Dietary Sodium, Adiposity, and Inflammation in Healthy Adolescents

AUTHORS: Haidong Zhu, MD, PhD,a Norman K. Pollock, PhD,a Ishita Kotak, MPH,a Bernard Gutin, PhD,a Xiaoling Wang, MD, PhD,b Jigar Bhagatwala, MBBS, MPH,a,b Samip Parikh, MBBS, MPH,a,b Gregory A. Harshfield, PhD,a and Yanbin Dong, MD, PhD

aGeorgia Prevention Center, Institute of Public and Preventive Health, and bInternal Medicine, Department of Medicine, Medical College of Georgia, Georgia Regents University, Augusta, Georgia

KEY WORDS
sodium intake, adiposity, leptin, TNF-α, 24-hour dietary recall, adolescents

ABBRévATIONS
AHA—American Heart Association
CRP—C-reactive protein
CV—coefficients of variation
ELISA—enzyme-linked immunosorbent assay
ICAM-1—intercellular adhesion molecule-1
SAAT—subcutaneous abdominal adipose tissue
SES—socioeconomic status
TNF-α—tumor necrosis factor-α
VAT—visceral adipose tissue

WHAT’S KNOWN ON THIS SUBJECT: High sodium intake is considered an indirect cause of obesity because it is often accompanied by higher energy intake and sugar-sweetened soft drink consumption. High sodium intake is associated with increased inflammatory response in adult patients.

WHAT THIS STUDY ADDS: This study shows that high sodium intake is positively associated with adiposity, leptin, and tumor necrosis factor-α independent of total energy intake and sugar-sweetened soft drink consumption in healthy white and African American adolescents.

abstract

OBJECTIVES: To determine the relationships of sodium intake with adiposity and inflammation in healthy adolescents.

METHODS: A cross-sectional study involved 766 healthy white and African American adolescents aged 14 to 18 years. Dietary sodium intake was estimated by 7-day 24-hour dietary recall. Percent body fat was measured by dual-energy x-ray absorptiometry. Subcutaneous abdominal adipose tissue and visceral adipose tissue were assessed using magnetic resonance imaging. Fasting blood samples were measured for leptin, adiponectin, C-reactive protein, tumor necrosis factor-α, and intercellular adhesion molecule-1.

RESULTS: The average sodium intake was 3280 mg/day. Ninety-seven percent of our adolescents exceeded the American Heart Association recommendation for sodium intake. Multiple linear regressions revealed that dietary sodium intake was independently associated with body weight (β = 0.23), BMI (β = 0.23), waist circumference (β = 0.23), percent body fat (β = 0.17), fat mass (β = 0.23), subcutaneous abdominal adipose tissue (β = 0.25), leptin (β = 0.20), and tumor necrosis factor-α (β = 0.61; all P < .05). No relation was found between dietary sodium intake and visceral adipose tissue, skinfold thickness, adiponectin, C-reactive protein, or intercellular adhesion molecule-1. All the significant associations persisted after correction for multiple testing (all false discovery rates < 0.05).

CONCLUSIONS: The mean sodium consumption of our adolescents is as high as that of adults and more than twice the daily intake recommended by the American Heart Association. High sodium intake is positively associated with adiposity and inflammation independent of total energy intake and sugar-sweetened soft drink consumption. Pediatrics 2014;133:e635–e642
As obesity has escalated to epidemic proportions, many causes, including dietary components, have been suggested. Recent evidence has suggested that sodium consumption may be an important contributor to this epidemic. For instance, animal studies have shown that a high sodium diet increases adipose tissue mass and adipocyte size, and leptin production.1-2 In humans, greater sodium consumption has been linked to higher body weight,3,4 possibly due to sodium’s effect on fluid intake because high sodium intake is often accompanied by high consumption of energy-dense foods and sugar-sweetened soft drinks.5-9 However, this may not always be the case because other studies have reported a positive relationship between dietary sodium intake and obesity independent of energy intake and sugar-sweetened beverage consumption.10-13 This apparent discrepancy may be attributed, in part, to differences in the population studied and the study design and instruments used. Furthermore, it is possible that other mechanisms exist by which high dietary sodium intake may be linked to obesity.

