Racial Differences in Hemodynamic Responses to Environmental Thermal Stress Among Adolescents

Robert M. Kelsey, PhD; Bruce S. Alpert, MD; Stephen M. Patterson, PhD; Marie Barnard, BA

Background—Previous studies by our laboratory and others have shown that blood pressure (BP) responses to many short-term laboratory stressors are greater in black than in white children. We sought to determine the cardiac and vascular contributions to these differences in BP reactivity and whether racial differences in vascular reactivity involve excessive vasoconstriction or deficient vasodilation.

Methods and Results—We evaluated BP, heart rate, and impedance cardiographic measures of preejection period (PEP) and total peripheral resistance (TPR) in healthy black (n=76) and white (n=60) adolescents (mean age, 14.8 years) during passive exposure to a vasoconstrictive cold chamber (8°C to 10°C) and a vasodilatory heat chamber (40°C to 42°C). Results indicated greater decreases in PEP and increases in TPR in blacks than whites during cold exposure (P<0.05) but no group differences during heat exposure. Covariance analyses indicated that the racial differences during cold exposure probably reflected greater β-adrenergic cardiac reactivity and α-adrenergic vasoconstrictive reactivity in blacks than whites.

Conclusions—Blacks and whites exhibited comparable myocardial and vasodilatory responses to heat stress, but blacks exhibited heightened myocardial and vasoconstrictive reactivity to cold stress. These results suggest that the locus of racial differences in vascular reactivity involves vasoconstrictive rather than vasodilatory function. The pattern of racial differences during cold stress raises the possibility that both myocardial and vasoconstrictive mechanisms may contribute to the increased risk of hypertension in blacks. (Circulation. 2000;101:2284-2289.)

Key words: stress • vasoconstriction • vasodilation • cardiac output • hemodynamics

The prevalence of essential hypertension among young adult black Americans is ~2 times greater than that for white Americans.1-2 Although the reasons for this increased risk among blacks are largely unknown, cardiovascular reactivity to stress has been identified as a possible mechanism, because numerous studies of adults and children have demonstrated racial differences in hemodynamic responses to a variety of stressors.3-10

One physical stressor frequently used in hypertension research is some variation of the cold pressor task, a potent stimulus for α-adrenergic vasoconstriction, which typically involves immersion of a limb in ice water or placement of a bag of ice water on the forehead.11-15 A number of studies have shown that the magnitude of cardiovascular responses during cold pressor is related to future resting blood pressure (BP) and the development of hypertension.16-18 Furthermore, studies of both adults and children indicate that increases in total peripheral resistance (TPR) during various limb and forehead cold pressor tasks are greater in blacks than in whites, suggesting a possible racial difference in vascular reactivity to cold stress.5,6,19-25 To the best of our knowledge, there has been no investigation of racial differences in cardiovascular reactivity to whole-body cold exposure (CE).

Racial differences in TPR reactivity are not restricted to cold pressor tasks. Studies of both adults and children have reported greater TPR increases, or smaller TPR decreases, in blacks than in whites during various stressors that typically elicit overall peripheral vasodilation, including dynamic exercise, video game challenge, public speaking, and competitive reaction time tasks.5,6,20-23 Consequently, it is not clear whether racial differences in vascular reactivity involve overzealous vasoconstriction, underzealous vasodilation, or both. Therefore, the present study investigated possible racial differences in cardiac and vascular reactivity during whole-body exposure to a vasoconstrictive cold environment and a vasodilatory hot environment, which elicit opposite changes in sympathetic vasoconstrictor tone.12,26

Methods

Subjects
Normotensive black (n=76; 36 male and 40 female subjects) and white (n=60; 27 male and 33 female subjects) adolescents (mean age, 14.8±1.6 years) were recruited from the Memphis, Tennessee, area for a project on early markers of hypertension. Children identified as having significant medical conditions or taking medications that would affect BP responses were excluded from the study. Informed consent and assent were obtained from the adoles-
cent and the parent or legal guardian. The University of Tennessee Institutional Review Board approved the protocol. Subjects received $60 for participating in the project.

**Cardiovascular Measures**

Systolic BP (SBP) and diastolic BP (DBP) were measured during each rest and task period with a SunTech automated blood pressure monitor (model 4240, SunTech Medical Instruments, Inc) with a cuff appropriate to the subject’s arm size. Mean arterial pressure (MAP) was calculated as \((1/3 \times \text{SBP}) + (2/3 \times \text{DBP})\). Preejection period (PEP), heart rate (HR), and cardiac output (CO) were measured with a Minnesota impedance cardiograph (model 304B, Instrumentation for Medicine, Inc) and a tetrapolar band-electrode system in accordance with established guidelines. Impedance cardiographic data were acquired, processed, and scored with commercial software (COP 4.0, Bio-Impedance Technology, Inc). TPR was derived from concurrent measures of CO and BP by TPR = (MAP/C0)×80.

