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 environment, which might reflect, for example, the intrauterine environment, existed to some extent later in life. The influence of genetic factors tended to decrease across age groups for systolic blood pressure (0.62 in individuals less than 65 years old; 0.12 in those 65 years and older) but not for diastolic blood pressure (0.22 for the middle-aged group; 0.26 for the older group). However, this declining trend for systolic blood pressure did not reach significance ($\chi^2=8.07, df=4, P=.09$). (Hypertension. 1994;24:663-670.)

Key Words  • blood pressure • genetics • environment • aging • twins, reared apart

Hypertension is a common disease and also one of the main risk factors for coronary heart disease. It is commonly accepted that blood pressure (BP) level is a function of genetic and environmental factors originating either early in utero, possibly as a consequence of maternal nutritional conditions, or later during adult life. Family and twin studies have been used to decompose genetic and environmental contributions to systolic and diastolic BP variation. Heritability estimates for systolic BP range from 13% to 82% and for diastolic BP from less than 1% to 64%, with average levels for both of approximately 50%.1

Typically, results from family studies have resulted in lower estimates than those from twin studies. Heritability estimates may be somewhat inflated in twin studies by the effects of genetic dominance. However, it is not clear whether or to what extent BP is affected by genetic dominance. Higher estimates of heritability in classic twin studies may also result when monozygotic twins have experienced more similar environments than fraternal twins. On the other hand, the family study design may underestimate heritability predominantly because of age differences between parents and offspring2 or possible violation of the equal environment assumption in twin studies. In classic studies of families or twins 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.3,4 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.2 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 95 mm Hg. The cut-off points for diastolic BP were higher for individuals 65 years of age or older. Since the fifth-phase Korotkoff sound was used as the diastolic reading, the cut-off point for systolic BP was 160 mm Hg. The intra- and interobserver variability was found to be good, as previously described elsewhere.2

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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>Older</td>
</tr>
<tr>
<td>n</td>
<td>121</td>
<td>62</td>
</tr>
<tr>
<td>SBP</td>
<td>150.5±19.5</td>
<td>157.5±24.3</td>
</tr>
<tr>
<td>DBP</td>
<td>89.8±9.9</td>
<td>87.8±10.7</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. 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. 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 program to estimate the genetic and environmental components of variance. The use of structural-equation models has become standard in twin research, and the application of these techniques to SATSA has been described previously.

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 ($V_C$), correlated environment ($V_G$), and nonshared environmental effects ($V_E$): (1) correlation of monozygotic twin pairs reared together ($Cor_{MZZ} = (V_A + V_C + V_G) / (V_A + V_E)$); (2) correlation of monozygotic twin pairs reared apart ($Cor_{MZA} = (V_A + V_E) / (V_A + V_C + V_E)$); (3) correlation of dizygotic twin pairs reared together ($Cor_{DZZ} = (V_A + V_E) / (V_A + V_C + V_E)$); (4) correlation of dizygotic twin pairs reared apart ($Cor_{DZA} = (V_A + V_E)^2 / (V_A + V_C + V_E) / V_T$).

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. $A^2$ 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 0.05. The proportion of variance due to genetic effects, $h^2$, and the proportion of variance due to different types of environmental effects could then be computed.

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.
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; Ens, 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 $\chi^2$ criteria. If the difference of $\chi^2$ 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