Animal studies show that excess salt intake can affect the innate immune system. High salt diets promote tissue inflammation and exacerbate autoimmune disease in mice.14,15 In patients with hypertension and myocardial infarction, high sodium intake has been associated with an increased inflammatory response and target organ damage.16-18 In another study, however, investigators did not observe an effect of sodium intake on inflammatory-related markers.19 Interestingly, in a recent clinical trial in hypertensive patients, investigators found that a very low sodium diet (480 mg/day) generated a pro-inflammatory phenotype, characterized by significant increases and decreases, respectively, in tumor necrosis factor-α (TNF-α), a marker of innate immunity and inflammation, and adiponectin, an antiinflammatory protein secreted from adipose tissue.20 Collectively, these aforementioned study findings suggest that the link between inflammation and sodium intake is more complex than commonly held and that not all classic components of the inflammatory response are similarly influenced by sodium intake. A limitation of the aforementioned dietary sodium-obesity-inflammation investigations was that study participants were adults. The impact of high sodium intake on inflammation in children and adolescents remains unknown. Therefore, we aimed to determine the relationships of sodium intake with robust measures of adiposity and markers of inflammation in a cohort of healthy white and African American adolescents.

METHODS

Study Participants

Seven hundred and sixty-six healthy adolescents aged 14 to 18 years including 389 whites and 377 African Americans (50.3% females) were recruited from local public high schools in Augusta, Georgia. Demographic information obtained from the school systems was used to select schools that enrolled both African American and white students. After receiving approval from the county superintendents and school principals, flyers were distributed to all students in the selected schools. Inclusion criteria for the study were white or African American race and age 14 to 18 years. Adolescents were excluded if they were diagnosed with any disease, were taking medications, or had any medical conditions that could affect growth, maturation, physical activity, nutritional status, or metabolism. Written informed consent was obtained from the 18-year-olds. For the 14- to 17-year-olds, parental consent and subject assent were obtained. Race was determined by self-report or by a parent if subject was under 18 years of age. The Institutional Review Board at the Medical College of Georgia approved the study. All measurements were performed between 2001 and 2005.21

Adiposity Measurements

Height and weight were obtained according to standard procedures using a wall-mounted stadiometer (Tanita Corporation of America, Arlington Heights, IL) and calibrated electronic scale (model CN20L, Cardinal Detecto, Webb City, MO). These measurements were used to calculate BMI. Before testing each week, the electronic scale was checked for accuracy by using known weights. By using a girth measuring tape (Seca 200, Hanover, MD), waist circumference was measured twice at the midpoint between the lowest rib and the iliac crest, and the values were averaged. A set of 5 skinfold thicknesses (biceps, triceps, subscapular, suprailiac, and medial calf) were measured 3 consecutive times on the left side of the body, with a Lange caliper (Cambridge Scientific, Cambridge, MA) according to the standard procedures, and the mean of 3 values were used.

Body fat percentage and fat mass were measured by dual-energy x-ray absorptiometry (QDR-4500W, Hologic Inc, Bedford, MA). For determination of measurement reproducibility, 1-way random effects model, single-measure intraclass correlation coefficients were calculated in participants 15 to 18 years of age (n = 219). Each participant was scanned twice within a 7-day period for percentage body fat (R = 0.97). Subcutaneous abdominal adipose tissue (SAAT) and visceral adipose tissue (VAT) were measured by using magnetic resonance imaging (1.5 T; GE Medical Systems, Waukesha, WI). Assessments of SAAT and VAT have been described in detail elsewhere.22
Briefly, a series of 5 transverse images was acquired from the lumbar region beginning at the inferior border of the fifth lumbar vertebra and proceeding toward the head; a 2-mm gap between images was used to prevent crosstalk. To calculate volumes for SAAT and VAT, the cross-sectional area from each slice was multiplied by the slice width (1 cm), and then the individual volumes were summed. The intraclass correlation coefficients for repeat analyses of the same scans on separate days were $R \geq 0.98$ for both SAAT and VAT.