**Thermal Stressors**

A walk-in thermal chamber in a laboratory of the Adult Clinical Research Center (A-CRC) served as the CE stimulus. A refrigerated ventilation system maintained the cold chamber at a constant temperature of 8°C to 10°C (85% to 95% humidity). The duration of CE was 10 minutes. A second ventilated walk-in thermal chamber directly opposite the cold chamber in the A-CRC laboratory served as the heat exposure (HE) stimulus. An electric forced-air heater installed in the ceiling, facing away from the subject, maintained the hot chamber at a constant temperature of 40°C to 42°C (35% to 45% humidity). The duration of HE was 20 minutes. The temperatures and exposure durations in the cold and hot chambers were based on previous studies of healthy children and children with chronic diseases during rest and strenuous exercise in ambient temperatures between 5°C and 42°C. While in the chambers, subjects were continuously observed through large observation windows.

**Procedure**

Informed consent and assent were obtained in the cardiovascular laboratory of the Pediatric Clinical Research Center (P-CRC). Subjects changed into a hospital gown after removing their shoes, shirt, and other upper outer garments. They were not required to remove lower garments. Height and weight were then measured, and electrodes for electrocardiography and impedance cardiography were applied. After performing several laboratory tasks in the P-CRC, subjects were taken by wheelchair to the laboratory of the A-CRC that housed the thermal chambers. The order of presentation of CE and HE was counterbalanced, with proportionate random assignment of black and white male and female subjects to each order. The following description is for CE followed by HE.

Subjects were connected to the automated BP monitor, an ECG, and the impedance cardiograph at the A-CRC and were seated in a chair in the A-CRC laboratory area (22°C ambient temperature) where they rested quietly for a 20-minute baseline period. Minute-by-minute baseline values for all cardiovascular measures were recorded during the last 3 minutes of this period. Subjects were then seated in the cold chamber and instructed to rest quietly but remain awake during the 10-minute CE period. Cardiovascular measures were recorded during minutes 1, 2, 5, 6, 9, and 10 of CE. After CE, subjects returned to the euthermic laboratory area for another 20-minute baseline period. Cardiovascular baseline measures were again recorded during the last 3 minutes of this period. After the second baseline period, subjects were seated in the hot chamber and instructed to rest quietly but remain awake during the 20-minute HE period. Cardiovascular measures were recorded during minutes 1, 2, 5, 6, 9, 10, 14, 15, 19, and 20 of HE. After HE, subjects returned to the euthermic laboratory area, where the electrodes were removed and any remaining questions by the subject and/or parent were answered. Once the subjects stated that they were again comfortable, they were escorted back to the P-CRC to complete the remainder of the study protocol.

**Data Reduction and Analysis**

Baseline means were computed for each cardiovascular measure by averaging data from the last 3 minutes of each baseline period. For CE, 3 mean scores were computed for each cardiovascular measure by averaging values from contiguous pairs of minutes (minutes 1 and 2, minutes 5 and 6, etc). Similarly, 5 mean scores were computed for each cardiovascular measure during HE. Cardiovascular reactivity was evaluated by subtracting the means for the appropriate pretask baseline period from the means for each time block during CE and HE. Preliminary analyses indicated that the order of presentation of CE and HE had a negligible impact on cardiovascular reactivity, so all analyses were collapsed over order. The cardiovascular data were analyzed in a series of multivariate repeated-measures trend analyses. The first set of analyses addressed baseline cardiovascular activity in a 2(race)×2(sex)×3(time block) design. The second set addressed cardiovascular reactivity during CE in a 2(race)×2(sex)×3(time block) design, and the third set addressed cardiovascular reactivity during HE in a 2(race)×2(sex)×5(time block) design. We conducted separate analyses for CE and HE because of the different number of time blocks for the 2 tasks and because we were interested primarily in racial differences in the patterns of cardiovascular reactivity elicited by vasoconstrictive and vasodilatory stimuli, rather than racial differences in the CE-HE response differential implied by a race-by-task interaction. For all analyses, the cardiovascular measures were divided into 2 subsets for separate analysis to control type I error while maximizing statistical power and minimizing potential multicollinearity. Two BP measures (SBP and DBP) made up 1 subset, whereas 3 cardiovascular measures that are under direct autonomic control (HR, PEP, and TPR) made up the second subset. This latter subset provides information on possible parasympathetic, \(\beta\)-adrenergic, and \(\alpha\)-adrenergic contributions to group differences in cardiovascular reactivity. As in previous research, all analyses included age and body mass index (BMI) as covariates. A value of \(P<0.05\) (2-tailed) was considered significant.

