

# Impaired Stress-Induced Pressure Natriuresis Is Related to Left Ventricle Structure in Blacks

Gregory A. Harshfield, Frank A. Treiber, Harry Davis, Gaston K. Kapuku

**Abstract**—The mechanisms through which stress may contribute to the racial difference in the prevalence of essential hypertension and associated target organ damage remain unclear. This study examined differences in stress-induced pressure natriuresis in 69 black and 52 white normotensives age 14 to 27 years, all with a positive family history of hypertension. Urine samples for sodium excretion were collected before and after a series of tasks (video game challenge, forehead cold stimulation). The average blood pressure across the 2 tasks and the average increase in blood pressure to the 2 tasks were calculated. Blacks had higher mean systolic ( $131 \pm 12$  versus  $126 \pm 12$  mm Hg,  $P < 0.02$ ) and diastolic ( $77 \pm 8$  versus  $72 \pm 9$  mm Hg,  $P < 0.001$ ) blood pressure and a greater average change in systolic blood pressure ( $15 \pm 9$  versus  $11 \pm 7$  mm Hg,  $P < 0.04$ ). This was associated with a smaller change in sodium excretion ( $2 \pm 6$  versus  $7 \pm 10$  mEq/h,  $P < 0.002$ ). The change in sodium excretion was related to the change in systolic ( $r = 0.31$ ,  $P < 0.03$ ) and diastolic ( $r = 0.27$ ,  $P < 0.05$ ) blood pressure in whites but not in blacks. Relative wall thickness was greater in blacks ( $0.31 \pm 0.04$  versus  $0.29 \pm 0.03$ ,  $P < 0.002$ ). In conclusion, impaired stress-induced pressure natriuresis in blacks may contribute to racial differences in essential hypertension and its sequelae. (*Hypertension*. 2002;39:844-847.)

**Key Words:** stress ■ sodium ■ race ■ blood pressure ■ echocardiography ■ hypertension, essential

The prevalence and consequences of essential hypertension are much greater in blacks than in whites.<sup>1</sup> The mechanisms through which stress might contribute to these differences remains unclear. The vast majority of studies to date examined and provided support for the “reactivity hypothesis” (reviews<sup>2-4</sup>). This hypothesis postulates that blacks show exaggerated blood pressure (BP) responses to stress, which produce vascular damage underlying the premature development of essential hypertension and associated target organ damage. However, the physiological response to stress is dynamic and includes both the response to the stressor per se and the changes that restore BP to prestress levels. This is accomplished in part through natriuresis, which reduces blood volume and therefore BP.<sup>5</sup> This part of the stress response is understudied but represents an alternative hypothesis to explain how stress may contribute to the racial differences.<sup>4,6-8</sup> Our “pressure natriuresis” hypothesis postulates that stress-induced impaired sodium regulation leads to an extended period of elevated BP in blacks. The resulting increased BP load leads to the early development of hypertension and its sequelae. The pressure natriuresis hypothesis is particularly appealing because of the well-known greater sensitivity of BP to sodium in blacks (reviews<sup>9-11</sup>).

The purpose of this study was to begin to test this hypothesis by examining racial differences in urinary sodium excretion ( $U_{NaV}$ ) and BP during a series of stressors. We then

examined the relationship of the patterns to left ventricular (LV) structure to examine the possible clinical significance of this response pattern.

## Methods

### Subjects

All procedures were approved by the Human Assurance Committee of the Medical College of Georgia, and the procedures were followed in accordance with the institutional guidelines. Informed consent and both parental consent and assent of the child (if  $> 18$  years) were obtained before testing. The 121 healthy normotensive subjects are part of ongoing longitudinal study that examines the precursors to the development of hypertension in high-risk youths. All of the subjects have a physician-verified family history of essential hypertension in 1 or both biological parents and  $\geq 1$  grandparents, as described previously.<sup>12,13</sup> The subject characteristics are presented in the Table.

### Procedures

On arrival, the subjects voided, and the sample was discarded. Next they drank 237 mL of Gatorade® to ensure they would be able to void after the testing session. An echocardiogram was performed and was followed by the collection of a pretest urine sample. The subject then performed 2 reactivity tasks, which were followed by the collection of a posttest urine sample.

### Reactivity Tasks

The procedures for the reactivity tests have been described in detail.<sup>14</sup> The 10-minute video game stressor “Break Out” (Atari Inc) was presented under a monetary incentive challenge based on the

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### Subject Characteristics and Casual Measurements

Subject Characteristics	Black (n=69)	White (n=52)
Males/females	39/30	32/20
Age, y	19±3	19±3
Height, m	1.7±.8	1.7±.9
Weight, kg	80±23	81±21
Quetlet index, kg/m <sup>2</sup>	27±7	27±8
Resting systolic BP, mm Hg	116±10	113±9
Resting diastolic BP, mm Hg*	65±9	60±7
LVM/height <sup>2.7</sup> , g/m <sup>2.7</sup>	31±6	30±6

Values are mean±SD.

