	−0.01*	1.00		
Height	0.40	−0.15	−0.62	1.00	
Pack years	−0.10	−0.14	−0.10	0.07*	1.00

All correlations were significant ($P<.05$), except where noted.
* Denotes $P<.10$.

Table 2. Linear regression results

Variable	Standardized Coefficients	$P<$
Age	−.379	.001
Gender	−.231	.001
Height	.197	.001
Pack years	−.075	.049

Adjusted $R^2=.32$

regression analyses were conducted. Mean APEFR was used as the dependent variable, and age, gender, height, and cigarette consumption (pack years), were included as independent variables. The model accounted for 32% of the variance in mean APEFR. Each of the variables were significant predictors, as shown in Table 2. The results of the linear regression and the associations found suggest that these variables are important in understanding individual variability in mean APEFR among the sample of African-American twins.

Quantitative Genetic Analyses

To conduct quantitative genetic analyses, the twin data were paired based on classification as MZ or DZ sibling pairs. Table 3 shows the phenotypic correlation between APEFR for all twin 1 and twin 2 combinations, and the correlations by zygosity. The magnitude of this correlation indicates the degree of similarity between pairs of twins. The intraclass correlations (also in Table 3) show the relative strength of the genetic, shared environmental, and nonshared environmental influences on APEFR. While the MZ correlation is greater than the DZ correlation (implying genetic influence), the similarity in the magnitude of the correlations indicates substantial shared environmental influences.

Quantitative genetic analyses were used to assess the relative influence of genetic and environmental factors on APEFR performance. Table 4 contains the chi-square values, chi-square changes, and significance tests for the full and reduced models.

The estimates of the proportions of variance for genetic, shared environmental, and nonshared environmental influences are summarized in Table 5.

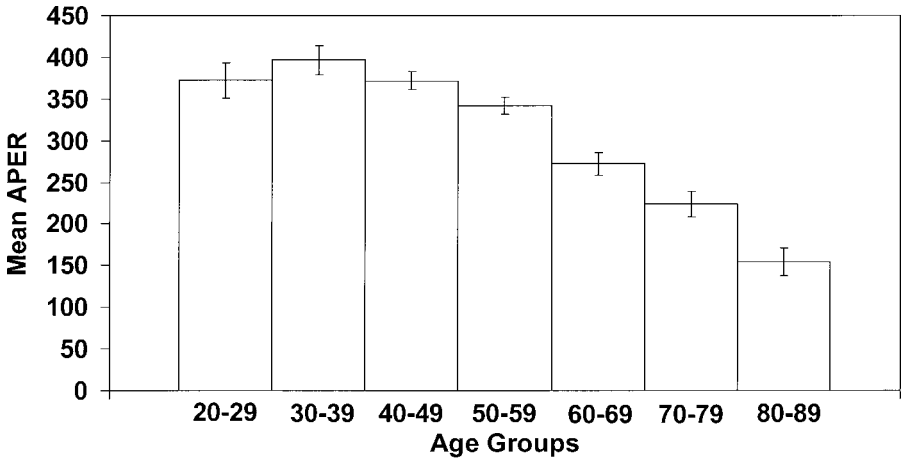

Fig 2. Average peak expiratory flow rate (APEFR) by age group

The significance of the genetic and shared environmental components were tested individually by dropping each path from the model, and assessing whether the change in the Chi-square was significant. Heritability (the proportion of variance due to genetic influences) was small, accounting for 14% of the variance on APEFR. Genetic influences could be dropped from the model without a significant decrease in fit (see Table 4).

Shared environmental influences were substantial, accounting for 30% of the variance on APEFR. After accounting for the non-significant genetic effect, the shared environmental influences could not be dropped from the model without a significant decrease in fit (see Table 4). Non-shared environmental influences accounted for the remaining 56% of variance.

CONCLUSIONS

While identifying significant genetic factors as sources of individual variation is intriguing, environmental sources of individual variation must be accounted for to better understand how genetic mechanisms are evidenced or evoked. One way to understand how the contribution of environmental influences may affect quantitative genetic estimates of sources of individual differences is to conduct estimates of the genetic and environmental influences from different populations. Therein, cultural (ie, environmental) influences can be examined.

