Reactivity as a Predictor of Subsequent Blood Pressure
Racial Differences in the Coronary Artery Risk Development in Young Adults (CARDIA) Study

Sarah S. Knox, Jeff Hausdorff, Jerome H. Markovitz

Abstract—This study investigated the association between cardiovascular reactivity and subsequent ambulatory blood pressure in 316 black and white men and women in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Cardiovascular laboratory reactivity was examined in subjects 20 to 33 years old, and ambulatory blood pressure and heart rate were measured 3 years later. Average ambulatory pressure during a 24-hour period was regressed separately on stress reactivity and standard covariate risk factors in each race/gender subgroup. Blacks had higher blood pressure and heart rates than whites, men had higher blood pressure than women, and women had higher heart rates than men. After controlling for age, baseline systolic pressure, familial history of hypertension, smoking, alcohol consumption, body mass index, and exercise, systolic blood pressure reactivity to star tracing and cold pressor stress were significantly associated with systolic ambulatory pressure in black men and women 3 years later (partial r=0.24 to 0.37). Heart rate reactivity to video challenge and star tracing were also significantly predictive of subsequent ambulatory heart rate in blacks. Diastolic star tracing reactivity was significantly associated with subsequent ambulatory blood pressure in black women (r=0.23), and diastolic reactivity to video and star tracing were significantly predictive of ambulatory diastolic pressure in white men (r=0.39). We conclude that hyperresponsivity to stress may be a risk factor for subsequent blood pressure elevation in blacks and may be one pathway leading to the higher prevalence of hypertension in blacks than in whites. (Hypertension. 2002;40:914-919.)

Key Words: blood pressure ■ race ■ stress

Blood pressure responsiveness to mental stress has been reported to be a significant predictor of exercise-induced myocardial ischemia\(^1\) and carotid artery atherosclerosis.\(^2\) Although it has also been reported to predict stable hypertension in borderline-hypertensive individuals,\(^3\) its utility as a prognostic measure has been questioned,\(^4\) and data concerning the association between stress reactivity and ambulatory blood pressure have been equivocal.\(^5–11\) A number of these studies are difficult to interpret because they were either based solely on correlations, only examined absolute levels during reactivity, or did not control for relevant covariates.\(^12–15\) There has been little research examining the effect of race and gender on the association between reactivity and subsequent ambulatory pressure, despite the fact that previous research has been fairly consistent in showing race as well as gender differences in reactivity and blood pressure measured at a single sitting.\(^16–19\)

The goal of the present study was to investigate whether cardiovascular reactivity to mental stress predicted subsequent ambulatory blood pressure differently in race/gender subgroups. Ambulatory blood pressure was chosen because it better reflects blood pressure variation and levels throughout the day than clinical measurements made at a single point in time.\(^20\) A second objective was to test whether previously reported higher nighttime blood pressure in blacks\(^21\) would be verified in a young, healthy cohort.

Methods

The Coronary Artery Risk Development in Young Adults Study (CARDIA) is an ongoing, prospective, epidemiologic study, conducted at four sites. A detailed description of the study design and recruitment methods can be found in an earlier publication.\(^22\) The data presented in this report are from a substudy conducted at one site, Birmingham, Alabama. The protocol was approved by the institutional review board, procedures followed were in accordance with institutional guidelines, and informed consent was obtained from each participant.

Subjects

Because of the high cost and time-consuming nature of cardiovascular reactivity testing and ambulatory blood pressure monitoring, these measurements were performed only at one site, Birmingham. The reactivity testing was performed in the second examination year, 1987, when the subjects were 20 to 33 years old. Ambulatory blood pressure monitoring was performed at the subsequent examination, in 1990, when the median age was 30 (range, 23 to 36 years old). A list of 400 Alabama participants consisting of 100 individuals from each of the four CARDIA sites were studied.
randomly selected from each of the four race/gender subgroups (black and white men and women) was generated at the CARDIA Coordinating Center. Partially because of the reluctance of already-burdened healthy participants to submitting to yet another long procedure, and partially because of the nature of certain types of employment (delivery people, truck drivers, and so forth, who could not stop and stretch their arms every 20 minutes for ambulatory measurements), it was not possible to recruit all 400 people. The total sample size was 316 (147 men and 169 women). There were 204 blacks (88 men and 116 women) and 112 whites (59 men and 53 women).

