

## Association of Ambulatory Blood Pressure and Dietary Caffeine in Adolescents<sup>1</sup>

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### Abstract:

**Background:** Although relatively little is known about the responsible factors, there is an increased prevalence of essential hypertension in youth. Our previous research using casual blood pressure (BP) suggests a role for caffeine intake. The objective of this study was to assess the association between caffeine intake and ambulatory BP patterns among adolescents and to replicate our previous findings that compared caffeine intake to BP values obtained at a single time point.

**Methods:** Eighty-two African-American and non-Hispanic white adolescents (15 to 19 years old) with normal systolic BP selected foods and beverages for a 4-day sodium-controlled diet. Subjects were stratified into three groups based on the amount of caffeine in these foods. Ambulatory BP measures (24-h) were recorded during 1 day of the 4-day diet. The effects of ethnicity, caffeine, and the interaction of ethnicity and caffeine on BP were assessed for daytime and nighttime hours controlling for gender and body mass index.

**Results:** The level of dietary caffeine was positively associated with daytime systolic BP ( $F_{2,76} = 3.1$ ,  $P = .05$ , partial  $R^2 = 0.07$ ) and daytime diastolic BP ( $F = 3.532, 76$ ,  $P = .03$ , partial  $R^2 = 0.07$ ). Caffeine's effect on systolic BP was most pronounced for African-American subjects. These results replicated our earlier findings. There was no association between caffeine intake and nighttime BP.

**Conclusions:** This investigation replicates and extends our previous findings that caffeine consumption impacts the BP of adolescents, during the daytime when sympathetic nervous system responses dominate BP control. Controlled studies that examine the pressor effects of caffeine intake at levels typical of the dietary patterns of today's adolescents are needed.

### Key Words:

Adolescents, ambulatory blood pressure, African Americans, caffeine, diet.

### Article:

There is a body of evidence providing support for the pressor effects of dietary caffeine among adults.<sup>1,2</sup> Relatively few studies extended this research into the pediatric population, in whom the prevalence of essential hypertension is rapidly increasing.<sup>3</sup> Our initial investigation in this area reported a positive association between caffeine intake from carbonated beverages consumed during a controlled diet and screening (ie, casual) systolic blood pressure (BP) in African-American youths.<sup>4</sup> This same relationship was not apparent in white youths. The purpose of this observational study was to replicate these findings and extend this research by examining the influence of caffeine intake on 24-h ambulatory blood pressure (ABP) recordings obtained during a sodium-controlled diet.

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## METHODS

### *Study Population*

The subjects were 82 healthy, normotensive youths (15 to 19 years old) who participated in an ongoing research program to examine hemodynamic responses to a competitive stress in healthy adolescents.<sup>5</sup> They included 41 African Americans (17 male and 24 female teenagers) and 41 non-Hispanic whites (29 male and 12 female teenagers). Subjects were volunteers throughout the public and private high schools in Richmond and Columbia Counties, Georgia. The Human Assurance Committee for the Medical College of Georgia approved the protocol. Written informed parental consent and subject assent were obtained before testing. Participation required following a 4-day sodium-controlled diet before the stress protocol. In addition, on 1 of the 4 days of the diet period, subjects were offered the opportunity to provide a 24-h ABP recording.

### *Laboratory Evaluation*

Measurements, which included systolic and diastolic BP readings as well as height and weight, were obtained during an initial orientation session. Normotensive status was determined using the mean of three successive BP readings. Subjects were considered normotensive if their mean BP reading was lower than the 95th percentile based on age, gender, and height norms.<sup>6</sup> Body mass index (BMI) was calculated as weight in kilograms divided by height in centimeters squared. The overnight rate of sodium excretion was determined from urine collected by each participant from bedtime to waking for each day of the 4-day diet. Sodium concentration was assessed using the NOVA 16 Analyzer (NOVA Biomedical, Waltham, MA).

