Genetic and Environmental Influences on Blood Pressure in Elderly Twins

Yuling Hong, Ulf de Faire, Debra A. Heller, Gerald E. McClearn, Nancy Pedersen

Abstract We used 289 pairs of Swedish twins reared apart or together to evaluate the importance of genetic and environmental influences on blood pressure. Unlike other twin and family studies, the adoption/twin design allows a distinction between estimates of the importance of shared rearing environments and genetic effects. Genetic factors were observed to play an important role for individual differences in blood pressure. Model-fitting analyses suggested upper limits of heritability for systolic and diastolic blood pressures in the entire sample of 0.44 and 0.34, respectively. More interestingly, substantial influences of shared family effects accounting for up to 27% of the variation were also revealed. Effects of correlated reared together, familial similarity may result from shared environment as well as shared genes. The Swedish Adoption/Twin Study of Aging (SATSA) combines a twin study with an adoption study, making it possible to avoid many limitations of the classic twin study with more accurate estimates of the genetic contributions. Furthermore, this study presents a unique opportunity to examine age differences in heritability for BP in an elderly twin population.

Methods

Study Samples

The SATSA sample of twins separated early in life was identified through the Swedish Twin Registry, which includes nearly 25,000 pairs of twins of the same gender born in Sweden between 1886 and 1958. The SATSA subregistry was compiled in 1984 by contacting pairs of twins identified in the registry as having been reared apart, along with a matched sample of twins who had been reared together. The SATSA sample has been described in detail elsewhere. The BP data presented here were obtained from a subset of 302 pairs of twins who were subjected to physical examinations during testing between 1986 and 1988. Three subjects without BP recordings and 12 who had had myocardial infarction in the past 2 years were excluded from the analyses. Table 1 shows the general characteristics of the study subjects.

This study was approved by the Ethics Committee of the Karolinska Institute and the Swedish National Data Inspection Authority. All subjects gave informed consent.

BP Measurement

BP was measured twice by trained nurses using a mercury sphygmomanometer with a cuff size of 17 cm by 67 cm with subjects in a supine position after 5 minutes of rest and after 1 minute standing. The fifth-phase Korotkoff sound was used as the diastolic reading. The pressure was read to the nearest 2 mm Hg. The supine measurement was used in the present study.

Definition of Hypertension

Subjects were identified as hypertensive if they displayed a systolic BP greater than 160 mm Hg and/or diastolic BP greater than 90 mm Hg.
TABLE 1. Blood Pressure Level by Medication, Age, and Gender

<table>
<thead>
<tr>
<th>Measure</th>
<th>No Medication</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td></td>
<td>Middle-aged</td>
<td>Older</td>
</tr>
<tr>
<td></td>
<td>121</td>
<td>62</td>
</tr>
<tr>
<td>SBP</td>
<td>150.5±19.5</td>
<td>164.0±22.6</td>
</tr>
<tr>
<td>DBP</td>
<td>89.6±9.9</td>
<td>86.2±8.9</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>58.7</td>
<td>54.8</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure, shown as mean±SD. Middle-aged, 50 to 65 years old; older, 65 years and older.

than 90 mm Hg or if they were taking antihypertensive medication.

Statistical Analyses

Analyses of BP variables included descriptive statistics and genetic analyses. Because age, gender, and antihypertensive medication may affect BP levels, multiple linear regression analyses were used to assess the influence of these variables. Intraclass correlations and model-fitting analyses were performed to evaluate quantitative contributions of genetic and environmental (shared and nonshared) components. The residuals from linear regression analyses were used for intraclass correlation calculations and model-fitting analyses. In the entire sample and when the sample was broken into two age groups, residuals from the linear regression model after adjustment for age, gender, and age-gender interaction were used for intraclass correlation analyses, and residuals after adjustment for gender were used for model-fitting analyses. When the sample was categorized into two gender groups, residuals after adjustment for age were taken for intraclass correlation analyses, and the levels of systolic and diastolic BP without adjustment were used in model-fitting analyses.

