Genetic and Environmental Influences on Blood Pressure and Pulse Pressure Among Adult African Americans

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Objective: The purpose of the present study was to identify sources of variability for systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure (PP) in a sample of adult African-American twins.

Design: The classic twin design was employed to examine genetic and environmental sources of variance in the outcome measures of interest.

Participants: Participants were 143 (71 MZ and 72 DZ) same-sex, intact twin pairs (mean age=49.87 years; SD 13.62), who took part in the Carolina African-American Twin Study of Aging (CAATSA).

Main Outcome Measures: Outcome measures of interest included SBP and DBP, and PP.

Results: For older twins, heritabilities were .52 for SBP, .36 for DBP, and .14 for PP. However, for younger twins, heritabilities were .44 for SBP, .27 for DBP, but no genetic influence on PP was observed.

Conclusion: The results indicate that genetic factors are a significant source of variance in hemodynamic indices, and also suggest that, with advancing age, genetic factors play an increasing role in determining blood pressure and PP in this population. (*Ethn Dis*. 2003;13: 193–199)

Key Words: African American, Twins, Aging, Pulse Pressure, Genetics, Environment, Heritability, Blood Pressure

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Introduction

One of the most critical health disparities experienced by African Americans as a group is the incidence of hypertension. African Americans have one of the highest rates of hypertension in the world,[1] with an estimated prevalence rate 2 times that of Caucasians.[2] This disease affects approximately 65% of African-American elders between the ages of 65 and 74 years, and is predictive of functional decline.[3]

Several theories have been proposed to account for the disparity in rates of hypertension. Some theories have suggested that genetic factors related to sodium retention are dominant in determining blood pressure among African Americans.[4,5] In contrast, other theories posit that environmental factors, such as racism,[6,7] or socioeconomic stress,[8] are dominant influences affecting blood pressure among African Americans. However, few studies have employed the twin or family design to address the relative contribution of genetic and environmental factors in determining blood pressure among African Americans.[9–13]

Previously, twin and family studies have been employed to estimate the heritability of blood pressure among Caucasian populations.[14] The results of these studies demonstrate that, among Caucasians, heritability estimates range from .44 to .64 for systolic blood pressure (SBP), and .34 to .73 for diastolic blood pressure (DBP).[15–17]

Other researchers have used the classic twin design to examine heritabilities of blood pressure and cardiovascular disease indices among both African descendants in Barbados, and African Americans.[10,11] The findings of these studies indicate that among African Americans and African descendants, genetic factors are a significant source of variability in SBP and left ventricular mass. The results were heritability estimates for SBP of .04 for the entire sample, and .70 for the male twin pairs from Barbados.[10]

Earlier studies have focused on understanding sources of variance in SBP and DBP, because of their predictive relationship to cardiovascular disease.[18–20] Pulse pressure (PP) is another hemodynamic index that has been demonstrated to have important implications for cardiovascular disease. For example, recent findings indicate that PP is a reliable predictor of cardiovascular morbidity and mortality, particularly for older adults.[19,21–23] Few data sources are available on genetic or environmental causes of variance for PP among African-American adults.

Researchers have noted that sample characteristics, such as age, gender, or ethnicity, have been shown to affect heritabilities.[14,17] To date, however, the few studies that utilized the twin design to explore the relative contribution of genetic and environmental factors to hemodynamic indices among African Americans were conducted with small numbers of twin pairs, and only assessed SBP.

The current study represents an important extension of this previous work, and includes a larger number of twin pairs, which allows for better, more stable estimates of genetic and environmental influences. The present study also includes measures of DBP, and PP, in addition to SBP. In addition, the current study is the first (to our knowledge)

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to estimate sources of individual variance for PP in an African-American sample. Finally, the present study employs model fitting to test the significance of parameter estimates for genetic and environmental components of variance for SBP, DBP, and PP.