### *Sodium-Controlled Diet*

The subjects received a sodium-controlled diet for 4 days.<sup>7</sup> During the orientation session, subjects planned their meals by selecting foods and beverages from a menu that include a wide array of breakfast, lunch, dinner, snack, and beverage items. Of the 15 beverage choices, six contained caffeine. There were also 10 chocolate-containing items with small amounts of caffeine. Controlling mean  $\pm$  SD sodium intake to  $4000 \pm 200$  mg/d was the only selection criterion. The preselected meals were packed into coolers. Subjects or parents picked up the cooler from the Georgia Prevention Institute along with a container for overnight urine collection, which was used to estimate subjects' compliance with the diet. Subjects were required to return any uneaten foods as well as packaging from the foods and beverages that were eaten. The amount of each food returned was recorded.

The total amount of food and beverages selected minus the amount returned was used to determine subjects' dietary intake during the 4 days. Caffeine content for all foods and beverages on the menu was determined using the University of Minnesota nutrient database (version 4.06\_34, July 2003). The amount of caffeine consumed during the 4 days was calculated for each subject based on the amount of caffeine in each food and the amount of the food consumed by the subject.

### *ABP Recordings*

The procedures for ABP recording have been previously described.<sup>8</sup> Briefly, an ABP monitor was fitted to the nondominant arm (model 90207, Space Labs, Redmond, WA). The ABP monitors were individually programmed for daytime and nighttime measurements based on subjects' estimates of their typical bed and wake times. Measurements were obtained every 20 min during daytime and every 30 min during nighttime. Both the subject and the parent were given instructions for wearing the monitor (eg, cessation of body movement at preinflation auditory cue while awake, and method for readjusting a slipped cuff). A telephone number for a research assistant was provided if problems arose. Adequacy of recordings were based on acceptable readings using previously established criteria<sup>9</sup> for  $\geq 21$  readings during the hours designated as daytime and six readings during those hours designated as nighttime.

### *Statistical Analyses*

Caffeine intake was treated as a categorical variable by stratifying subjects into three caffeine-intake categories based on their mean daily caffeine intake. This was done because of the skewed distribution of this variable due

to a large number of subjects consuming 1550 mg/d of caffeine. This categorization was also used in our previous investigation. For ABP, hourly averages for systolic and diastolic BP were calculated across periods designated as daytime and nighttime. A general linear model was used to assess the effects of ethnicity and category of caffeine intake on daytime systolic and diastolic BP and determine whether the association between caffeine intake and BP varied by ethnicity. Gender and BMI were controlled for in the statistical models (ie, entered as covariates). The overnight sodium excretion corresponding to the specific day when each subject wore the ABP monitor was also considered as a possible confounding effect.