Significant multivariate effects in the CE and HE analyses were followed by univariate F tests and F-to-remove tests. The former tests permit comparisons with previous research on cardiovascular reactivity to stress. The latter tests, which are more appropriate in a multivariate context, use ANCOVA techniques to determine the unique contribution of each cardiovascular measure to a multivariate effect after controlling for the other measures in the subset. For example, controlling for HR and TPR in an F-to-remove test on PEP reactivity should control statistically for preload and afterload effects on left ventricular performance, leaving primarily residual \(\beta\)-adrenergic sympathetic effects. Conversely, controlling for PEP and HR in an F-to-remove test on TPR reactivity should control statistically for \(\beta\)-adrenergic and indirect parasympathetic effects on the vasculature, leaving primarily residual \(\alpha\)-adrenergic vasoconstrictive effects. Finally, controlling for PEP and TPR in an F-to-remove test on HR reactivity should control statistically for most sympathetic effects on the heart, leaving primarily residual parasympathetic effects.

**Results**

**Baseline**

Table 1 presents age, BMI, and baseline cardiovascular data for each group. There were no significant group differences in age, BMI, or baseline BP. However, there were significant differences in baseline cardiac measures as a function of sex (multivariate \(P<0.05\)) and race (multivariate \(P<0.005\)). Overall, PEP was longer in male than in female subjects (\(P<0.05\)), and HR was slower in blacks than in whites (\(P<0.005\)). The latter effect was qualified by a race-by-sex interaction (\(P<0.0005\)), indicating that the lower resting HR of blacks occurred primarily in male subjects. There were no group differences across baseline periods.
TABLE 1. Age, BMI, and Baseline Cardiovascular Levels in Black and White Adolescents

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
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<th>White</th>
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<th>Group Differences</th>
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<tr>
<td></td>
<td>Male (n=36)</td>
<td>Female (n=40)</td>
<td>Male (n=27)</td>
<td>Female (n=33)</td>
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<tr>
<td>Age, y</td>
<td>15.0±0.9</td>
<td>14.2±2.1</td>
<td>15.0±1.1</td>
<td>14.9±1.6</td>
<td>NS</td>
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<tr>
<td>BMI, kg/m²</td>
<td>21.2±2.4</td>
<td>21.8±2.9</td>
<td>21.3±3.1</td>
<td>20.9±3.1</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-CE baseline</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>127±19</td>
<td>118±15</td>
<td>134±27</td>
<td>126±18</td>
<td>NS</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>69±10</td>
<td>69±9</td>
<td>70±8</td>
<td>69±7</td>
<td>NS</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>74±10</td>
<td>87±10</td>
<td>89±13</td>
<td>85±12</td>
<td></td>
</tr>
<tr>
<td>PEP, ms</td>
<td>141±15</td>
<td>132±17</td>
<td>133±13</td>
<td>131±15</td>
<td></td>
</tr>
<tr>
<td>TPR, dyne · s · cm⁻²</td>
<td>1529±334</td>
<td>1287±312</td>
<td>1402±354</td>
<td>1502±504</td>
<td>NS</td>
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<tr>
<td>Pre-HE baseline</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>129±21</td>
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<td>NS</td>
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<td>DBP, mm Hg</td>
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<td>68±8</td>
<td>72±9</td>
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<td>NS</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>72±12</td>
<td>82±10</td>
<td>85±15</td>
<td>82±12</td>
<td></td>
</tr>
<tr>
<td>PEP, ms</td>
<td>142±16</td>
<td>131±17</td>
<td>133±16</td>
<td>130±17</td>
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<tr>
<td>TPR, dyne · s · cm⁻²</td>
<td>1598±341</td>
<td>1383±370</td>
<td>1526±386</td>
<td>1573±534</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD.

Stress

Overall Reactivity

Table 2 presents the adjusted means for overall cardiovascular reactivity during CE and HE for each group, along with the adjusted pooled SD for each cardiovascular measure. Both thermal stimuli elicited significant decreases in PEP (both P<0.0005), but they had opposite effects on SBP, DBP, and TPR, with CE eliciting increases and HE eliciting decreases in each case (all P<0.0005). Thus, as expected, CE elicited a vasoconstrictive response, whereas HE elicited a vasodilatory response. Although HR decelerated significantly during CE (P<0.0005), it did not deviate from baseline during HE (P=NS). There were no significant group differences in overall BP reactivity during either stressor.