Intraclass Correlations

Genetic analyses were based on quantitative genetic theory, which defines a phenotype as the sum of the effects of both genotype and environment.3 The goal was to decompose the phenotypic variance into its genetic and environmental components by comparing the similarity within the twin pairs (measured by intraclass correlation) in each of four zygosity and rearing groups. For example, monozygotic twins share identical genotypes, so any differences between them are theoretically caused by their environments. Dizygotic twins, in contrast, share on average 50% of their segregating genes. The extent to which monozygotic twins are more alike than dizygotic twins should therefore reflect genetic influences. In the classic twin method, the difference between intraclass correlations for monozygotic twins and those for dizygotic twins is doubled to estimate heritability.5 The remaining population variation can then be attributed to environmental factors.

The study of twins reared apart is a powerful method for evaluating not only genetic influences but also different types of environmental effects. The influence of a shared rearing environment is estimated by comparing the intraclass correlations for twins reared together with those for twins reared apart: If twins reared together are more similar than twins reared apart, this finding indicates the importance of a shared rearing environment. However, even twins reared apart may share similar, or “correlated,” environments. Factors producing a correlated environment, for twins reared both together and apart, may include prenatal influence, postrearing contact, or similarities in aspects of adult lifestyle such as dietary habits. The effects of correlated environment become apparent when the similarity of a pair of twins cannot be explained by either zygosity or the type of rearing. In a study of twins reared together, estimates of the influence of a shared environment are derived from resemblances that cannot be explained by genetic effects. Such studies cannot separate the relative contributions of these two different environments. Unlike traditional studies of twins reared together, the study of twins reared apart allows separate quantification of the effects of a shared rearing environment and those of a correlated environment.

Residual variance that cannot be explained by heredity, the shared rearing environment, and/or correlated environments is attributed to the effects of a nonshared environment that is unique to the individual and the effects of random errors.

Model-Fitting Analyses

In the classic twin study, estimates of genetic and environmental effects that are based on comparisons of intraclass correlations have relatively low power and large standard errors and do not simultaneously use all available information. Model-fitting approaches are more powerful and permit the analysis of groups of twins simultaneously, making assumptions explicit and testing the relative fit of nested models. In our study, intrapair correlation and asymptotic covariance matrices among twin pairs from the PRELIS program were subjected to structural-equation modeling with the LISREL 7 program6 to estimate the genetic and environmental components of variance. The use of structural-equation models has become standard in twin research,7 and the application of these techniques to SATSA has been described previously.2,8

The models in this study are based on the following four equations, which describe twin correlations in terms of the contributions to total variance (\(V_T\)) of additive genetic effects (\(V_A\)), shared rearing environment (\(V_S\)), and nonshared environmental effects (\(V_E\)): (1) correlation of monozygotic twin pairs reared together (\(r_{MZA} (0, 0) = V_A + V_S + V_E\)), (2) correlation of monozygotic twin pairs reared apart (\(r_{MZA} (0, 0) = V_A + V_E\)), (3) correlation of dizygotic twin pairs reared together (\(r_{DZT} (0, 0) = V_A + V_S + V_E\)), and (4) correlation of dizygotic twin pairs reared apart (\(r_{DZA} (0, 0) = 0.5 \cdot V_A + V_E\)) and \(\text{covariate within models to obtain estimates for genetic and environmental effects (V_A, V_S, V_E).} \text{The Figure shows a path diagram for genetic and environmental effects on BP phenotypes of twin pairs.} \text{The LISREL 7 computer program simultaneously analyzed intrapair correlation and asymptotic covariance matrices from the four rearing/zygosity groups and produced maximum likelihood estimates of the model parameters.} \text{A χ² and probability value for the test of the fit for the model was provided, as well as standard errors of the estimates. A model is considered to fit the data when the probability value is greater than .05. The proportion of variance due to genetic effects, i.e., heritability (h²), and the proportion of variance due to different types of environmental effects could then be computed.} \text{Since there may be a relation between age and the variables under study, a model without taking age into account will bias the estimates. Hence, age in years was also included as a covariate within models to obtain estimates for genetic and environmental factors that are independent of linear effects of age within a cohort.} \text{Separate models with and without}
Path diagram shows genetic and environmental effects on blood pressure phenotypes of twin pairs. MZ indicates monozygotic twins; DZ, dizygotic twins; TRT, twins reared together; TRA, twins reared apart; Ens, nonshared environmental factor; G, genetic factor; Ec, correlated environmental factor; es, nonshared environmental effects; h, genetic effects; es, shared environmental effects; ec, correlated environmental effects; AgeL, standardized latent variable of age; BP1 and BP2, blood pressure levels for twin 1 and twin 2; and Age, age in years for twin 1 and twin 2.