METHOD

Sample

The sample for the analysis consisted of 143 same-sex African-American twin pairs who participated in the Carolina African-American Twins Study of Aging (CAATSA). Birth records from North Carolina registries were used to identify participants for the CAATSA study. Details on the sample can be found elsewhere.[24] The sample consisted of 71 monozygotic (26 male-male and 45 female-female) and 72 dizygotic (27 male-male and 45 female-female) twin pairs. In-person interviews were conducted, and included health status and psychosocial measures.

Zygosity for the present study was established using a physical similarity questionnaire[25] derived from physical similarity criteria established by research by Nichols and Bilbro.[25] In their study, physical similarity criteria were used to predict zygosity with 93% accuracy, compared to genetic markers from blood.[25]

Measures

Blood Pressure

Blood pressure was taken by using an oscillometric automated device (A & D model UA-767; Milpitas, Calif). Three measurements were taken with the subject in a sitting position, from the same arm, using an appropriately sized cuff,[26] and the average SBP and DBP values were used in the analysis.

Pulse Pressure

PP was calculated for each subject by subtracting the average sitting DBP value from the average sitting SBP value.

Antihypertension Medication Use

The status of antihypertensive medication use was ascertained from subjects' self-report.

Procedures

Blood pressure measurements were taken at the mid-point of the 2.5 hour interview, following a 5-minute rest period, and to allow time for the subject to become acclimated to the interviewer, in order to reduce arousal and anxiety.[26] The rest period was introduced to attenuate any minor psychological stress that may have been produced during the interview. The blood pressure cuff was placed on the participant's bare arm. The measurements lasted approximately 5 minutes and were taken while the subject sat upright in a comfortable chair.

Interviews were scheduled and took place during the morning hours of 9AM–11AM, whenever possible. However, interviews were performed at the participants' convenience, resulting in some variability in interview times (within and across twin pairs).

Statistical Analyses

Analyses of the hemodynamic variables included descriptive statistics, linear regressions, and quantitative genetic analyses. Age, gender, and medication may affect BP levels, and have been examined in twins elsewhere.[17] Multiple linear regressions were used to examine the contribution of these factors to individual variability in the hemodynamic indices. Intra-class correlations were used to estimate the genetic and environmental (shared and non-shared) contributions to individual variability.[27] The results of these analyses were used to inform the quantitative genetic analyses.

Quantitative Genetic Analysis

Quantitative genetic designs frequently take the form of comparisons between identical, or monozygotic (MZ), and same-sex fraternal, or dizygotic (DZ), twin pairs: the "classic twin study." These types of designs assume MZ twin pairs share 100% of their segregating genes and DZ twin pairs share 50%, on average. Operating under this strong assumption, data from twin pairs are used to calculate the heritability of a trait. Heritability is considered the proportion of phenotypic variance due to additive genetic variation. Additive genetic variation is the sum of the effects from genes influencing a trait. A simple and widely used method for estimating heritability is to calculate twice the difference between the intra-class correlations of MZ and DZ twin pairs (for the calculation of intra-class correlations see reference 28).

Using these same intra-class correlations, environmental effects are partitioned into those that are common (shared) or unique (non-shared) (see reference 28). Common shared environmental variation is the phenotypic variation due to the subjects living in the same family, thus sharing aspects of a particular environment.[28] The formula used to calculate this proportion of variance is twice the DZ correlation minus the MZ correlation. Unique environmental variation is the component of phenotypic variance that can be attributed to environmental factors not shared by family members, which are unique to the individual. This component of variation is the remainder of the