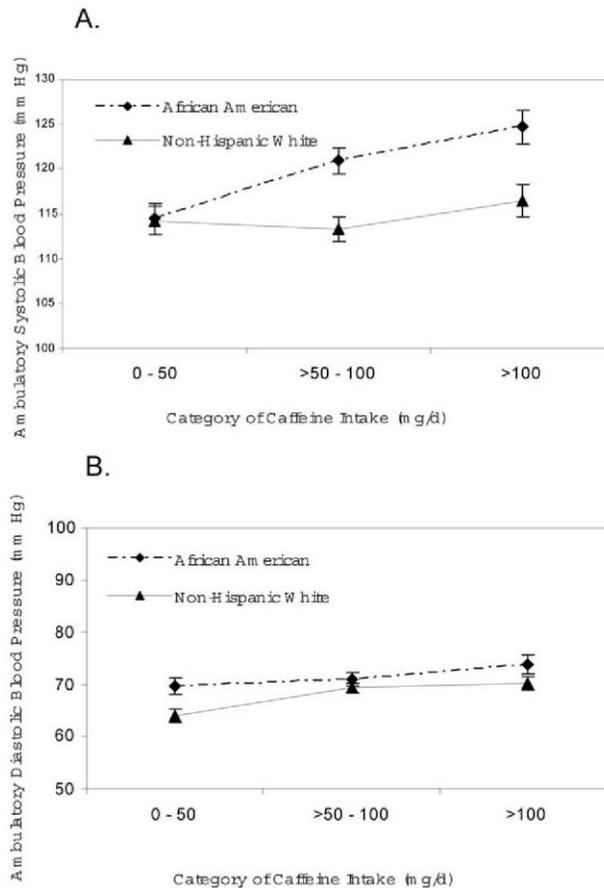
## RESULTS

### *Caffeine Intake*

Participants were stratified into three caffeine intake categories (0 to 50 mg/d, n = 27; >50 to 100 mg/d, n = 33; and >100 mg/d, n = 23). Based on the amount of caffeine in a 12-oz. regular cola (37.2 mg of caffeine), the mean caffeine intake in each successive category was equivalent to 0.59 can (22 mg), 2 cans (75 mg), and 3.8 cans per day (144 mg). Twenty-seven of the 42 African-American subjects were found in the lowest caffeine category, followed by 18 in the midcaffeine category, and only four in the highest caffeine intake category. In contrast, only 7 of the 41 non-Hispanic white subjects were found in the lowest caffeine category, followed by 15 in the midcaffeine category, and only 19 in the highest caffeine intake category ( $\chi^2 = 17.4$ ,  $P = .0002$ ). Those African Americans in the highest intake group consumed less caffeine (mean  $\pm$  SE,  $114.0 \pm 21.0$  mg/d) than non-Hispanic whites in the same group ( $149.8 \pm 9.7$  mg/d).

### *ABP Measures*

**Systolic BP** After controlling for gender and BMI, there were statistically significant main effects for ethnicity and caffeine category with daytime systolic BP as the dependent variable. First, African Americans had higher daytime systolic BP ( $115.9 \pm 1.7$  mm Hg v  $110.5$



**FIG. 1** Daytime ambulatory blood pressures for African American and non-Hispanic white subjects compared across category of caffeine intake for (A) systolic blood pressure and (B) diastolic blood pressure. Data points are least square means adjusted for sex and body mass index and error bars represent standard error of the means.

$\pm 2.1$  mm Hg,  $F_{1,76} = 7.33$ ,  $P = .0084$ , partial  $R^2 = 0.08$ ). Second, daytime systolic BP increased from the lowest to the highest caffeine intake group ( $113.2 \pm 1.6$  mm Hg,  $117.2 \pm 1.4$  mm Hg, and  $119.5 \pm 1.9$  mm Hg,  $F_{2,76} = 3.1$ ,  $P = .05$ , partial  $R^2 = 0.07$ ) regardless of ethnicity. Fig. 1A illustrates the increases in daytime systolic BP across category of caffeine intake for both African-American and non-Hispanic white subjects. The interaction between ethnicity and caffeine intake category was not statistically significant ( $F_{2,76} = 1.65$ ,  $P = .20$ , partial  $R^2 = 0.03$ ). However, there appears to be a trend that the increase in daytime systolic BP with increasing caffeine consumption was greater in African Americans than in whites.

African Americans had higher nighttime systolic BP compared to non-Hispanic whites ( $108.6 \pm 2.0$  mm Hg v  $104.5 \pm 2.2$  mm Hg,  $F_{1,76} = 2.09$ ,  $P = .04$ , partial  $R^2 = 0.045$ ). There was no statistically significant difference in nighttime systolic BP across the caffeine intake categories ( $F_{2,76} = 1.31$ ,  $P = .27$ , partial  $R^2 = 0.03$ ) nor was there an interaction between caffeine intake category and ethnicity ( $F_{2,76} = 1.46$ ,  $P = .24$ , partial  $R^2 = 0.03$ ).