**Biochemical Parameters**

Fasting blood samples were collected for assessment of the following adipokine and inflammatory markers: leptin, adiponectin, C-reactive protein (CRP), TNF-α, and intercellular adhesion molecule-1 (ICAM-1). Serum leptin concentrations were measured by using enzyme-linked immunosorbent assay (ELISA; R & D Systems, Minneapolis, MN) and run in duplicate, with intra- and interassay coefficients of variation (CV) of 2.2% and 5.3%, respectively. Adiponectin was measured in plasma that was assayed in duplicate by ELISA (Linco Research, St Charles, MO), with intra- and interassay CV of 7.4% and 8.4%, respectively. Plasma CRP concentrations were assayed by using high-sensitivity ELISA (ALPCO Diagnostics, Salem, NH) and run in duplicate, with intra- and interassay CV of 3.8% and 7.0%, respectively. TNF-α and ICAM-1 were measured in serum that was assayed in duplicate by ELISA (R & D Systems, Minneapolis, MN). Intra- and interassay CV were 4.3% and 7.3%, respectively, for serum TNF-α and 3.3% and 6.0%, respectively, for serum ICAM-1.

**Dietary Intake**

Diet was assessed with individual, nonconsecutive, 24-hour recalls that covered the period from midnight to midnight for the previous day using the Nutrition Data System for Research (Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN) by trained dietitians. The first 2 recalls were performed in person at our institute within 1 week of testing with the use of food models, portion booklets, or serving containers to assist in estimating serving size, and the remaining interviews were conducted by telephone weekly, with all 7 recalls completed within a period of 12 weeks. We sought to obtain 7 recalls from each participant, 1 for each day of the week. To minimize the potential for underreporting during the time frame for 24-hour recalls, subjects were blinded to the telephone recall schedule. Three-, 4-, 5-, 6-, and 7-day dietary recalls were collected in 3.3%, 8.7%, 17.2%, 18.4%, and 50.2% of the adolescents, respectively. Ninety-eight ($n = 750$) and 95% ($n = 725$) of the adolescents in our study completed at least 3- and 4-day dietary recalls, respectively. Dietary intakes of energy, sodium, potassium, dietary fat, and sugar-sweetened beverages were an average of the intakes from all the recalls collected from each participant.

**Physical Activity**

Free-living physical activities were assessed using CSA/MTI Actigraph monitors (model 7164; MTI Health Services, Fort Walton Beach, FL) as previously described. Subjects were instructed to wear the monitor for 7 days, remove it for sleep and any activity that might cause harm to either the monitor or another person (eg, during contact sports), and return the monitor 1 week later. Data from day 1 and day 7 were discarded because a full day of information was not available for those days. Daily movement counts were converted to average minutes per day spent in moderate physical activity (3–6 metabolic equivalents) and vigorous physical activity (>6 metabolic equivalents) by the software accompanying the device.

**Pubertal Maturation**

Pubertal maturation stage (or Tanner stage) was measured with a 5-stage scale ranging from I (prepubertal) to V (fully mature) as described by Tanner. Using this gender-specific questionnaire, participants reported their pubertal stage by comparing their own physical development to the 5 stages in standard sets of diagrams. A parent or research coordinator then reviewed the results with the children to make sure they understood the questionnaire. When an individual reported discordant stages of pubic hair and breast or genital development, the higher of the 2 stages was used. The validity and reliability of this instrument were well established previously.

**Socioeconomic Status and Birth Weight**

Parents completed questionnaires regarding their education and occupation. Family socioeconomic status (SES) was calculated by using the Hollingshead Four-Factor Index of Social Status, a weighted average of parental educational (scale 1–7) and occupations (scale 1–9). The validity and reliability of this instrument were established by Cirino et al. Birth weight data were also collected via questionnaires, which were also completed by the parents.

**Statistical Analyses**

Normal distribution and homogeneity of variances were confirmed by Shapiro-Wilks W and Levene tests, respectively. Racial group differences for adiposity, adipokines, inflammatory markers, dietary intake, physical activity, and SES were determined by using independent samples 2-tailed t tests if data were distributed normally and
Mann-Whitney U tests otherwise. Group differences in categorical variables were tested by using $\chi^2$ tests. Descriptive statistics for raw variables are presented as mean ± SD.