correction for medication were performed to evaluate the effects of medication on twin similarity for BP.

Age and Gender Difference in Genetic Factors

To evaluate age group differences, this twin sample was divided into two age cohorts: a middle-aged twin group (less than 65 years) and an old twin group (65 years or older). Intraclass correlations and the results of model-fitting analysis were then compared across age groups and gender. Cohort and gender differences in genetic and environmental factors were evaluated by comparing models in which parameter estimates were constrained to be equal across age or gender groups with models in which the estimates were allowed to differ. The relative fits of these constrained and unconstrained models were then evaluated by χ² criteria. If the difference of χ² values between constrained and unconstrained models is statistically significant (P<.05), we can conclude that there are differences in parameter estimates across age or gender groups.

Results

Sample Characteristics

Study subjects were 63±8 years old (mean±SD). Table 1 lists mean levels of systolic and diastolic BP. In general, individuals using antihypertensive medication had higher mean levels of systolic and diastolic BP than those without medication. Medication was a significant independent predictor for both systolic and diastolic BP when age, gender, and age-gender interaction were accounted for (Table 2). Gender was a predictor for both systolic and diastolic BP independent of age and age-gender interaction. There was an effect of age-gender interaction on systolic BP: Older men had a lower mean level of systolic BP than older women, and middle-aged men had a higher mean level of systolic BP than middle-aged women. After additional adjustment for medication, there were still gender differences of borderline significance for systolic and diastolic BP (Table 2). There were no significant age differences in BP in the present study.

Intraclass Correlations

Table 3 shows the intraclass correlation coefficients by rearing and zygosity groups for the total sample, for middle-aged and older twins, and for male and female twins separately. In general, correlation coefficients for monozygotic twins were higher than those for dizygotic twins, indicating the existence of genetic influences for BP levels. This effect was more apparent among younger twins compared with older twins, suggesting a greater effect of genetic factors in middle-aged twins. On average, the correlations for twins reared together were not higher than those for twins reared apart, indicating the existence of shared rearing environmental effects. The correlations for monozygotic twins reared apart were not higher than those for dizygotic twins reared apart in some of the subgroups, suggesting the effects of correlated environment. On average, the differences of correlation coefficients between monozygotic and dizygotic twins in men were larger than those in women for both

<table>
<thead>
<tr>
<th>Measure</th>
<th>Age</th>
<th>Gender</th>
<th>Age-Gender Interaction</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta</td>
<td>P</td>
<td>Beta</td>
<td>P</td>
</tr>
<tr>
<td>SBP</td>
<td>0.279</td>
<td>.498</td>
<td>-31.516</td>
<td>.032</td>
</tr>
<tr>
<td></td>
<td>0.319</td>
<td>.426</td>
<td>-26.865</td>
<td>.061</td>
</tr>
<tr>
<td>DBP</td>
<td>-0.282</td>
<td>.151</td>
<td>-14.119</td>
<td>.044</td>
</tr>
<tr>
<td></td>
<td>-0.268</td>
<td>.167</td>
<td>-12.494</td>
<td>.072</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.
TABLE 3. Intraclass Correlations for Total Study Sample, Gender Group, and Age Group by Zygosity and Rearing Status