**Diastolic BP** After controlling for gender and BMI, there were significant effects for ethnicity and caffeine category with daytime diastolic BP as the dependent variables. African Americans had higher daytime diastolic BP than non-Hispanic whites ( $69.1 \pm 1.1$  mm Hg v  $65.8 \pm 1.4$  mm Hg,  $F = 6.31_{1,76}$ ,  $P = .01$ , partial  $R^2 = .07$ ). Daytime diastolic BP increased from the lowest to the highest caffeine intake group ( $67.4 \pm 1.1$  mm Hg,  $70.1 \pm 0.9$  mm Hg, and  $71.9 \pm 1.2$  mm Hg,  $F = 3.53_{2,76}$ ,  $P = .03$ , partial  $R^2 = 0.07$ ). The interaction between ethnicity and caffeine was not statistically significant ( $F = 0.98_{2,76}$ ,  $P = .40$ , partial  $R^2 = 0.02$ ). Fig. 1B illustrates the similar but small changes in daytime diastolic BP across the caffeine intake categories for both ethnic groups. African Americans had higher nighttime diastolic BP compared to non-Hispanic whites ( $58.7 \pm 1.4$  mm Hg v  $56.2 \pm 1.6$  mm Hg,  $F_{1,76} = 1.92$ ,  $P = .058$ , partial  $R^2 = 0.045$ ). There was no statistically significant difference in

nighttime diastolic BP across the caffeine intake categories ( $F_{2.76} = 0.36$ ,  $P = .70$ , partial  $R^2 = 0.01$ ) nor was there an interaction between caffeine intake category and ethnicity ( $F_{2.76} = 0.94$ ,  $P = .40$ , partial  $R^2 = 0.02$ ).

### *Overnight Sodium Excretion*

The mean overnight hourly rate of sodium excretion (UNaV/h) was  $5.60 \pm 3.3$  mEq/h. There was no statistically significant difference in overnight UNaV/h across the caffeine intake categories ( $F_{2.79} = 0.90$ ,  $P = .42$ ,  $R^2 = 0.02$ ). In a statistical model containing gender, ethnicity, BMI, caffeine intake category, overnight UNaV/h, and the interaction of caffeine intake category by overnight UNaV/h, there was no relationship between overnight UNaV/h and daytime systolic BP ( $F_{1.73} = 0.06$ ,  $P = .80$ , partial  $R^2 = .0001$ ) nor was there a relationship between the interaction of overnight UNaV/h with the caffeine category and daytime systolic BP ( $F_{2.73} = 1.39$ ,  $P = .26$ , partial  $R^2 = 0.036$ ). A similar result was found for the relationship of daytime diastolic BP and overnight UNaV/h ( $F_{1.73} = 0.59$ ,  $P = .44$ , partial  $R^2 = 0.008$ ) and the interaction of UNaV/h with caffeine intake ( $F_{2.73} = 0.32$ ,  $P = .72$ , partial  $R^2 = 0.009$ ).

## DISCUSSION

The major finding of this observational study is that dietary caffeine is associated with daytime BP in adolescents. Specifically, both daytime systolic and diastolic BP increased with greater caffeine intake. There was a trend for African-American subjects to experience larger increases in systolic BP as caffeine intake increased compared to non-Hispanic whites. Daytime diastolic BP increased along with caffeine intake regardless of race. There was no association between caffeine intake and nighttime BP.

The present results replicate and extend our previous findings<sup>4</sup> where adolescents' caffeine intake during the controlled sodium diet was related to BP measured during the study's screening (ie, BP taken at one point in time). In this earlier study, the screening systolic BP for African-American subjects associated with each successive caffeine category were 105.8, 105.4, and 118.25 mm Hg. The primary difference in results between the two studies is that in the present study we found evidence for a dose–response relationship between caffeine intake and daytime systolic BP (112.7, 116.8, and 119.1 mm Hg), regardless of ethnic group. Although not statistically significant in this present study, a more linear response was found among African-American subjects where the daytime systolic BP among African-American subjects for each successive caffeine category were 114.4, 120.9, and 124.7 mm Hg compared to white subjects, 114.2, 113.3, and 116.4 mm Hg.