Results from this analysis of African-American twins differ from those found

Table 3. Cross-twin and intraclass correlations corrected for age, height, gender, and pack years

	Cross-Twin Correlation
	APEFR TWIN 1
APEFR TWIN 2	r=.40*
MZ TWINS	
	APEFR TWIN 1
APEFR TWIN 2	r=.44*
DZ TWINS	
	APEFR TWIN 1
APEFR TWIN 2	r=.37*

* Correlation is significant (P<.0001), phenotypic and intraclass correlations corrected for age, height, gender, and pack years.

Table 5. Genetic and environmental proportions of variance

Components of Variance	Standardized Coefficients	Proportions of Variance
Genetic	.374	14%
Shared environment	.548	30%
Non-shared environment	.748	56%

Proportions of variance are calculated as the square of the standardized coefficients.

in American and European studies, but resemble those found in a sample of Russian twins. The relationships found between APEFR and age, gender, cigarette consumption, and height, were similar to those found by previous studies. As in previous research on these variables in general, each was found to be a predictor of individual variability in mean APEFR.

While the contributions of these variables was similar to those demonstrated by previous research, differences were observed in the distribution of genetic and environmental sources of individual differences. Studies of Europeans (Swedish) and European Americans observed significant contributions of genetic influence to individual variance in mean APEFR.[12,14–16] In the present study, and in a study of Russian twins, only small and nonsignificant proportions of genetic influence were observed.

Assuming that there are not substantial genetic differences at the population level between ethnic groups, the difference in results among these studies is due to environmental variability. While there could be allelic differences between the populations, due to the complexity of this phenotype, there are likely to be multiple genes involved, and that the probability of allelic differences across multiple sites that affect this phenotype in a significant manner is probabilistically low.

There are many potential hypotheses as to how the contextual and situational factors could influence genetic and environmental estimates, such that African-American twins more closely resemble Russian twins than European-American twins. The most simple assumption is that social and political constraints and oppression affect twin similarity such that dizygotic twins are more similar than expected from a genetic explanation. In other words, the variability found in contextual gradients of environmental forces substantially affects the phenotype of interest, such that the genetic effects are suppressed. One interesting difference between the Russian and African-American sampled is the magnitude of the average APEFR, and interclass twin correlations between the populations. The study of Russian twins had larger phenotypic correlations (r=0.70) and mean APEFR (415.40 mL) compared to the African-American sample (r=0.44, mean=329.29 mL). The specific contextual or situational factors that contribute to cultural differences in APEFR need to be identified and investigated.

In conclusion, the present analyses indicate that shared environmental effects play a more significant role in mean APEFR for African-American twins than has been observed in studies from other countries. This analysis contributes to the growing evidence regarding the influence of culture on genetic

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Table 4. Structural equation modeling results

MODEL	χ^2	*P*	*df*	χ^2 Change*	*df* Change
1. Full model	0.00	1.00	3		
2. No G	0.25	.993	4	0.25	1
3. No C	2.76	.599	4	2.76†	1
4. No C or G	33.64	.000	5	33.64‡	2

* Change in χ^2 compared to full model.
† Denotes a significant change in χ^2 at P<.10 level.
‡ Denotes a significant change in χ^2 at P<.01 level.

and environmental estimates. These findings also demonstrate that sources of individual differences may not be static across cultures, and that further investigation of the environmental mediation of estimates of genetic and environmental influences is warranted. Investigations of health differentials across ethnic groups, solely on the basis of genetic differences, will not yield accurate identification of the mechanisms responsible for health disparities. Attempting to account for the differential health burden ethnic minorities experience by investigating genetic differences seems to go against probability, given that there are small genetic differences across racial groups and variability within each group. The role of genetic influences, however, cannot be completely dismissed. The potential role genes play in creating health differentials requires further explanation. It is not the fact that genes define individuals from different ethnic or cultural groups that is key to the elucidation of health differentials per se. Instead, describing health differentials as arising from insults to a complex system represented by the interaction between genes and environments which creates excess burden of chronic illness and disease within some groups is a more accurate perspective.

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