<table>
<thead>
<tr>
<th>Measure and Grouping</th>
<th>MZA</th>
<th>MZT</th>
<th>DZA</th>
<th>DZT</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total*</td>
<td>0.33 (43)</td>
<td>0.60 (64)</td>
<td>0.37 (95)</td>
<td>0.17 (85)</td>
</tr>
<tr>
<td>Age*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle-aged</td>
<td>0.44 (22)</td>
<td>0.72 (22)</td>
<td>0.34 (65)</td>
<td>0.08 (40)</td>
</tr>
<tr>
<td>Older</td>
<td>0.25 (21)</td>
<td>0.45 (22)</td>
<td>0.41 (30)</td>
<td>0.23 (45)</td>
</tr>
<tr>
<td>Gender†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.27 (19)</td>
<td>0.75 (22)</td>
<td>0.51 (30)</td>
<td>0.05 (39)</td>
</tr>
<tr>
<td>Women</td>
<td>0.37 (24)</td>
<td>0.53 (42)</td>
<td>0.28 (65)</td>
<td>0.29 (46)</td>
</tr>
<tr>
<td>DBP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total*</td>
<td>0.19 (43)</td>
<td>0.54 (64)</td>
<td>0.18 (95)</td>
<td>0.18 (85)</td>
</tr>
<tr>
<td>Age*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle-aged</td>
<td>0.20 (22)</td>
<td>0.60 (22)</td>
<td>0.19 (65)</td>
<td>0.10 (40)</td>
</tr>
<tr>
<td>Older</td>
<td>0.17 (21)</td>
<td>0.43 (22)</td>
<td>0.23 (30)</td>
<td>0.23 (45)</td>
</tr>
<tr>
<td>Gender†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.26 (19)</td>
<td>0.33 (22)</td>
<td>0.32 (30)</td>
<td>0.13 (39)</td>
</tr>
<tr>
<td>Women</td>
<td>0.16 (24)</td>
<td>0.61 (42)</td>
<td>0.11 (65)</td>
<td>0.23 (46)</td>
</tr>
</tbody>
</table>

MZA indicates monozygotic twins reared apart; MZT, monozygotic twins reared together; DZA, dizygotic twins reared apart; DZT, dizygotic twins reared together; SBP, systolic blood pressure; and DBP, diastolic blood pressure. Number of twin pairs is shown in parentheses. Middle-aged, 50 to 65 years old; older, 65 years and older.

*Adjusted for age, gender, and age-gender interaction.
†Adjusted for age.

systolic and diastolic BP, indicating that there were gender differences in heritability for BP.

Comparisons of correlation coefficients obtained with and without adjustment for antihypertensive medication revealed general declines in correlation coefficients after correction for medication (Table 4). This could imply that treatment for antihypertensive medication may influence to some extent the similarity between twins in BP levels.

Table 5 shows the intraclass correlations for systolic and diastolic BP from the subsample of subjects who were free of antihypertensive medication. These results are quite similar to the results from the entire sample without medication adjustment.

Quantitative Genetic Results

Because a significant difference of variance across the four zygosity and rearing groups was found in middle-aged and male twins for systolic BP, and in the entire sample for diastolic BP, intrapair correlation and asymptotic covariance matrices were used in the model-fitting analyses instead of variance-covariance matrices. The model-fitting results for the entire sample without adjustment for medication are summarized in Table 6, which shows the estimates for the percentages of variances obtained from LISREL modeling. Heritability was 44% for systolic BP and 34% for diastolic BP in the entire study group. Heritability in the middle-aged group was 62% for systolic BP and 22% for diastolic BP; in the older group, heritability was 12% for systolic BP and 26% for diastolic BP. Although the difference between a constrained model that assumed equal estimates across the two age groups and the combination of the two separate age group models for systolic BP were not significant ($\chi^2=8.07$, df=4, $P=.09$), the heritability appeared to be much lower in the older group than in the middle-aged group.