\* $P<0.05$ , blacks greater than whites.

protocol of Murphy et al.<sup>15</sup> Hemodynamic readings were obtained during minutes 1, 3, 5, 7, and 9 of the video game task. The video game controller was secured at a position comfortable for use with the subject's right hand, even if they were left-handed. Previous data obtained on 47 left-handed and 522 right-handed subjects during this task demonstrated similar performance scores ( $597\pm269$  versus  $602\pm288$  points for left- versus right-handed subjects.) The forehead cold stimulation task was based on a protocol developed in our laboratory.<sup>13</sup> A plastic bag containing 6 cups of crushed ice and 1.5 cups of water was placed on the subject's forehead for 1 minute. Hemodynamic measurements were obtained immediately on completion of each stressor and at minutes 15 and 20 during recovery.

### Hemodynamic Measurements

The subject was fitted with equipment for recording BP and heart rate (Dinamap Model 1846 SX, Critikon Inc). Cardiac index (CI) was determined using thoracic bioimpedance (NCCOM-3, Bo Med Medical Manufacturing Ltd). The total peripheral resistance index (TPRI) was calculated using concurrently derived BP and CI as follows:  $[(\text{systolic BP} + 2 \times \text{diastolic BP})/3]/\text{CI}$ , expressed in wood units ( $\text{mm Hg} \cdot \text{L}^{-1} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ).

### Echocardiograms

Our echocardiographic procedures have been described previously.<sup>16</sup> LV posterior wall thickness, interventricular septal thickness, and LV internal dimension were measured in diastole according to the American Society of Echocardiography convention.<sup>17</sup> Wall thickness was determined as the sum of interventricular septal thickness and LV posterior wall thickness divided by 2. LV mass (LVM) was derived using the Devereux formula.<sup>18</sup>  $\text{LVM}/\text{height}^{2.7}$  was used in statistical analyses.<sup>19</sup>

### Analyses

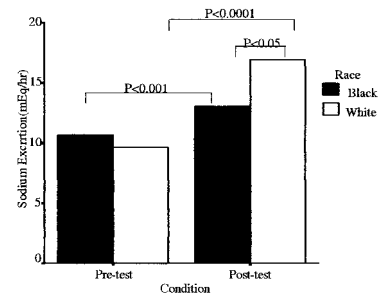
The analyses were performed with SPSS version 10. *T* tests were performed to examine racial differences in  $\text{U}_{\text{NaV}}$  and BP. Pearson correlation coefficients were obtained to examine the relationships between the changes in  $\text{U}_{\text{NaV}}$  and BP.

An expanded Methods section can be found in an online data supplement available at <http://www.hypertensionaha.org>.

## Results

### Racial Differences in Change in Sodium Excretion

The levels of pretest and posttest  $\text{U}_{\text{NaV}}$  for blacks and whites are presented in Figure 1. Both groups had similar levels of  $\text{U}_{\text{NaV}}$  during the pretest, with higher  $\text{U}_{\text{NaV}}$  for whites during the posttest. Both groups showed significant increases in  $\text{U}_{\text{NaV}}$  from pretest to posttest, with a greater increase in whites than blacks ( $7\pm10$  versus  $2\pm6$ ,  $P<0.002$ ).



**Figure 1.** Racial differences in sodium excretion during the protocol.

### Racial Differences in Hemodynamic Responses

Blacks had significantly higher mean systolic BP (SBP) across the tasks ( $131\pm12$  versus  $126\pm12$  mm Hg,  $P<0.02$ ), which was correlated ( $r=0.53$ ,  $P<0.001$ ) with the significantly higher TPRI in blacks ( $29\pm10$  versus  $32\pm10$  mm Hg  $\cdot \text{L}^{-1} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ,  $P<0.001$ ). Blacks also had significantly higher diastolic BP (DBP) ( $77\pm8$  versus  $72\pm8$ ,  $P<0.001$ ), which was correlated ( $r=0.5$ ,  $P<0.001$ ) with the significantly higher TPRI as shown above. In addition, blacks had a significantly greater mean change SBP ( $15\pm9$  versus  $11\pm7$  mm Hg,  $P<0.04$ ), which was correlated with the change in TPRI ( $r=0.56$ ,  $P<0.001$ ). Heart rates did not differ.