There is limited research on caffeine's effects among adolescents or young adults who regularly consume caffeinated beverages. Strickland et al<sup>10</sup> investigated the cardiovascular reactivity effects of two levels of caffeine in coffee (3 mg and 250 mg) in a crossover study among healthy young women (aged 17 to 22 years) who consumed no more than two caffeinated beverages a day. They found that systolic BP during stress was 5 mm Hg greater for the higher dose, regardless of family history of hypertension or ethnicity. Myers et al,<sup>11</sup> examining the cardiovascular reactivity effects of 3 mg and 250 mg of caffeine among regular coffee drinkers (men aged 18 to 35 years), found that caffeine had a positive relationship with BP before, during, and after stress, regardless of ethnicity or family history of hypertension. A meta-analysis of the effects of chronic coffee consumption on BP found that in 11 trials where coffee treatment (median caffeine intake = 630 mg) was compared with control, systolic and diastolic BP increased by 2.4 mm Hg and 1.3 mm Hg, respectively.<sup>2</sup> Six of the 11 trials used ambulatory measures. Relevant to our present investigations, this effect was greater in trials with younger participants. The questions remain whether adolescents receiving controlled amounts of caffeine comparable to quantities obtained from typical carbonated beverage consumption will demonstrate pressor effects and whether African-American and white teens will respond similarly.

Regarding caffeine and ambulatory measures, Lane et al<sup>12</sup> observed that among habitual coffee drinkers, caffeine administered in a double-blind placebo design increased both ABP and urinary excretion of epinephrine during waking hours (nighttime hours were not recorded). The elevation of epinephrine, a major hormone of the sympathetic nervous system suggests that caffeine may contribute to sympathetic reaction to the stresses of daily living. This hypothesis is consistent with our findings where greater caffeine intake was only

associated with higher BP during daytime when the sympathetic nervous system mediates BP responses to the physiologic and psychologic demands of the day. In contrast, differences were not seen at night during which time volume regulatory systems are the dominant BP control system.

Although corrected for statistically, a limitation of this observational study was that we were not able to control the level of caffeine intake across the participants, therefore gender and ethnic subgroups would be equally represented in successive caffeine intake categories. Furthermore, the sample size was relatively small, limiting the statistical modeling of the interactive effects (ie, low statistical power). Clinical research is needed on the direct effects of caffeine in adolescents in doses that are comparable to their normal range of caffeine intake. A second limitation is that we were not able to consider the effects of other characteristics that are related to BP control and may have been present in those who consumed greater amounts of caffeine. For example, Musante and Treiber<sup>13</sup> found that adolescents who had higher anger expression reported consuming more caffeinated soda and coffee. Narkiewicz et al<sup>14</sup> demonstrated an interactive effect between coffee and cigarette consumption on daytime systolic BP in young adults. The clustering of BP-related characteristics within adolescents at risk for hypertension needs to be better understood.

In conclusion, dietary and lifestyle factors leading to obesity have been proposed to explain the emergence of essential hypertension as a pediatric disorder.<sup>15</sup> Our studies suggest that caffeine consumption may be an additional factor, particularly in African Americans. Caffeinated beverage consumption is ever-present in the diets of American youths. The present research highlights the need for additional studies that examine the direct effect of caffeine from beverages on adolescent BPs and consider why caffeine's effects may not be consistent across racial groups. This is particularly important because of the elevated risk of hypertension among African-American youth.<sup>16</sup> If caffeine has a direct effect on BP in youth at risk for hypertension, it may be possible to design relevant intervention strategies and offer a straightforward public health message that could help reduce the risk of hypertension among young African Americans and other vulnerable populations.<sup>17</sup>

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