When men and women were evaluated separately, heritability estimates in men were 67% for systolic BP and 11% for diastolic BP; in women, heritability estimates were 31% for systolic BP and 25% for diastolic BP. However, comparison between gender-constrained models and the combinations of two separate gender group models indicated that the differences in estimates for men and women were not statistically significant for systolic or diastolic BP.

Differences in the environmental contributions to variance were evident. For systolic BP, effects of shared rearing environment were detected in middle-aged twins and male and female twins but not in older twins. Correlated environmental effects (including, perhaps, maternal nutritional status, postrearing contact, etc) were marked in the entire sample, older twins, and female twins but not in middle-aged twins and male twins. For diastolic BP, shared rearing environmental effects were apparent in the entire sample, middle-aged twins, older twins, and female twins but not in male twins, whereas correlated environmental effects were found in male twins. However, these differences are not statistically significant because of a lack of power.

Discussion

A significant genetic influence on BP was observed for the entire study population as well as across different age and gender groups. The observed heritabilities were somewhat higher than corresponding heritabilities found in family studies but lower than the results from previous classic twin studies on twins reared to-
TABLE 4. Intraclass Correlations for Total Study Sample, Gender Group, and Age Group by Zygosity and Rearing Status Adjusted for Medication

<table>
<thead>
<tr>
<th>Measure and Grouping</th>
<th>MZA</th>
<th>MZT</th>
<th>DZA</th>
<th>DZT</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total*</td>
<td>0.18 (43)</td>
<td>0.53 (64)</td>
<td>0.35 (95)</td>
<td>0.11 (85)</td>
</tr>
<tr>
<td>Age*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle-aged</td>
<td>0.41 (22)</td>
<td>0.64 (42)</td>
<td>0.31 (65)</td>
<td>0.01 (40)</td>
</tr>
<tr>
<td>Older</td>
<td>0.05 (21)</td>
<td>0.40 (22)</td>
<td>0.39 (30)</td>
<td>0.20 (45)</td>
</tr>
<tr>
<td>Gender†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.18 (19)</td>
<td>0.77 (22)</td>
<td>0.38 (30)</td>
<td>-0.03 (39)</td>
</tr>
<tr>
<td>Women</td>
<td>0.17 (24)</td>
<td>0.43 (42)</td>
<td>0.33 (65)</td>
<td>0.25 (46)</td>
</tr>
<tr>
<td>DBP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total*</td>
<td>0.17 (43)</td>
<td>0.51 (64)</td>
<td>0.19 (95)</td>
<td>0.15 (85)</td>
</tr>
<tr>
<td>Age*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle-aged</td>
<td>0.18 (22)</td>
<td>0.58 (42)</td>
<td>0.16 (65)</td>
<td>0.05 (40)</td>
</tr>
<tr>
<td>Older</td>
<td>0.15 (21)</td>
<td>0.37 (22)</td>
<td>0.22 (30)</td>
<td>0.22 (45)</td>
</tr>
<tr>
<td>Gender†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.22 (19)</td>
<td>0.36 (22)</td>
<td>0.27 (30)</td>
<td>0.11 (39)</td>
</tr>
<tr>
<td>Women</td>
<td>0.15 (24)</td>
<td>0.55 (42)</td>
<td>0.16 (65)</td>
<td>0.20 (46)</td>
</tr>
</tbody>
</table>

Definitions are as in Table 3. Number of twin pairs is shown in parentheses. Middle-aged, 50 to 65 years old; older, 65 years and older.

* Adjusted for age, gender, age-gender interaction, and medication.
† Adjusted for age and medication.

As pointed out above, family studies usually result in lower heritability estimates than twin studies partly because of age differences in parents and offspring.2 The inclusion of genetic dominance variance in monozygotic twins, and possible violations of the equal environment assumption in twins. In the present study, there was no indication of genetic dominance because the correlation coefficient in monozygotic twins reared apart was less than twice the correlation coefficients in dizygotic twins reared apart for both systolic and diastolic BP.