### Racial Differences in Pressure Natriuresis

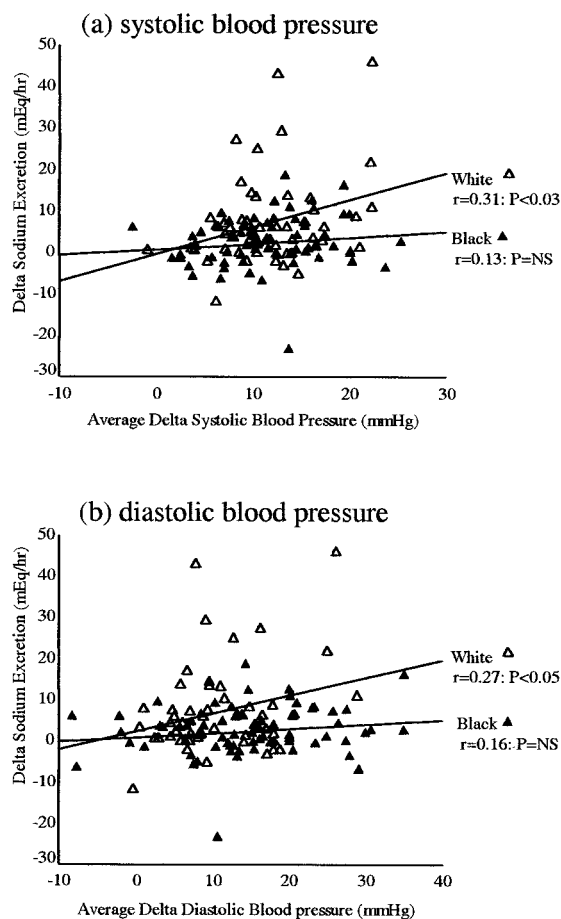
Blacks showed a greater average change in SBP ( $14\pm9$  versus  $11\pm6$  mm Hg,  $P<0.04$ ) but similar changes in DBP and heart rate. The relationships between the changes in BP and  $\text{U}_{\text{NaV}}$  are presented in Figure 2. The change in  $\text{U}_{\text{NaV}}$  was related to the change in SBP in whites but not in blacks, as shown in Figure 2a. The change in BP was related to the change in TPRI in both white ( $r=0.46$ ,  $P<0.001$ ) and black subjects ( $r=0.59$ ,  $P<0.001$ ). A similar pattern was observed for DBP, as shown in Figure 2b. The change in DBP was related to the change in TPRI in both white ( $r=0.46$ ,  $P<0.001$ ) and black subjects ( $r=0.67$ ,  $P<0.0001$ ). The changes in heart rate were not related to the change in  $\text{U}_{\text{NaV}}$  in blacks or whites.

### Racial Differences in LV Structure

Blacks and whites had similar LVM ( $127\pm35$  versus  $123\pm30$  grams, respectively),  $\text{LVM}/\text{height}^{2.7}$  ( $30\pm7$  versus  $29\pm6$  g/m<sup>2.7</sup>, respectively), and LV cavity diameter ( $4.9\pm0.4$  versus  $4.9\pm0.4$  cm). However, blacks compared with whites had a greater wall thickness ( $0.76\pm0.11$  versus  $0.73\pm0.08$  cm,  $P<0.02$ ) and relative wall thickness ( $0.31\pm0.04$  versus  $0.29\pm0.04$ ,  $P<0.006$ ). The only significant correlations between hemodynamic measures and echocardiographic measures were between relative wall thickness and the average TPRI across the stress period, which was significant for both blacks ( $r=0.38$ ,  $P<0.03$ ) and whites ( $r=0.42$ ,  $P<0.005$ ).

## Discussion

Previous studies by our group and others<sup>2-4,20</sup> support the hypothesis that exaggerated stress-induced increases in BP to



**Figure 2.** Racial differences in the relationship between the change in sodium excretion and systolic BP (a) and in sodium excretion and diastolic BP (b).

acute stress may contribute to racial differences in hypertension and its sequelae. This is the first study to test and provide support for an alternative pressure natriuresis hypothesis, which focuses on long-term BP control systems that return BP to prestress levels rather than the stress response per se. Specifically, the black subjects had lower  $U_{Na}V$  despite a higher BP across the stress period. Furthermore, the average change in BP during the reactivity tasks was related to the change in  $U_{Na}V$  in the white subjects as expected but was not related in the black subjects. Both of these findings indicate that the black subjects showed impaired stress-induced pressure natriuresis. Finally, this pattern of response was linked to cardiac remodeling in the blacks, as evidenced by greater wall thickness and relative wall thickness.

Our results are consistent with a previous study that examined racial differences in pressure natriuresis during an extended stress period (1 hour) in 14 black and 14 white subjects.<sup>21</sup> The black subjects tended to show lower  $U_{Na}V$  during stress, with 6 of the black and 2 of the white subjects showing a reduction in  $U_{Na}V$ . An earlier study by Light et al<sup>7</sup> found that another high-risk group showed this pattern, ie, those with a positive family history of hypertension. It is of interest to note that we observed slower stress-induced natriuresis in the black subjects compared with white subjects

despite the fact that all of the subjects had a genetic risk for the development of hypertension as determined by a positive family history of hypertension. This suggests that the influence of environmental factors on this phenotype (stress-induced pressure natriuresis) is stronger in blacks than in whites. Our results are also consistent with the results of animal studies that demonstrated slowing of natriuresis during stress in animals at risk for the development of hypertension (reviews<sup>8,22,23</sup>).

In summary, this study is the first to our knowledge to demonstrate racial differences in stress-induced pressure natriuresis during a series of acute stressors. Furthermore, this is the first study to link this response pattern to BP-related target organ changes. These results support the impaired pressure natriuresis hypothesis to help explain how stress contributes to racial differences in the prevalence of essential hypertension and its sequelae. Further studies are necessary to determine the mechanisms underlying impaired stress-induced pressure natriuresis and to determine its effects on BP after stress.

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