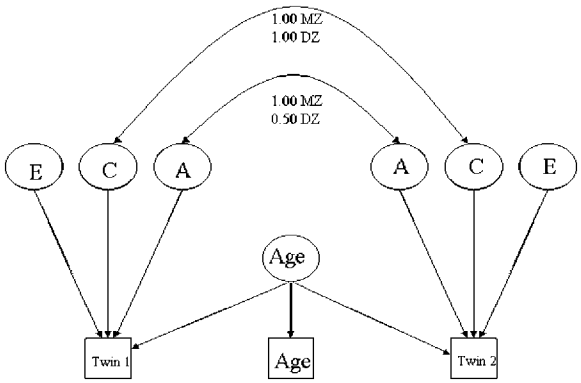

Fig 1. This is a pictorial representation of the age regression model used for the Quantitative Genetic Analysis. A represents additive genetic influences, C represents common environmental influences, and E represents unique environmental influences. Expected intraclass correlations for additive genetic influence for MZ and DZ twin pairs are 1.00 and .50 respectively; expected intraclass correlations for common environmental influence are 1.0 for both MZ and DZ twin pairs

variance after shared and additive genetic variance has been estimated.

Age

To evaluate the impact age may have on estimates of genetic and environmental influences, we separated the sample into young and old age groups, based on the mean age of the total sample. The age groups consisted of: a younger adult group (≤49 years of age; *N*=134) and an older adult group (>49 years of age; *N*=152). MZ and DZ twins did not differ significantly on age.

Figure 1 provides an example of an age regression twin model. The analyses will use this mode to estimate additive genetic, common and shared environmental components, as well as to determine the contribution of age, for the SBP, DBP, and PP.

RESULTS

Sample Characteristics

Descriptive statistics for the sample are presented in Table 1. The mean age of the subjects was 49.87 years (SD=13.62). In Table 2, the average blood pressures are presented by age groups, gender, and antihypertensive medication status. The results show that subjects who were using antihypertensive medications had higher SBP and DBP, and PP, compared to those who were not. The only exception to this pattern was that older women taking antihypertensive medication had lower DBP compared to those who were unmedicated.

Table 3 shows the results of the regression analysis. As expected, age was a significant predictor of SBP and PP. In addition, medication use was also a significant predictor of SBP. However, neither gender nor medication use were significant predictors of SBP or PP values.

Intra-class Correlations

Table 4 shows the intra-class correlation coefficients by zygosity group for the entire sample, and separately by age group. The correlation coefficients were uniformly higher for MZ twins, compared to DZ twins, on measures of systolic and diastolic blood pressure. Among the older age group, MZ twins had correlation coefficients more than twice those of DZ twins. This differential in correlations suggests a dominance effect on blood pressure. However, a similar finding may result from epistasis, or a large shared environmental influence.

Table 4 also shows the intra-class correlation coefficients by zygosity group for the entire sample, and separately by age group, after removing the linear effect of antihypertensive medication. Comparisons of intra-class correlation coefficients for SBP, DBP, and PP, with and without adjustment for antihypertensive medication, revealed a general decrease, with DZs experiencing the greatest differential after adjustment. A similar trend occurred for SBP and DBP across both younger and older age groups, with the younger DZs experiencing the greatest decrease in similarity once medication was taken into account. For PP however, there was a slight increase in the intra-class correlation for younger twins, and a decrease for older twin pairs.

Quantitative Genetic Results

The comparison of intra-class correlations, with and without correction for antihypertensive medication, revealed some differences. As a result, the subsequent model-fitting estimates were calculated for the entire sample, with a correction for antihypertensive medication.

Table 1. Descriptive statistics

	MZ	DZ	Total
N	142	144	286
Age	49.76 (15.19)	49.97 (11.92)	49.87 (13.62)
Gender (% male)	36.6	37.5	37.1

Note: standard deviations in parentheses.
MZ=monozygotic twins; DZ=dizygotic twins.