<p>| TABLE 2. Results From Multiple Linear Regression Analyses |
|-------------------------------|------------------|------------------|------------------|------------------|</p>
<table>
<thead>
<tr>
<th>Measure</th>
<th>Age</th>
<th>Gender</th>
<th>Age-Gender Interaction</th>
<th>Medication</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Beta</td>
<td></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>
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<tbody>
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<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 (23)</td>
<td>0.72 (42)</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 (65)</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 (42)</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 ($\chi^2=8.07, df=4, P=0.09$), 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[12-17] but lower than the results from previous classic twin studies on twins reared to-
correlated environments to some extent, although these
firmed the effects of shared rearing environment and/or
estimate the relative contribution of shared rearing
Environmental Effects
partly because of age differences in parents and off-
As pointed out above, family studies usually
were more notable for systolic BP. Tambs et al
found a decrease in heritability for diastolic BP from
BP have been reported to decrease with age. Sims et al
associations remain unsettled.
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 envi-
ronment from other correlated environmental influ-
ences. Our findings indicate that twins reared together
had higher correlation coefficients than twins reared
apart, suggesting the existence of shared rearing envi-
ronmental effects. The model-fitting techniques con-
firmed 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 cor-
related 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 sim-
ilarities in aspects of adult lifestyle, McCarty et al reported a powerful influence of maternal environment
on the development of BP in adult rats. Barker et al 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 postrear-
ing contact. Shared rearing effects were more pro-
nounced 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 envi-
ronment) 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 al
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 al
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 heritabil-
ity 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 \(\chi^2=8.07, df=4, P=.09\) 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 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 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>
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<td>0.31 (65)</td>
<td>0.01 (40)</td>
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</tr>
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<td>Gender†</td>
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<td>-0.03 (39)</td>
</tr>
<tr>
<td>Men</td>
<td>0.17 (24)</td>
<td>0.43 (42)</td>
<td>0.33 (65)</td>
<td>0.25 (46)</td>
</tr>
<tr>
<td>Women</td>
<td>0.16 (65)</td>
<td>0.51 (64)</td>
<td>0.19 (95)</td>
<td>0.15 (85)</td>
</tr>
<tr>
<td>Age</td>
<td>0.17 (43)</td>
<td>0.51 (64)</td>
<td>0.19 (95)</td>
<td>0.15 (85)</td>
</tr>
<tr>
<td>Middle-aged</td>
<td>0.17 (43)</td>
<td>0.51 (64)</td>
<td>0.19 (95)</td>
<td>0.15 (85)</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>
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<tr>
<td>Gender†</td>
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<td>0.36 (22)</td>
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<td>Men</td>
<td>0.15 (24)</td>
<td>0.55 (42)</td>
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<td>0.20 (46)</td>
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<tr>
<td>Women</td>
<td>0.20 (45)</td>
<td>0.11 (39)</td>
<td>0.31 (65)</td>
<td>0.39 (30)</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.

Together,16-22 As pointed out above, family studies usually
result in lower heritability estimates than twin studies
partly because of age differences in parents and off-
spring,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.
TABLE 5. Intraclass Correlations for Total Study Sample by Zygosity and Rearing Status, Subjects With Medication Excluded

<table>
<thead>
<tr>
<th>Measure</th>
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<th>MZA</th>
<th>MZT</th>
<th>DZA</th>
<th>DZT</th>
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</thead>
<tbody>
<tr>
<td>SBP</td>
<td>Total*</td>
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<td>0.59 (40)</td>
<td>0.41 (62)</td>
<td>0.07 (51)</td>
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<tr>
<td>DBP</td>
<td>Total*</td>
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<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>10%</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>24%</td>
</tr>
<tr>
<td>Constrained model</td>
<td>56%</td>
<td>6%</td>
</tr>
<tr>
<td>Difference</td>
<td>8.07</td>
<td>4</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>9.08</td>
<td>5</td>
</tr>
<tr>
<td>DBP</td>
<td>34%</td>
<td>55%</td>
</tr>
<tr>
<td>By age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle-aged</td>
<td>22%</td>
<td>51%</td>
</tr>
<tr>
<td>Older</td>
<td>26%</td>
<td>65%</td>
</tr>
<tr>
<td>Constrained model</td>
<td>24%</td>
<td>57%</td>
</tr>
<tr>
<td>Difference</td>
<td>6.28</td>
<td>4</td>
</tr>
<tr>
<td>By sex group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>11%</td>
<td>15%</td>
</tr>
<tr>
<td>Women</td>
<td>25%</td>
<td>48%</td>
</tr>
<tr>
<td>Constrained model</td>
<td>32%</td>
<td>56%</td>
</tr>
<tr>
<td>Difference</td>
<td>5.19</td>
<td>4</td>
</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 al26 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 al22 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. However, 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 adjustment when adjusted for the mean effects of medication. Therefore, we compared the intraclass correlations without adjustment for medication with those with adjustment for medication. 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. 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. In individuals taking antihypertensive medication, BP levels were even higher than in 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 indicates that several genes at multiple genetic loci as well as the interaction between environmental stimuli and individuals’ genotypes are involved in the genesis of hypertension. The present study used a quantitative genetic method to evaluate the importance of polygenic influences, i.e., effects of many genes of small effects. To establish the molecular genetic background, further studies using linked genetic markers such as human leukocyte antigens, restriction fragment length polymorphism, or quantitative trait loci are needed instead of researching only a single gene.

In conclusion, genetic factors seem to play an important role in individual differences in BP levels. Substantial influences of shared family effects accounting for up to 27% of the BP variance were also revealed. Furthermore, 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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Genetic and environmental influences on blood pressure in elderly twins.
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