**Procedure**

**Reactivity Testing**

The procedure for reactivity testing has been described in detail elsewhere.\(^{23}\) There were three tasks: a video game (Atari Breakout, Atari Corporation), a mirror star-tracing task, and a cold pressor task elsewhere.\(^{23}\) There were three tasks: a video game (Atari Breakout, Atari Corporation), a mirror star-tracing task, and a cold pressor task.

Ambulatory blood pressure and heart rate were monitored for 24 hours with a Suntech Accutracker II, which was inflated approximately every 20 minutes. The inflation schedule was variable, to reduce the effects of anticipation. If any value outside preset limits (>220 or <80 mm Hg, systolic; and >130 or <40 mm Hg, diastolic) was detected during a reading, a rejection code was given for that measurement and another measurement was immediately made. In addition, a change of 50 mm Hg in systolic pressure, of 40 mm Hg in diastolic pressure, or of 50 mm Hg in pulse pressure also triggered a rejection code and a new reading.

Blood pressure dipping was defined as the difference between average daytime pressure and the average nighttime pressure.

**Statistical Methods**

To isolate the effects of blood pressure reactivity from other factors that are known to influence blood pressure levels, analyses were calculated by regressing ambulatory blood pressure on blood pressure reactivity, controlling for average blood pressure during an 8-minute baseline habituation period; smoking status (smoker, non-smoker, ex-smoker); familial history of hypertension in one or both parents; alcohol consumption (self-report) in milliliters per day; body mass index (BMI); and physical activity score calculated from the physical activity score.

**Results**

**Race/Gender Differences in Ambulatory Pressure**

Because ambulatory blood pressure was not measured at the examination in which the reactivity testing was done, the baseline measures for blood pressure at the reactivity examination consist of the average of 4 resting baseline measures. These results can be seen in Table 1. ANOVA revealed no significant race differences in blood pressure or heart rate; however, the race differences in ambulatory systolic pressure showed a tendency toward significance \(P<0.06\). Black and white men did not differ significantly, but white women had significantly lower pressure than all three groups, accounting for most of the borderline significance.

A comparison of mean ambulatory blood pressure by race and gender at different times of the day, 3 years later, can be seen in Tables 2 and 3. Blacks had higher overall systolic and diastolic blood pressure and heart rate than whites and higher pressure during each of the separate periods of the day. These differences were all significant except for diastolic blood pressure and heart rate in the morning. There were also significant gender differences in blood pressure, which were consistent across time periods with the exception of morning diastolic pressure. Men had significantly higher mean systolic and diastolic pressures than women. With respect to heart rate, blacks had

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**TABLE 1. Descriptive Statistics: Cohort of 316 Men and Women**

<table>
<thead>
<tr>
<th></th>
<th>Black Men (n=88)</th>
<th>White Men (n=59)</th>
<th>Black Women (n=116)</th>
<th>White Women (n=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>29.6 (3.5)</td>
<td>30.7 (3.6)</td>
<td>29.7 (3.9)</td>
<td>30.8 (3.6)</td>
</tr>
<tr>
<td>Diastolic (Exam 2)*</td>
<td>70.8 (1.2)</td>
<td>69.6 (1.5)</td>
<td>68.8 (1.0)</td>
<td>68.7 (1.5)</td>
</tr>
<tr>
<td>Systolic (Exam 2)*</td>
<td>119.1 (1.1)</td>
<td>116.3 (1.3)</td>
<td>111.1 (0.9)</td>
<td>107.2 (1.4)</td>
</tr>
<tr>
<td>Education, y</td>
<td>13.6 (1.9)</td>
<td>14.3 (2.6)</td>
<td>13.9 (1.9)</td>
<td>14.4 (2.4)</td>
</tr>
<tr>
<td>Smokers, %</td>
<td>36.5</td>
<td>32.7</td>
<td>25.0</td>
<td>37.8</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.7 (4.3)</td>
<td>26.6 (5.0)</td>
<td>27.7 (5.8)</td>
<td>25.0 (5.5)</td>
</tr>
<tr>
<td>Alcohol users, %</td>
<td>78.4</td>
<td>84.7</td>
<td>57.8</td>
<td>75.4</td>
</tr>
<tr>
<td>Alcohol, mL/day (users)</td>
<td>22.2 (32.1)</td>
<td>21.4 (40.5)</td>
<td>11.9 (23.9)</td>
<td>7.2 (12.9)</td>
</tr>
<tr>
<td>Antihypertensive medication, n</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>51.2 (14.5)</td>
<td>41.5 (9.5)</td>
<td>54.0 (13.1)</td>
<td>52.5 (13.5)</td>
</tr>
<tr>
<td>LDL-C, mg/dL</td>
<td>116.1 (31.2)</td>
<td>121.2 (30.4)</td>
<td>105.1 (29.0)</td>
<td>110.6 (31.4)</td>
</tr>
<tr>
<td>Total cholesterol mg/dL</td>
<td>184.1 (35.4)</td>
<td>186.8 (33.5)</td>
<td>172.4 (29.3)</td>
<td>181.3 (33.8)</td>
</tr>
</tbody>
</table>