Table 2. Average blood pressure by age group, gender, and medication status

	No Med				Med			
	Men		Women		Men		Women	
	Younger	Older	Younger	Older	Younger	Older	Younger	Older
N	35	26	77	43	7	38	15	45
Sitting SBP	131.19	136.62	121.31	136.17	135.05	142.39	140.33	137.53
	(15.12)	(16.03)	(15.29)	(20.84)	(6.96)	(16.24)	(18.81)	(18.56)
Sitting DBP	81.59	81.86	77.14	83.49	90.43	84.37	89.58	80.39
	(14.01)	(10.08)	(10.64)	(13.51)	(7.17)	(9.93)	(11.04)	(12.13)
PP	49.60	54.76	44.17	52.68	44.62	58.02	50.76	57.133
	(9.92)	(13.58)	(10.89)	(14.38)	(5.87)	(12.59)	(11.39)	(16.16)
% Hypertensive	45.8	57.7	24.7	60.5	100	100	100	100

Note: standard deviations in parentheses. Hypertension is defined as a SBP >140 mm Hg, or a DBP >90 mm Hg, or antihypertensive medication use.

The results of the model fitting are presented in Table 5, which shows the estimates for the percentages of variances obtained from structural equation modeling. For the entire sample, the heritability estimate for SBP was 47%; for DBP, 44%; and 2% for PP. Dividing the twins into age groups, we found the heritability for SBP for the older group was 52%; for DBP, 36%; and 14% for PP. In the younger age group, SBP had a heritability of 44%; DBP was 27%; and no heritability was found for PP.

Shared environmental effects were also calculated in the model fitting. Only pulse pressure showed the presence of shared environmental effects. These estimates accounted for 39%, 32%, and 36% of the variance for the entire sample, the older age group, and the younger age group, respectively.

DISCUSSION

The results demonstrate that a large proportion of the individual variability in blood pressure for African-American adults derives from genetic sources. Heritabilities for SBP and DBP in the total sample ranged from .44 to .52, after controlling for the effects of antihypertensive medication. These heritability estimates are similar to the results found in most previous studies that used the "classic twin" approach with other racial groups. A review by Harrap[14] reports that genetic factors account for 30% to 60% of the variance in blood pressure.

The results of the present study are markedly different from the findings of a previous study that employed the twin method to examine sources of genetic influences on blood pressure among African descendants in Barbados. Grim et al[9] reported heritability estimates of .04 for the entire sample, and .70 for the male twin pairs for SBP. This wide range in estimates may be the result of the limited number of pairs analyzed (37 pairs in the final analysis).

As noted by Harrap,[14] sample characteristics, such as age, may affect estimates of genetic and environmental influences. In previous research, heritabilities tended to decrease with age during the adult years. For example, Ditto,[15] using a sample of 100 young twin pairs (mean age 20, SD=5) from Montreal, Canada, reported heritabilities of .63 and .58 for resting systolic and diastolic blood pressures, respectively. Fagard et al[16] tested 53 young male twin pairs and found the heritabilities for conventional blood pressure measures to be .64 for systolic, and .73 for diastolic.[11] Hong et al[17] examined genetic and environmental influences on blood pressure in a sample of 289 elderly twin pairs (mean age 63, SD=8) from the Swedish Adoption/Twin Study of Aging. Heritability estimates were .44 for SBP and .34 for SBP.[17] These studies demonstrate an apparent decline in the genetic influence on blood pressure with advancing age.

This decline is contrary to the current study's results, which found a larger contribution from genetic factors on blood pressure among older twins. Heritabilities for the younger twins in the

Table 3. Multiple linear regression analysis for SBP, DBP, and PP

	Age		Gender		Age × Gender		Medication		Zygosity	
	Beta	Prob.	Beta	Prob.	Beta	Prob.	Beta	Prob.	Beta	Prob.
SBP	.227*	.016	−.198	.353	.063	.776	.150*	.015	.092	.098
DBP	.026	.795	−.103	.650	.006	.979	.115	.080	.101	.087
PP	.283†	.003	−.177	.407	.080	.719	.102	.096	.035	.525

* $P<.05$.
† $P<.01$.