Role of Shared and Correlated Environmental Effects

This study on twins reared apart made it possible to estimate the relative contribution of shared rearing environments more accurately than conventional twin or family studies and to separate the shared rearing environment from other correlated environmental influences. Our findings indicate that twins reared together had higher correlation coefficients than twins reared apart, suggesting the existence of shared rearing environmental effects. The model-fitting techniques confirmed the effects of shared rearing environment and/or correlated environments to some extent, although these effects are not statistically significant because of a lack of power. The results indicated that shared environmental effects are more evident for diastolic BP, whereas correlated environmental influences are more important for systolic BP. The shared rearing environmental effects suggest the importance of early rearing experience in determining BP variations in adults and the elderly. As to the effects of correlated environments, which might reflect prenatal influences, postrearing contacts, or similarities in aspects of adult lifestyle, McCarty et al23 reported a powerful influence of maternal environment on the development of BP in adult rats. Barker et al24 found that intrauterine environment had an important effect on BP and hypertension in adult humans. The correlated environmental influences detected in the elderly in the present study may reflect long-lasting effects of prenatal factors or alternatively more postrearing contact. Shared rearing effects were more pronounced for diastolic BP, whereas correlated effects were more notable for systolic BP. Shared family effects such as diet may have a greater influence on diastolic BP, and the intrauterine environment (correlated environment) had greater influences on systolic BP later in life. However, the precise mechanisms behind these associations remain unsettled.

Age and Gender Differences

Heritability estimates for both systolic and diastolic BP have been reported to decrease with age. Sims et al25 found a decrease in heritability for diastolic BP from 68% for young adult twins to 38% for middle-aged twins. The same trend was found for systolic BP. Tambs et al26 reported age effects on the genetic contribution in a study of parents aged 36 years or more and their offspring. To the best of our knowledge, however, no study has been published on the differences in heritability for BP between middle-aged adult and elderly twins. Our study of middle-aged adult (less than 65 years old) and elderly (65 years and older) twins indicates substantially lower heritability estimates in older age groups for systolic BP, although the differences found were not statistically significant (χ²=8.07, df=4, P=.09) partly because of small sample sizes in the subgroups. The marked difference in heritability across age groups for systolic BP may reflect an increase in the importance of
Table 5. Intraclass Correlations for Total Study Sample by Zygosity and Rearing Status, Subjects With Medication Excluded

<table>
<thead>
<tr>
<th>Measure</th>
<th>Grouping</th>
<th>MZA</th>
<th>MZT</th>
<th>DZA</th>
<th>DZT</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>Total*</td>
<td>0.43 (26)</td>
<td>0.61 (40)</td>
<td>0.41 (62)</td>
<td>0.07 (51)</td>
</tr>
<tr>
<td>DBP</td>
<td>Total*</td>
<td>0.19 (26)</td>
<td>0.61 (40)</td>
<td>0.16 (62)</td>
<td>0.06 (51)</td>
</tr>
</tbody>
</table>

Definitions are as in Table 3. Number of twin pairs is shown in parentheses.

Table 6. Genetic and Environmental Contributions to Blood Pressure Variance

<table>
<thead>
<tr>
<th>Measure and Grouping</th>
<th>Percentage of Variance</th>
<th>Goodness of Fit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>h²</td>
<td>Es</td>
</tr>
<tr>
<td>SBP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>44%</td>
<td>...</td>
</tr>
<tr>
<td>By age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle-aged</td>
<td>62%</td>
<td>5%</td>
</tr>
<tr>
<td>Older</td>
<td>12%</td>
<td>...</td>
</tr>
<tr>
<td>Constrained model</td>
<td>56%</td>
<td>6%</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>By gender group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>67%</td>
<td>5%</td>
</tr>
<tr>
<td>Women</td>
<td>31%</td>
<td>3%</td>
</tr>
<tr>
<td>Constrained model</td>
<td>56%</td>
<td>4%</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>34%</td>
<td>11%</td>
</tr>
<tr>
<td>By age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle-aged</td>
<td>22%</td>
<td>27%</td>
</tr>
<tr>
<td>Older</td>
<td>26%</td>
<td>8%</td>
</tr>
<tr>
<td>Constrained model</td>
<td>24%</td>
<td>19%</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>By sex group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>11%</td>
<td>...</td>
</tr>
<tr>
<td>Women</td>
<td>25%</td>
<td>27%</td>
</tr>
<tr>
<td>Constrained model</td>
<td>32%</td>
<td>12%</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
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</tr>
</tbody>
</table>