There were significant racial differences in overall cardiovascular reactivity during CE (multivariate P<0.006). Univariate tests indicated that PEP shortened significantly more in blacks than in whites (P<0.005) and that blacks showed marginally less HR deceleration and marginally greater TPR elevation compared with whites (both P<0.09). Subsequent F-to-remove tests revealed that the racial difference in PEP reactivity remained significant after controlling for HR and TPR [F(1, 128)=6.79, P<0.01] and that the racial difference in TPR reactivity became stronger after controlling for HR and PEP [F(1, 128)=3.96, P<0.05]. The racial difference in HR deceleration disappeared after controlling for PEP and TPR [F(1, 128)<1, P=NS]. As the adjusted means in the Figure indicate, the overall reduction in PEP and elevation in TPR during CE were significantly greater in blacks than in whites. Although the multivariate test failed to reveal significant sex differences in overall cardiovascular reactivity during CE, there was a univariate effect for PEP reactivity.

TABLE 2. Adjusted Means (Controlling for Age and BMI) and Adjusted Pooled SD for Overall Cardiovascular Reactivity (Changes From Baseline) During CE and HE in Black and White Adolescents

<table>
<thead>
<tr>
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<td>Male</td>
<td>Female</td>
<td></td>
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<td></td>
<td>Pooled SD</td>
<td>Group Differences</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>6.9</td>
<td>5.7</td>
<td>1.5</td>
<td>6.1</td>
<td>10.1</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>5.9</td>
<td>4.0</td>
<td>2.3</td>
<td>4.4</td>
<td>6.7</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>−4.4</td>
<td>−5.8</td>
<td>−8.6</td>
<td>−6.1</td>
<td>7.7</td>
</tr>
<tr>
<td>PEP, ms</td>
<td>−8.5</td>
<td>−4.3</td>
<td>−3.3</td>
<td>−1.5</td>
<td>8.0</td>
</tr>
<tr>
<td>TPR, dyne · s · cm⁻²</td>
<td>139.0</td>
<td>218.2</td>
<td>109.1</td>
<td>93.4</td>
<td>253.4</td>
</tr>
<tr>
<td>HE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>−4.7</td>
<td>−8.9</td>
<td>−5.9</td>
<td>−4.3</td>
<td>11.0</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>−5.3</td>
<td>−5.6</td>
<td>−6.7</td>
<td>−6.4</td>
<td>5.5</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>0.4</td>
<td>−0.4</td>
<td>0.9</td>
<td>1.5</td>
<td>5.9</td>
</tr>
<tr>
<td>PEP, ms</td>
<td>−7.8</td>
<td>−1.8</td>
<td>−4.1</td>
<td>−1.6</td>
<td>7.8</td>
</tr>
<tr>
<td>TPR, dyne · s · cm⁻²</td>
<td>−193.8</td>
<td>−120.9</td>
<td>−208.1</td>
<td>−125.8</td>
<td>212.3</td>
</tr>
</tbody>
</table>
The present results extend prior pediatric and adult research on racial differences in cardiovascular reactivity to cold stimuli. A number of previous studies found greater blood pressure and vascular reactivity during limb and forehead cold pressor tasks in blacks compared with whites. The present study is the first to demonstrate racial differences in cardiac and vascular reactivity during whole-body cold stress. Traditional laboratory cold pressor tasks (ie, limb or forehead) typically involve limited regional body surface exposure to very cold and often painful ice-water slurries (≈4°C), so it was unclear whether the cardiovascular effects of such tasks would generalize to whole-body CE. The results of this study, therefore, not only demonstrate further racial differences in vascular reactivity to cold stimuli but also help bridge the gap between traditional laboratory cold pressor tasks and naturalistic environmental phenomena.

The effects of whole-body CE on TPR and BP were similar to those for various limb and forehead cold pressor tasks, all of which evoke peripheral vasoconstriction. However, limb and forehead cold pressor tasks tend to evoke divergent cardiac responses. Hand and foot cold pressor tasks typically elicit HR acceleration and some increase in myocardial performance (eg, PEP shortening), whereas forehead cold pressor tasks tend to elicit HR deceleration, characteristic of the "dive reflex," with little change in myocardial performance. The cardiac effects of whole-body CE involved HR deceleration and PEP shortening, suggesting an amalgam of the cardiac effects of limb and forehead cold stimuli. Thus, the cardiovascular response pattern elicited by whole-body cooling may be a synthesis of the patterns evoked by the limited regional cooling of limb and forehead cold pressor tasks.