Table 4. IntraClass correlations for SBP, DBP, and PP before and after controlling for medication use

Before Adjustment			After Adjustment		
Measure & Group	MZ	DZ	Measure & Group	MZ	DZ
SBP			SBP		
Total Sample	.58 (71)	.29 (72)	Total Sample	.54 (71)	.12 (72)
Younger	.50 (34)	.30 (33)	Younger	.45 (34)	.09 (33)
Older	.53 (37)	.21 (39)	Older	.50 (37)	.13 (39)
DBP			DBP		
Total Sample	.45 (71)	.22 (72)	Total Sample	.44 (71)	.19 (72)
Younger	.42 (34)	.27 (33)	Younger	.29 (34)	.14 (33)
Older	.48 (37)	.19 (39)	Older	.48 (37)	.17 (39)
PP			PP		
Total Sample	.54 (71)	.54 (72)	Total Sample	.51 (71)	.45 (72)
Younger	.32 (34)	.45 (33)	Younger	.33 (34)	.46 (33)
Older	.56 (37)	.50 (39)	Older	.53 (37)	.45 (39)

Note: number of pairs given in parentheses.

present study were .44 and .27 for SBP and .52 and .36 for SBP for older twins. The difference in these results, compared to those of previous research, may be due to factors related to ethnicity. We propose that environmental forces, such as stress associated with racism or the struggle for economic security, may be especially influential on blood pressure at younger ages for African-American adults.[6–8] However, with advancing age environmental forces seem to exert less influence on blood pressure, allowing genetic factors to have a greater impact on blood pressure variance.

A compelling feature of the sample was the considerable variability in age within the age groupings. This wide within-group variation may mean there are other important ages at which meaningful differences occur that our analysis failed to determine. There may be age-related "critical periods" at which genetic and environmental mechanisms culminate to produce important increases in age-related variability in blood pressure. This suggests the existence of important sources of genetic and environmental variance correlated with age that were not included in the present analysis.

Creating two age cohorts provided an important examination of possible sources of variability within and across age cohorts. The analysis of the blood pressure data from the older twins revealed a large genetic effect. Examination of the intra-class correlations suggests that dominance, as well as additive genetic effects, may be involved in the source of genetic influence on blood pressure in this group. However, a formal test of dominance was not performed here, due to the relatively small sample size. Previous literature indicates that hypertension resulting from a single dominant gene is a rare phenomenon.[29] Therefore, we interpret these preliminary results as evidence of a multi-factoral combination of genetic influences at play in the regulation of blood pressure in this population.[29] Evidence suggests that biochemical mechanisms link DNA variation in the renin-angiotensin system with the hypertension phenotype. The focus of much of this work has been on angiotensin I converting enzyme (ACE) and variants of angiotensinogen (AGT) genes.[30,31] Given the present findings, these genes might represent excellent starting points for future investigations of genetic influences on blood pressure and hypertension in African Americans.

It is interesting to note that gender was not a significant predictor of SBP, DBP, or PP, probably as a result of the similarity in blood pressure and PP values between men and women in the sample (Table 2). Cross gender similarity in blood pressure is unusual (men typically have higher values than women), and may be due to a number of factors. For example, the increased similarity between the mean values for men and women in the older cohort, relative to the younger, could be due to selective survival of men. Older men with higher

Table 5. Model fitting results

	Age	A	C	E	χ^2	*df*	*P*
Total							
SBP	.10†	.47†	.00	.43	0.70	7	.998
DBP	.01	.44†	.00	.55	1.58	7	.979
PP	.13†	.02	.39†	.46	4.88	7	.675
Older							
SBP	.00	.52†	.00	.48	1.60	7	.979
DBP	.09†	.36†	.00	.55	1.13	7	.997
PP	.11†	.14	.32†	.43	4.33	7	.741
Younger							
SBP	.07†	.44†	.00	.49	7.98	7	.436
DBP	.17†	.27*	.00	.56	9.09	7	.334
PP	.02	.00	.36†	.62	.60	7	1.00

* $P<.05$.
† $P<.001$.
A=additive genetic influence; C=common or shared environmental influence; E=unique environmental influence.

