Effect of Home Blood Pressure and Gender on Estimates of the Familial Aggregation of Blood Pressure

The Tecumseh Blood Pressure Study

Kenneth A. Jamerson, Nicholas Schork, and Stevo Julius

Blood pressure (BP) readings from a single clinic visit are often used in population studies investigating the genetic basis of BP. We examined first-degree relatives in the Tecumseh Blood Pressure study to compare heritability estimates of BP readings obtained in the clinic-office setting (the average of two seated readings) with self-reported home BP readings (the average of 14 readings) taken over a 1-week period. The hypothesis tested was that repeated BP readings obtained in the home over the 1-week period would have fewer artifacts (i.e., environmentally induced variability in BP) and thus would better estimate the true "basal" BP that, in turn, would improve heritability estimates. We and others assume that the true basal BP level is heritable. We therefore expected that this "true" BP, by reducing BP variability of offspring, would show a stronger between-sibling correlation and that it would correlate better to parental BP as measured in a clinic setting. Correlation coefficients were calculated between siblings in the present Tecumseh study using self-reported home BP and clinic BP readings. Among 380 siblings (average age, 31.4 years), correlation coefficients for the home readings were of the same magnitude as for office readings (home, r=0.23, p<0.01; office, r=0.24, p<0.01). When offspring clinic BP readings were compared with archived BP data on parents, the correlation between offspring clinic and parental clinic BP readings was stronger (r=0.24, p<0.05) than the correlation of offspring home BP readings to parental clinic BP readings (r=0.17, p<0.05). This overall weak correlation was chiefly because sons' home BP did not correlate to parents' clinic BP (r=0.08, p=NS), whereas daughters' home BP readings exhibited a stronger correlation (r=0.27, p<0.01). The difference in BP between home and office readings was taken as a measure of BP "reactivity." This difference of home-to-clinic BP in sons correlated to parents' clinic BP. Furthermore, the clinic-to-home difference in the sons of hypertensive parents was 7.0 mm Hg compared with 3.6 mm Hg in offspring of normotensive parents (p<0.05). Self-reported home BP readings do not improve estimates of aggregation of BP in siblings. Male offspring show a tendency for heritability of the reactivity BP component. Sons of hypertensive parents are more likely to exhibit "white coat" reactivity. In analyzing heritability, it may be important to consider white coat reactivity as well as baseline BP as potentially different BP characteristics. In addition, a familial tendency for white coat reactivity may influence BP heritability estimates in epidemiological studies, at least of male subjects.

Key Words • blood pressure • genetics • gender

Familial aggregation of blood pressure (BP) between first-degree relatives has been consistently demonstrated.1-5 Heritability of BP is traditionally estimated from regression data based on casual office readings, although such a practice may be confounded by "white coat" hypertension, i.e., persons with hypertension in the office but normotensive home BP. It is now accepted that the use of 24-hour ambulatory monitoring may give a more accurate estimate of average BP and be a better predictor of cardiovascular morbidity and mortality.6-10 It is likely that multiple BP determinations taken in both the office and home environments would likewise be a better predictor of a subject's "true" average or basal BP than a few casual office readings alone. It is generally assumed that the true average BP ought to be the heritable characteristic of BP measurements. With this in mind, it is important to study the effect of the white coat on estimates of familial aggregation of BP.

BP readings from a single occasion in a clinic could contain artifacts that would obscure the estimation of true baseline BP in population studies.11 Data from Framingham12 and the Australian Trial in Mild Hypertension Study13 illustrate some of the artifacts inherent in using clinic BP readings, since repeat measures from these populations demonstrate the overestimation of
BP by a single walk-in clinic reading. These studies showed later, repeated BP measures, subsequent to the initial readings, exhibited marked regression toward a true mean. Previous population studies are further limited by the difference in age between parents and offspring at the time of cross-sectional comparison. Although the differences in age can be adjusted by statistical analysis, it is doubtful that this removes true biological effects of age on heritability.

The aim of the present analysis was to determine heritability estimates between first-degree relatives by using some unique features of the Tecumseh Blood Pressure Study population. The Tecumseh study contains information on present subjects and on their parents' BP readings at various times in their lives. We examined clinic BP readings, self-reported home BP readings, and the difference in BP levels between the clinic and home environments in a group of 380 siblings and compared them with archived BP data on their parents when they were of similar age to their offspring. In contradistinction to previous population studies, the Tecumseh data set permitted us to evaluate white coat reaction in the clinic and true baseline BP as well as how these data might affect heritability estimates of BP.