*Mean of 4 resting measures.
higher average ambulatory heart rate than whites (82 versus 79 beats per minutes, \( P < 0.02 \)).

**Laboratory Reactivity as a Predictor of Subsequent Ambulatory Pressure and Heart Rate**

After controlling for age, baseline systolic pressure, familial history of hypertension, BMI, physical activity, smoking status, alcohol consumption, and eliminating the persons receiving antihypertensive medication, star tracing and cold pressor systolic reactivity in black men and women were significantly associated with mean overall systolic ambulatory pressure 3 years later. There were no significant associations between systolic reactivity and subsequent systolic ambulatory pressure in whites. With respect to diastolic pressure, reactivity to star tracing was significantly associated with overall diastolic ambulatory pressure in black women, and diastolic reactivity to video and star tracing was significantly associated with subsequent ambulatory pressure in white men. These results can be seen in Tables 4 and 5.

After controlling for baseline heart rate and other covariates, video and star tracing heart rate reactivity in the laboratory were significantly associated with subsequent ambulatory heart rate in black men and women only. These results can be seen in Table 6.

Because an earlier CARDIA report on the full cohort reported that baseline heart rate was a predictor of hypertension across 5 examinations, average ambulatory pressure at examination 3 was regressed on baseline heart rate at examination 2, adjusting for examination 2 blood pressure, as was done in the earlier analyses. There were no significances, probably because of the limited range of time.

Dipping was defined as average daytime pressure minus nighttime pressure. There were no racial differences in nighttime dipping of blood pressure.

**Discussion**

The use of ambulatory blood pressure monitoring has increased steadily with increasing evidence that blood pressure measured in a single session has limited generalizability to average daytime levels, and with the knowledge that ambulatory measures are more closely correlated with cardiovascular risk than multiple office blood pressure measurements. The rationale for investigating cardiovascular reactivity in relation to subsequent ambulatory pressure is the long-standing hypothesis that if an individual has an increased magnitude of response in stressful situations, and this type of response occurs fairly often, secondary vascular changes in the form of an increase in wall-to-lumen ratio in hypertensive resistance vessels will occur, causing an increase in peripheral resistance accompanied by permanent blood pressure elevation. This is called the “recurrent activation model.”

In support of this theory, it has been shown in a follow-up study lasting 45 to 57 years that blood pressure reactivity to cold pressor stress, one of the tasks investigated in the current study, is a strong predictor of subsequent hypertension. Based on these data, the fact that blacks in our study were more reactive to cold pressor than whites would suggest that they may be more likely to have hypertension. However, controlled investigations of reactivity with the use of animal models have demonstrated that the associations are not linear, and that high blood pressure reactors do not get hypertension without the addition of other genetic or environmental factors. Isolating influences of single factors on blood pressure is far more difficult to do in humans because not all factors influencing blood pressure can be experimentally controlled. The aim of the present study was simply to isolate the effects of cardiovascular reactivity as much as possible from parental history of hypertension and health-related behaviors that influence blood pressure, so that the association between reactivity and subsequent blood pressure could be measured independent of these influences. In addition to controlling for baseline blood pressure, age, and parental history, we adjusted for smoking, physical activity, and alcohol consumption. Dietary data were not collected at the ambulatory pressure examination, so BMI was used as the best proxy for energy intake and expenditure.