Separate multivariate linear regression analyses were conducted to examine associations of dietary sodium intake with adiposity and adipokine measurements (weight, BMI, waist circumference, skinfold thickness, percentage body fat, SAAT, VAT, leptin and adiponectin) and inflammatory markers (CRP, ICAM-1, and TNF-α). Pearson’s correlation coefficient was first used to assess the correlations of adiposity, adipokines, and markers of inflammation with potential confounding factors, including Tanner stage, physical activity, birth weight, SES, dietary fat, and sugar-sweetened soft drink and potassium intake.9–13,27,28 Only related confounding variables were included in the analyses.

Before the regression analyses, percent body fat, SAAT, VAT, leptin, adiponectin, and CRP were log-transformed so that each of these variables followed an approximate normal distribution. To control for multiple testing, a standard false discovery rate correction was applied to the set of raw $P$ values, using the conventionally accepted false-positive rate of 5%.29 Data were analyzed by using IBM SPSS statistics for windows, Version 20.0 (Armonk, NY) and statistical significance was set at $P < .05$.

## RESULTS

Participant characteristics are presented in Table 1. The sample was composed of 766 white and African American adolescents aged 14 to 18 years (50% female, 49% African American). The gender distribution, age, percent body fat, VAT, CRP, TNF-α, physical activity, dietary fat, and sugar-sweetened beverage consumption were not different between racial groups. However, white adolescents were found to have lower weight, BMI, waist circumference, skinfold thickness, SAAT, serum leptin, Tanner stage, and higher plasma adiponectin, serum ICAM-1, birth weight, SES, energy intake, and potassium intake than African American adolescents (all $P < .05$). Furthermore, while adolescents consumed more dietary sodium than African American adolescents (3359 vs 3197 mg/day, $P = .045$). In the total sample, dietary sodium intake was 3280 mg/day (range, 690–9590 mg/day); this amount is approximately twice as much than the 1500 mg/day or less recommendation by the American Heart Association (AHA).

Multiple linear regression, adjusting for age, gender, race, Tanner stage, birth weight, physical activity, energy intake, potassium intake, and sugar-sweetened beverages, revealed that dietary sodium intake was associated with adiposity including weight ($\beta = 0.23$), BMI ($\beta = 0.23$), waist circumference ($\beta = 0.23$), percent body fat ($\beta = 0.17$), fat mass ($\beta = 0.23$), SAAT ($\beta = 0.25$), leptin ($\beta = 0.20$), and TNF-α ($\beta = 0.61$) (all $P < .05$; Table 2). No relations were found between dietary sodium intake and VAT, skinfold thickness, or adiponectin (all $P > .05$).