Methods

The aims and nature of the Tecumseh Blood Pressure Study have been previously reported elsewhere. The study subjects were aged 18–42 years (average 32.9), previously healthy, and taking no antihypertensive medications. In this article we report comparisons of BP data collected on 380 subjects from the latest Tecumseh Blood Pressure Study (average age, 31.4±4.5 years) with their parents' BP readings obtained in the course of previous Tecumseh Health Study surveys when the average age of the parents was 31.2 years. Offspring BP data were obtained from 1987 to 1990, and parental data were obtained primarily during a data collection from 1958 to 1961.

The present implementation of the Tecumseh Blood Pressure Study calls for BP measurements at home and in the clinic-office setting. Subjects were first taught to measure BP in their home by a trained technician auscultating through a "Y"-connected stethoscope. A subject was considered properly trained when his or her readings were within 5 mm Hg of the technician's. The coefficient of variation of the 14 home readings (7 days of BP monitoring with morning and evening readings) was 4.4% and 6.3% for systolic (SBP) and diastolic (DBP) BP, respectively. The validity and reproducibility of these readings have been analyzed in a separate report. Clinic BP readings were obtained by a physician who took three BP readings after the subject had been in the seated position for 2 minutes and in the recumbent position for 15 minutes.

A battery of psychosocial, hemodynamic, and biochemical measures were obtained on each subject at this clinic visit. The Spielberger State/Trait Personality Index was administered by a trained technician. The interpretation and limitations of these standardized questionnaires have been well described.

Statistical Analysis

Estimates of the familial aggregation of BP were obtained with Pearson product-moment correlation coefficients and linear regression techniques. Group differences were assessed by t tests, analysis of variance, and analysis of covariance where appropriate.

Results

Comparison of Clinic Blood Pressure Readings Between Parents and Offspring

The correlation coefficient for casual systolic office BP readings (clinic BP) between mid-parent (the average of readings from mother and father) and offspring pairs (son or daughter) was r=0.24, p<0.05 (Table 1). The correlation of SBP between father and offspring (r=0.21, p<0.05) appeared to be stronger than mother and offspring (r=0.15, p<0.05). The correlation coefficients for diastolic readings were in the same direction but weaker. Regression analysis (Table 2) for mid-parent and offspring BP readings suggested that approximately 24% of variability in SBP readings among first-degree relatives derives from inheritable factors. There was no significant BP correlation between husband and wife, or nonrelated children residing in the same household (Figure 1).

### Table 1. Correlation Between Parental Clinic and Offspring Home and Clinic Systolic and Diastolic Blood Pressures in Tecumseh, Michigan

<table>
<thead>
<tr>
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<th>Clinic BP</th>
<th></th>
<th>Home BP</th>
<th></th>
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<tbody>
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<td>Son</td>
<td>Daughter</td>
<td>Son or daughter</td>
<td>Son</td>
</tr>
<tr>
<td>Mother</td>
<td></td>
<td></td>
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<td></td>
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<td>0.15*</td>
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</tr>
<tr>
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<td>0.21†</td>
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<tr>
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<tr>
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</tr>
<tr>
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<td>0.25†</td>
<td>0.24†</td>
<td>0.08</td>
</tr>
<tr>
<td>DBP</td>
<td>0.15*</td>
<td>0.22*</td>
<td>0.15</td>
<td>-0.03</td>
</tr>
</tbody>
</table>

BP, blood pressure; SBP, systolic BP; DBP, diastolic BP; mid-parent, average of readings from mother and father.

*p<0.05, †p<0.005.
Comparison of Blood Pressure Readings Between Sibling Pairs

Figure 1 indicates that correlation of the SBP values between siblings was of the same magnitude (r=0.24) whether the correlation was calculated for a single clinic reading or for an average of 14 readings obtained at home.

Comparison of Offspring Home Blood Pressure Readings to Parental Clinic Values

Figure 1 shows that correlation of home BP readings of the offspring to the parental clinic readings was strong for the daughters (r=0.27, p<0.05) but not significant for sons (r=0.08, p=NS).

The magnitude of difference in BP between clinic and home readings (ΔBP) was considered to represent an alerting or white coat response (Figure 2). The sons' ΔBP correlated to parents' clinic reading (r=0.19, p<0.05), whereas in daughters this correlation was not significant (r=0.06, p=NS). It therefore appears that men tend to show more of an alerting response than women and that the "reactivity" component of the BP in the sons accounts for the correlation of sons' BP to parents' clinic BP readings.