Because blood pressure regulation occurs at several levels, for example, in the central nervous system, at the bulbar level and locally (eg, heart, resistance vessels), pressure elevation can be, and usually is, a result of multiple interacting factors involving genes, biological factors, and environmental influences. Even though identification of hypertension genotypes has not progressed to the point of enabling investigations of environmental interactions with a specific genotype, the characterization of phenotypes is progressing. The Tecumseh Study reported that a subgroup of 37% of its borderline hypertensives had hyperkinetic circulation, displaying high sympathetic arousal characterized by increased heart rate, cardiac index, forearm blood flow and plasma norepinephrine. A hyperkinetic phenotype would be consistent with a larger magnitude of response to laboratory stress. Unfortunately, the Tecumseh study did not identify subjects by race or gender, making it impossible to know whether racial differences existed. Even though the current study controlled for parental history of hypertension, we could not control for parental genotype, or even parental phenotype, and our results still beg the question. What we have shown is that racial differences exist and appear to be independent of relevant health related behaviors and parental history of hypertension. Whether the racial differences were due to genotype, hyperalertness resulting from more frequently oc-

### Table 2. Ambulatory Systolic Pressure

<table>
<thead>
<tr>
<th></th>
<th>Black Men</th>
<th>White Men</th>
<th>Black Women</th>
<th>White Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>123.3</td>
<td>118.4</td>
<td>114.7</td>
<td>111.9</td>
</tr>
<tr>
<td>Afternoon</td>
<td>111.6</td>
<td>103.5</td>
<td>103.9</td>
<td>97.7</td>
</tr>
<tr>
<td>Evening</td>
<td>125.5</td>
<td>120.4</td>
<td>114.8</td>
<td>111.5</td>
</tr>
<tr>
<td>Night</td>
<td>112.6</td>
<td>104.0</td>
<td>103.4</td>
<td>97.7</td>
</tr>
</tbody>
</table>

### Table 3. Ambulatory Diastolic Pressure

<table>
<thead>
<tr>
<th></th>
<th>Black Men</th>
<th>White Men</th>
<th>Black Women</th>
<th>White Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>73.1</td>
<td>72.1</td>
<td>71.4</td>
<td>69.5</td>
</tr>
<tr>
<td>Afternoon</td>
<td>61.7</td>
<td>58.3</td>
<td>58.6</td>
<td>55.8</td>
</tr>
<tr>
<td>Evening</td>
<td>71.9</td>
<td>67.8</td>
<td>68.1</td>
<td>66.3</td>
</tr>
<tr>
<td>Night</td>
<td>61.9</td>
<td>58.2</td>
<td>58.5</td>
<td>55.6</td>
</tr>
</tbody>
</table>
burring stress, or a combination of gene/environment interactions cannot be answered and will have to await future studies.

With respect to the association between blood pressure reactivity and hypertension, one perspective has been that enhanced blood pressure reactivity may be an indication, rather than a predictor of hypertension, since it has been observed independent of increased heart rate reactivity. This is supported by rat models of hypertension, which have shown that early elevations in heart rate and relatively high stress-induced increases in heart rate are a general distinguishing characteristic of animals at high risk for hypertension. Our results show that though the average blood pressure of both groups was normal, ambulatory heart rate and blood pressure were higher in blacks than in whites, and blacks showed more consistent associations between blood pressure and heart rate reactivity and subsequent ambulatory measures than whites. This combination would be consistent with the hyperkinetic phenotype described in Tecumseh. In that study, hyperreactors at 32 years of age had normal blood pressure as children and young adults but elevated childhood heart rates, indicating that increased heart rate preceded the elevated blood pressure. Moreover, in CARDIA, an earlier study analyzing the entire cohort reported that baseline heart rate (clinical measurement) was an independent predictor of subsequent diastolic blood pressure (clinical measurements) across 5 examination periods in whites and in black men. Although heart rate did not predict blood pressure in the subset analyzed in the current study, this may have been due to the diminished time frame (3 years instead of 10 in the earlier study). The fact that ambulatory heart rate was measured as a pulse rather than with chest electrodes, both during reactivity testing and ambulatory monitoring. The second is that the rest periods between reactivity tasks were only 3 minutes long, meaning that recovery time may have been insufficient. However, the latter caveat may actually have made the stressors more similar to real-life situations (eg, a stressful workday) than a