### TABLE 1 Participant Characteristics

<table>
<thead>
<tr>
<th>Total Sample</th>
<th>Whites</th>
<th>African Americans</th>
<th>$P^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>766</td>
<td>389</td>
<td>377</td>
</tr>
<tr>
<td>Age, y</td>
<td>16.1 ± 1.2</td>
<td>16.1 ± 1.2</td>
<td>16.2 ± 1.2</td>
</tr>
<tr>
<td>Female, %</td>
<td>50.3</td>
<td>50.1</td>
<td>50.4</td>
</tr>
<tr>
<td>Wt, kg</td>
<td>66.0 ± 16.1</td>
<td>63.0 ± 13.9</td>
<td>69.2 ± 17.6</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.2 ± 5.2</td>
<td>22.0 ± 4.1</td>
<td>24.5 ± 5.8</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>74.5 ± 11.1</td>
<td>73.3 ± 9.8</td>
<td>75.9 ± 12.2</td>
</tr>
<tr>
<td>Sum of skinfold thickness, mm</td>
<td>80.7 ± 45.3</td>
<td>76.8 ± 58.1</td>
<td>84.8 ± 51.4</td>
</tr>
<tr>
<td>Percent body fat, %</td>
<td>24.0 ± 10.2</td>
<td>24.1 ± 9.1</td>
<td>23.9 ± 11.2</td>
</tr>
<tr>
<td>SAAT, cm³</td>
<td>887 ± 770</td>
<td>761 ± 570</td>
<td>1002 ± 901</td>
</tr>
<tr>
<td>VAT, cm³</td>
<td>99 ± 68</td>
<td>104 ± 62</td>
<td>95 ± 74</td>
</tr>
<tr>
<td>Adiponectin, μg/mL</td>
<td>8.5 ± 5.0</td>
<td>9.3 ± 5.1</td>
<td>7.1 ± 4.8</td>
</tr>
<tr>
<td>Leptin, ng/mL</td>
<td>12.0 ± 12.9</td>
<td>10.2 ± 11.3</td>
<td>14.2 ± 14.3</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>1.1 ± 2.2</td>
<td>1.0 ± 2.0</td>
<td>1.2 ± 2.4</td>
</tr>
<tr>
<td>TNF-α, ng/mL</td>
<td>0.9 ± 0.8</td>
<td>0.8 ± 0.6</td>
<td>0.9 ± 0.9</td>
</tr>
<tr>
<td>ICAM-1, ng/mL</td>
<td>217 ± 76</td>
<td>248 ± 61</td>
<td>184 ± 78</td>
</tr>
<tr>
<td>Tanner stage</td>
<td>4.3 ± 0.7</td>
<td>4.3 ± 0.7</td>
<td>4.4 ± 0.7</td>
</tr>
<tr>
<td>Birth wt, lb</td>
<td>7.4 ± 3.1</td>
<td>7.7 ± 1.2</td>
<td>7.2 ± 1.4</td>
</tr>
<tr>
<td>SES</td>
<td>35.9 ± 9.1</td>
<td>36.3 ± 9.0</td>
<td>30.0 ± 9.2</td>
</tr>
<tr>
<td>Moderate/vigorous physical activity, min/d</td>
<td>44 ± 29</td>
<td>44 ± 28</td>
<td>44 ± 30</td>
</tr>
<tr>
<td>Dietary intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy, kcal/d</td>
<td>1957 ± 590</td>
<td>2048 ± 647</td>
<td>1915 ± 652</td>
</tr>
<tr>
<td>Sodium, mg/d</td>
<td>3280 ± 1150</td>
<td>3359 ± 1150</td>
<td>3197 ± 1167</td>
</tr>
<tr>
<td>Potassium, mg/d</td>
<td>1970 ± 761</td>
<td>2125 ± 829</td>
<td>1808 ± 648</td>
</tr>
<tr>
<td>Fat, g/d</td>
<td>75.9 ± 29.5</td>
<td>76.5 ± 29.6</td>
<td>75.3 ± 29.4</td>
</tr>
<tr>
<td>Sugar-sweetened beverages, mL/d</td>
<td>578 ± 363</td>
<td>570 ± 390</td>
<td>588 ± 327</td>
</tr>
</tbody>
</table>

* Values are means ± SD.

$^a$ Tests of significance between racial groups were based on independent samples t test (2 tailed).

$^b$ Tests of significance between groups were based on the $\chi^2$ test.

$^c$ Data available for 490 participants.

$^d$ Data available for 908 participants.

$^e$ Data available for 648 participants.

$^f$ Data available for 636 participants.

$^g$ Data available for 177 participants.

$^h$ Data available for 544 participants.

$^i$ Data available for 660 participants.
We further tested if the associations between dietary sodium intake and TNF-α was dependent on adiposity because adiposity is often associated with heightened inflammation status. After further adjustment for percent body fat, the association remained significant (P = 0.03, Table 3). In addition, the associations between dietary sodium intake and adiposity, leptin, and TNF-α survived corrections for multiple testing (all false discovery rates <0.05, Table 2).

Although 98% of the adolescents (n = 750) provided at least 3 days of 24-hour diet recalls, we also analyzed the data excluding participants with only 1 or 2 days of 24-hour diet recalls. Our results remain unchanged (data not shown); therefore, participants with only 1 or 2 days of 24-hour diet recalls were not excluded from analyses.

**DISCUSSION**

To the best of our knowledge, this is the first study to assess relationships of dietary sodium intake with a wide range of robust measurements of adiposity. We found that the average dietary sodium consumed by our white and African American adolescents was as high as that of adults and more than twice the AHA recommendation. Higher sodium intake was positively associated with adiposity independent of intakes of energy and sweetened soft drinks. In addition, high sodium intake was positively and independently associated with leptin and TNF-α.