h² indicates heritability; Es, shared environmental effects; Ec, correlated environmental effects; Ens, nonshared environmental effects; SBP, systolic blood pressure; and DBP, diastolic blood pressure. Ellipses show that parameter estimates were fixed in the models.

Accumulated experiences unique to individuals. This difference may also reflect cohort effects or selective attrition. However, no significant difference of heritability estimates between middle-aged and older groups was found for diastolic BP, indicating that genetic effects on diastolic BP persisted in the older age group.

With respect to gender differences in genetic contributions to BP variation, mixed results have previously been found. McIlhany et al observed higher heritabilities in females than in males for both systolic BP (78% versus 41%) and diastolic BP (61% versus 56%) in a study of 200 twin pairs aged 14 years on average. Schieken et al could not detect any gender differences in heritability for systolic BP (66% for each) in a group of 251 twin pairs aged 11 years on average. For diastolic BP, a higher estimate for males (64%) than for females (51%) was observed. Our study, which investigated a middle-aged adult and elderly twin population, showed that males had somewhat higher heritability estimates than females for systolic BP but slightly lower heritability estimates than females for diastolic BP. However, these differences were not statistically significant. Unfortunately, sample sizes were too small to evaluate differences in heritabilities by gender and age group simultaneously.

Medication Effects

Antihypertensive medication obviously reduces BP levels, but data on the possible effect of antihypertensive medication on twin similarity in BP levels are scant. The intraclass correlation estimates from the subsample of subjects who were free of medication are quite similar to the results from...
the entire sample without adjustment for medication. How-
 ever, medication was given regularly for all hypertensive
 subjects and was very frequent in this elderly population.
 Because of the frequency of medication use, we felt it was
 relevant to test whether estimates of twin similarity differ
 when adjusted for the mean effects of medication. Therefore,
 we compared the intraclass correlations without adjust-
 ment for medication with those with adjustment for medica-
 tion. The results indicated that antihypertensive medication may
 influence twin similarity for BP levels, particularly for systolic
 BP in the elderly and women. Correction for medication use
 may have decreased twin similarity for BP because twin
 similarity for behaviors such as willingness to seek professional
 help and to take medication was removed as well. It is not
 clear whether twin similarity for antihypertensive medication
 use simply reflects genetic effects on BP or possibly genetic
 variance for personality as well. Further investigations using
 multivariate genetic models are warranted.

 Representativeness of the Study Population
 Regarding BP Levels

 The prevalence of hypertension and mean BP levels were
 higher in the present study population than corresponding
 measures from most other studies on elderly populations,27-30
 approximately two of three twins had hypertension. However,
 the mean levels were somewhat lower than another Swedish
 population study that reported mean levels (±SD) of systolic
 and diastolic BP to be 167.1±26.9 and 92.9±12.9 mm Hg,
 respectively, in a population aged 70.1±6.8 years.31 In individu-
 als taking antihypertensive medication, BP levels were even
 higher than those not taking medication, indicating that
 hypertension was not optimally controlled. It is unlikely,
 however, that genetic estimates are affected, as all twins
 irrespective of treatment or no treatment were included in the
 analyses.