The results show that fatal cardiovascular events were best predicted by PP in the elderly (aged 60 and older), compared to either systolic or diastolic pressure alone.[19]

values may die at earlier ages, leaving healthier men with lower BP values alive longer. In addition, the effect of psychosocial factors related to blood pressure, such as John Henryism[32] may underpin this similarity. Future research using this sample will address these possibilities.

Pulse Pressure

Pulse pressure (PP) is an independent risk factor for cardiovascular morbidity and mortality.[18,19,21–23] Pulse pressure (PP) provides an index of large artery stiffness.[22] For example, Alderman[18] suggests that PP combined with SBP is a better predictor of cardiovascular events than SBP alone. In another study, Lee et al[19] examined the use of PP, compared to using SBP or DBP alone, as a predictor for fatal cardiovascular events in the elderly. The results show that fatal cardiovascular events were best predicted by PP in the elderly (aged 60 and older), compared to either systolic or diastolic pressure alone.[19] Consistent with previous literature,[19,23] the results of the present study show increased PP with advancing age.

Previous longitudinal studies found that PP values greater than 65 were associated with the highest risk for cardiovascular disease. However, values between 45 and 60 were associated with lower, but still significant, CVD risk.[18,21] The average PP for the present study's total sample was greater than 50. Given the rates of cardiovascular disease and hypertension among African Americans, this is not surprising. However, the relatively high PP values across the age groups suggest that PP may be predictive of cardiovascular morbidity at younger ages in this population.

The results of this study show no significant genetic influence on PP for the total sample. The individual variability in PP was driven almost equally by shared and unique environmental influences.

A particularly interesting finding is that PP showed a significant shared environmental component of variance. By contrast, neither SBP nor DBP have a significant shared environmental component. This finding appears to be counter-intuitive. However, PP is an index of arterial stiffness and has a separate conceptual meaning other than the values from which it derives (ie, SBP and DBP). As a result PP may have different estimates for sources of variance. We interpret the findings for PP to reflect some early environmental influence, present in families, and resistant to age. For example, a nutritional mechanism, such as dietary fat, may contribute to atherosclerotic processes.[33–35]

Once age was considered in the analysis of PP, a small proportion of genetic variance was found for the older age group, but not for the younger group. As with blood pressure, it appears that aging causes genetic factors to play a greater role in individual variability in PP. An alternative interpretation is that there may be less environmental variability in later life, so that genetic factors play a more prominent role with age. Young people may be in different environments and/or they may react differently to environmental challenges than older adults. Continued examination of individual differences in reactivity and blood pressure variability will remain important future avenues for research to understand better how the impact of the environment may vary with age.

Antihypertensive Medication

Antihypertensive medication is used to reduce blood pressure levels, but few previous studies have accounted for the possible effects these medications may have on twin similarity. Hong et al[17] found that twin similarity decreased, after accounting for antihypertensive medication. In our results, controlling for antihypertensive medication also decreased twin similarity for most of the intra-class correlations. This reduction in twin similarity was greater for DZ twins. However, there was a general increase in heritabilities for SBP, DBP, and PP, after accounting for antihypertensive medications. Hong et al[17] suggested that the correction may have eliminated twin similarity for behaviors such as willingness to seek professional help and to take medication, as well as for the direct effects of medication itself.

SUMMARY

The results indicate that both genetic and environmental factors play significant roles in determining blood pressure and PP measures, even after medication is taken into account. The data indicate that genetic factors are substantive in determining measures of SBP and DBP, particularly for older African-American subjects. We interpret these findings to indicate that genetic factors become especially influential as African Americans age. By contrast, shared and unique environmental factors are most important in determining PP. Future studies of these African-American twins will consist of identifying Quantitative Trait Loci (specific genes), and examining other possible sources of environmental influence on hemodynamic indices.

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