### Table 4

<table>
<thead>
<tr>
<th></th>
<th>Black Men</th>
<th></th>
<th></th>
<th>Black Women</th>
<th></th>
<th></th>
<th>White Women</th>
<th></th>
<th></th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>β</strong></td>
<td></td>
<td></td>
<td><strong>β</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Video SBP</td>
<td>0.21</td>
<td>0.14</td>
<td>0.14</td>
<td>0.13</td>
<td>0.17</td>
<td>0.46</td>
<td>0.16</td>
<td>0.11</td>
<td>0.15</td>
<td>0.18</td>
</tr>
<tr>
<td>Star SBP</td>
<td>0.25</td>
<td>0.13</td>
<td>0.05</td>
<td>0.16</td>
<td>0.13</td>
<td>0.20</td>
<td>0.25</td>
<td>0.11</td>
<td>0.03</td>
<td>0.11</td>
</tr>
<tr>
<td>Cold SBP</td>
<td>0.23</td>
<td>0.10</td>
<td>0.03</td>
<td>0.15</td>
<td>0.09</td>
<td>0.11</td>
<td>0.22</td>
<td>0.08</td>
<td>0.01</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*After controlling for age, baseline systolic pressure, familial history of hypertension, smoking status, alcohol consumption, body mass index, and physical activity. SE indicates standard error; SBP, systolic blood pressure.

Because the limited range of blood pressure in this cohort actually reduces power to detect associations, and power is further reduced by the number of covariates in the equations, small but true differences could have gone undetected. However, these facts also suggest that the significant results that were found probably are robust and reflect true differences. The young age of CARDIA participants and the prospective design of the study have the advantage of providing a unique opportunity for identifying risk factors before the emergence of manifest disease. The fact that these analyses also controlled for baseline blood pressure, parental history of hypertension, and health-related behaviors raises the possibility that enhanced cardiovascular reactivity to acute stress has an independent association with subsequent blood pressure and may be a risk factor for hypertension in blacks.

Although it has earlier been reported that blacks demonstrated less blood pressure dipping than whites, those results were not replicated in the current study. This may be due to the fact that racial differences in dipping are partially mediated by parental status, which was controlled for in the present analyses, or it may also be that one measure of nighttime dipping is not a reliable reflection of nighttime blood pressure. A small study of 21 individuals who were monitored twice with ambulatory blood pressure, showed little test-retest reliability across the two settings with respect to nighttime dipping. In the current study, only one night was available for analysis, raising the question of whether the measure was reliable.

There are two limitations to the present results. One is that heart rate was measured as a pulse rather than with chest electrodes, both during reactivity testing and ambulatory monitoring. The second is that the rest periods between reactivity tasks were only 3 minutes long, meaning that recovery time may have been insufficient. However, the latter caveat may actually have made the stressors more similar to real-life situations (eg, a stressful workday) than a
protocol allowing long, restful recovery between tasks. In any event, to the extent that this caused bias, it was the same for all groups, meaning that the stronger association of reactivity with subsequent ambulatory pressure in blacks, particularly black women, is still a meaningful distinction. Whether these differences are indicative of greater vulnerability to specific environmental stressors in blacks than in whites or whether the association occurs in conjunction with more frequently occurring or sustained stress cannot be answered by the data presented in this study but warrants further investigation.

**Perspectives**

Although average ambulatory pressure in both blacks and whites in this young adult cohort was within the normal range, systolic and heart reactivity to laboratory stressors were more predictive of subsequent ambulatory measures in blacks than in whites. These results were independent of resting measures of blood pressure, age, parental history of hypertension, physical activity, smoking, alcohol consumption, and body mass index. Because average blood pressure was normal but heart rate was higher in blacks than in whites, we interpret the hyperreactivity to acute stress as a precursor rather than result of elevated blood pressure. Seen in the context of other findings, these results may indicate that blacks in this study had a hyperkinetic phenotype. Future studies of gene/environment interactions are needed to elucidate this issue.

**Acknowledgments**

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**References**


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