To assess a possible relation between hypertension and blood pressure reactivity or white coat reactivity, the parent population was divided into normotensive and hypertensive groups based on a parental BP reading of ≥140/90 mm Hg. The percent change in the offspring BP in the clinic versus home environment was calculated (Table 3). Sons of hypertensive parents had a larger difference between the clinic and the home BP than sons of normotensive parents in both the SBP (6.5% versus 3.3%, p<0.05) and the DBP (7% versus 3.3%, p<0.05). However, the difference of the clinic-to-home BP in the daughters of hypertensive and normotensive parents was similar.

It is known that BP levels of subjects may be influenced by environmental and genetic components. Forward selection multiple regression of various nature/nurture factors (i.e., weight, parental BP level, anxiety, and curiosity from the Spielberger State/Trait anxiety survey) was performed to predict their influence on the change in BP from the office to the home environment. Measures of anxiety did not significantly contribute to the white coat reactivity in sons or daughters.

Discussion

We examined the familial aggregation of BP by comparing readings in both the home and office environments and found that the correlation coefficient BP between sibling pairs was similar whether the average of the clinic values from a single occasion or the average of multiple readings taken over a 1-week period in the home was used. We observed correlation coefficients of clinic SBP between first-degree relatives of the same magnitude as previous population studies.1-3,14 On the theory that the true BP is better approximated by repeat BP readings taken at home and that true BP level (as opposed to BP oscillations) ought to be genetically determined, a more robust within-sibling home BP correlation was expected. However, this expectation was not confirmed in the present study, and it appears that home BP determination does not enhance estimates of heritability among siblings. The data do not allow us to fully describe the usefulness of home BP readings for heritability estimates between parents and offspring because no home BP readings are available for the parents.

We analyzed the correlations of home BP readings of offspring to clinic BP readings of parents. Although there are inherent methodological concerns in the comparison of clinic to home BP readings, the analysis uses home and clinic BP readings to test the notion that repeated BP readings should predict the BP level better than a casual reading. Accordingly, an average home
Our basic finding was that white coat-induced BP variability as well as baseline BP levels are affected by gender and therefore may confound heritability estimates of clinic-determined BP levels. White coat reactivity was significantly higher in male offspring of hypertensive parents when compared with those of normotensive parents. A familial tendency for the white coat phenomenon in hypertensive families could result in overestimation of the BP level and of the incidence of true hypertension if clinic values alone are used. The sex-specific nature of white coat phenomenon deserves special attention. At age 32, 5.6% of the total Tecumseh Blood Pressure Study population had borderline hypertension, and 75% of these subjects were men. 15,16 Similarly, white coat hypertension is seen in about 6% of the population, and two thirds of these subjects are men. 14,19

We are unable to explain why daughters of hypertensive parents did not show the same tendency for the white coat phenomenon, but again note that at age 32, borderline hypertension appears to be a disorder of men. It is interesting to speculate as to the relative importance of being born male versus the environmental factors associated with being male. From our personality surveys, neither anger, anxiety, nor curiosity were distributed differently in men versus women, suggesting that the immediate perception of the environment was not an important determinant of the BP reactivity. Thus, it is likely that there is a sex-specific inheritance in the development of white coat reactivity in BP.

The present study demonstrates that both the artifact that is inherent in casual clinic BP readings and the baseline (average) appear to aggregate in first-degree relatives. Further, both white coat reactivity and baseline BP may be inherited, but this inheritance is differentially affected by gender. The use of home BP readings in population studies may identify individuals with white coat reactivity, but deleting this type of artifact from BP measurements does not provide a more accurate estimate of the BP aggregation in first-degree relatives. Research to isolate the genetic basis of hypertension must therefore consider confounders of BP measurements as well as baseline BP levels. We call attention to the white coat response as a possible distinguishing characteristic of the sons of hypertensive parents in whom hypertension may be more likely to develop in the future. The natural history of the white coat phenomenon deserves further study. Its evolution in Tecumseh will be the subject of future reports.

References

FIGURE 2. Bar graphs show comparison of parents' systolic blood pressure (BP) with offsprings' home systolic BP values by gender in 380 parent/offspring pairings (left side of figure). Difference in office and clinic systolic BP in offspring is correlated with parents' systolic BP (right side of figure).


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