 Despite numerous studies on the mechanisms of BP
 regulation, the primary cause of hypertension in most
 patients remains unknown. Accumulated evidence indi-
 cates that several genes at multiple genetic loci as well as the
 interaction between environmental stimuli and indi-
 viduals' genotypes are involved in the genesis of hyper-
 tension.32-37 The present study used a quantitative ge-
 netic method to evaluate the importance of polygenic
 influences, ie, effects of many genes of small effects. To
 establish the molecular genetic background, further
 studies using linked genetic markers such as human
 leukocyte antigens,38 restriction fragment length poly-
 morphism,39 or quantitative trait loci40 are needed in
 stead of researching only a single gene.

 In conclusion, genetic factors seem to play an impor-
 tant role in individual differences in BP levels. Substan-
 tial influences of shared family effects accounting for up to
 27% of the BP variance were also revealed. Further-
 more, effects of correlated environments, which might
 partly reflect the intrauterine environmental effects, exist
to some extent later in life. The influence of genetic
 factors tends to decrease across age groups for systolic
 BP but not for diastolic BP. However, this declining
trend for systolic BP did not reach significance.

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 References

 1. Hopkins PN, Williams RR. Human genetics and coronary heart
 2. Tambs K, Eaves LJ, Mourn T, Holmen J, Neale MC, Naess S,
 Lund-Larsen PG. Age-specific genetic effects for blood pressure.
 3. Pedersen NL, Friberg L, Flocerus-Myrbach B, McClearn GE,
 Plomin R. Swedish early separated twins: identification and char-
 4. Pedersen NL, McClearn GE, Plomin R, Nesselroade JR, Berg S,
 De Faire U. The Swedish Adoption Twin Study of Aging: an
 5. Falcinner DS. Introduction to Quantitative Genetics. 3rd ed.
 and Application. 2nd ed. Chicago, Ill: SPSS; 1989.
 7. Neale MC, Cardon LR. Methodology for Genetic Studies of Twins
 and Families: Dordrecht, the Netherlands: Kluwer Academic
 8. Boomsma DI, Martin NG, Neale MC. Genetic analysis of twin and
 family data: structural modeling using LISREL. Behav Genet.
 1989;19:3-161.
 GE, Matthews KA. Genetic and environmental influences for type
 A-like measures and related traits: a study of twins reared apart and
 Genetic and environmental influences on serum lipid levels in
 11. Neale MC, Martin NG. The effects of age, sex, and genotype on
 self-report drunkenness following a challenge dose of alcohol.
 12. De Faire U, Iselius L, Lundman T. Biological and cultural deter-
 13. Iselius L, Morton NE, Rao DC. Family resemblance for blood
 14. Ward R. Familial aggregation and genetic epidemiology of blood
 pressure in 7- to 12-year-old Chinese twins, with special reference
 15. Muldoon MF, Terreri DF, Bunker CH, Manuck SB. Family history
 studies in hypertension research: review of the literature. Am J
 PG, Naess S. Genetic and environmental effects on blood pressure
 17. Mongeau JG. Heredity and blood pressure in humans: an overview.
 RR. Genetic heritability and common environmental components
 of resting and stressed blood pressure, lipids, and body mass index
 19. Hayakawa K, Shimizu T. Blood pressure discordance and lifestyle:
 Japanese identical twins reared apart and together. Ada Genet Med
 Huang FY, Lan CC, Yang KH, et al. Chronological changes in
 hypertensive disease: a public health perspective. Ada Genet Med
 22. Schieken RM, Eaves U, Hewitt JK, Mosteller M, Bodurtha JN,
 Moskowitz WB, Nunce WE. Univariate genetic analysis of blood
 pressure in children (the Medical College of Virginia Twin Study).
 Am J Cardiol. 1989;64:1331-1337.
 23. McCarty R, Cerpiall MA, Murphy CA, Lee JH, Fields-Okostcha C.
 Maternal involvement in the development of cardiovascular phe-

 Hong et al  Genetic Influences on Blood Pressure  669
Genetic and environmental influences on blood pressure in elderly twins.
Y Hong, U de Faire, D A Heller, G E McClearn and N Pedersen

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