Our whole-body CE protocol allowed the duration of CE to be extended safely and ethically beyond what is acceptable with typical cold pressor tasks. This permitted a more thorough evaluation of the time course of cardiovascular reactivity during cold stress. Although TPR reactivity increased over time during CE, cardiac reactivity declined in a manner similar to the typical decline in cardiac reactivity during repeated psychological stress. Thus, the cardiac response during CE might have reflected the psychological stress of CE. In contrast, the myocardial and vasodilatory effects of HE were relatively stable over time.

The racial difference in overall PEP reactivity during CE remained significant after controlling for HR and TPR in the F-to-remove test, suggesting that β-adrenergic effects, rather than preload or afterload, were responsible for the heightened PEP reactivity in Blacks. The marginal racial difference in overall HR reactivity during CE disappeared after controlling for PEP and HR in the F-to-remove test, suggesting that sympathetic rather than parasympathetic effects were primarily responsible for the diminished HR deceleration in blacks. In contrast, the racial difference in overall TPR reactivity during CE became stronger after controlling for PEP and HR in the F-to-remove test, suggesting that β-adrenergic vasoconstriction partially masked α-adrenergic vasoconstriction in Blacks. Taken together, these results suggest that blacks exhibited both heightened β-adrenergic myocardial and α-adrenergic vasoconstrictive reactivity to cold stress. This pattern is strikingly similar to the results of a β-adrenergic blockade study of undergraduate men, which indicated that...
both β-adrenergic myocardial and α-adrenergic vasoconstrictive influences were greater in blacks than in whites.

In contrast to CE, blacks and whites exhibited comparable myocardial and vasodilatory responses to HE. Thus, our data indicate that the locus of racial differences in vascular reactivity involves vasoconstrictive rather than vasodilatory function. Moreover, inasmuch as cold stress induces peripheral vasoconstriction through an increase in sympathetic stimulation of α-adrenergic receptors,26 and heat stress induces peripheral vasodilation through a withdrawal of such sympathetic stimulation,26 our findings imply a racial difference in α-adrenergic receptor function rather than a difference in sympathetic efferent discharge. Alternatively, these results may reflect racial differences in nonadrenergic vasoconstrictive mechanisms, involving substances such as angiotensin II or endothelin-1.35,36

In addition to racial differences in cardiovascular reactivity, we found sex differences in PEP and TPR reactivity. PEP decreases during CE and HE were greater in male than in female subjects, suggesting a general augmentation of β-adrenergic myocardial reactivity in male subjects. These results are consistent with previous research indicating greater SBP and epinephrine reactivity in male than in female subjects.37,38 The decrease in TPR during HE was also greater in male than in female subjects, suggesting either enhanced β-adrenergic vasodilation or enhanced withdrawal of α-adrenergic vasoconstriction in male subjects. Consistent with evidence of diminished vascular adrenergic receptor function in female subjects,29 F-to-remove tests indicated that both mechanisms probably contributed to the sex difference in TPR reactivity.

There are important racial differences in morbidity and mortality from essential hypertension, with a disproportionate incidence in black Americans.1,2 Determining the causes of hypertension is crucial to the design and implementation of improved primary prevention and intervention strategies. The discovery of reliable early markers for later-onset hypertension may clarify the mechanisms by which the hemodynamics of established hypertension, normal cardiac output with elevated TPR, develop between childhood and adulthood. Classic physiological models have postulated that a hyperdynamic myocardial phase precedes the hypertensive state. The pattern of race and sex differences in PEP reactivity that we observed during CE is consistent with such models, because it indicates that the greatest PEP reactivity occurred in black male subjects, who are at greatest risk for early development of hypertension. On the other hand, the racial difference in TPR reactivity that we observed during CE is consistent with findings from other researchers who discovered racial differences in TPR responses to various stressors in healthy children and adolescents with a family history of cardiovascular disease, as well as with a recent review of adult studies that concluded that blacks tend to show excessive BP responses to stressors that elicit predominantly α-adrenergic vascular responses. Thus, the racial differences in cardiovascular reactivity that we observed during whole-body CE raise the possibility that both myocardial and vasoconstrictive mechanisms may contribute to the increased risk of hypertension in blacks.

Acknowledgments
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References


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