The AHA recommends that all Americans reduce the amount of sodium in their diet to <1500 mg a day. Ninety-seven percent (741 of 766) of our adolescents exceeded the AHA recommendation for sodium intake. More than 80% (615 of 766) exceeded the level of 2300 mg/day recommended in the Dietary Guidelines for Americans, which is in agreement with the recent report. The sodium intake consumed by our adolescent sample is comparable to the national data among children and adolescents from NHANES 2003–2008.

In humans, greater sodium consumption has been linked to higher body weight, possibly due to sodium’s effect on fluid intake because high sodium intake is often accompanied by high consumption of energy-dense foods and sugar-sweetened soft drinks. By contrast, we showed that higher sodium intake was positively associated with several adiposity measures independent of intakes of energy and sweetened soft drinks, which echoes the recent findings in European children and adolescents. Libuda et al reported that a high intake of processed salty foods was associated with higher body weight status independent of energy intake and soft drink consumption. Moreover, data from the Korean National Health And Nutrition Examination Survey suggest that high sodium intake may be a potential risk factor for weight gain independent of calorie intake. These findings including ours raise the possibility that high sodium intake could be a direct cause of obesity, which is further supported by animal literature. First, salted food has been shown to stimulate the brain reward and pleasure centers and increase caloric consumption, augmenting the incidence of overeating, obesity, and related illness in rats.

Second, independent of energy intake, chronic salt overload induced adipocyte hypertrophy and increased mass of adipose depots and high plasma leptin concentration by enhancing the adipocyte insulin sensitivity for glucose uptake, the insulin-induced glucose metabolism, and lipogenic capacity of white adipose tissue in rats.

We also found that sodium intake was positively and independently associated

<table>
<thead>
<tr>
<th><strong>TABLE 2</strong></th>
<th>Associations of Dietary Sodium Intake With Adiposity Measures and Markers of Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiposity measures&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Standardized β Coefficient</td>
<td>Adjusted R²</td>
</tr>
<tr>
<td>Wt</td>
<td>0.23</td>
</tr>
<tr>
<td>BMI</td>
<td>0.23</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.23</td>
</tr>
<tr>
<td>Sum of skin folds</td>
<td>0.15</td>
</tr>
<tr>
<td>Percent body fat</td>
<td>0.17</td>
</tr>
<tr>
<td>Fat mass</td>
<td>0.23</td>
</tr>
<tr>
<td>SAAT</td>
<td>0.25</td>
</tr>
<tr>
<td>VAT</td>
<td>0.16</td>
</tr>
<tr>
<td>Leptin</td>
<td>0.20</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>0.09</td>
</tr>
<tr>
<td>Inflammatory markers&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>ICAM-1</td>
<td>0.03</td>
</tr>
<tr>
<td>CRP</td>
<td>0.06</td>
</tr>
<tr>
<td>TNF-α</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Value for the null hypothesis. FDR, false discovery rate.

<sup>a</sup> Multiple linear regression analyses were conducted between dietary sodium intake and measurements of adiposity, adjusted for age, gender, race, Tanner stage, birth weight, physical activity, energy intake, potassium intake, and sugar-sweetened beverages.

<sup>b</sup> Multiple linear regression analyses were conducted between dietary sodium intake and measurements of adiposity, adjusted for age, gender, race, Tanner stage, family socioeconomic status, physical activity, energy intake, potassium intake, and dietary fat intake.

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**TABLE 3** Dietary Sodium Intake as an Independent Predictor of TNF-α With Adjustment of Adiposity

<table>
<thead>
<tr>
<th>Regression Models</th>
<th>β</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-α</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base model&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.61</td>
<td>0.02</td>
</tr>
<tr>
<td>Base model + percent body fat</td>
<td>0.57</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Data are presented as standardized β-coefficients.

<sup>a</sup> Multiple linear regression analyses were conducted between dietary sodium intake and measurements of adiposity, adjusted for age, gender, race, Tanner stage, family socioeconomic status, physical activity, energy intake, potassium intake, and dietary fat intake.
with increased circulating levels of leptin. Leptin is one of the most important adipokines secreted by fat cells, with a variety of physiologic roles related to the control of metabolism, maintenance of energy homeostasis and body weight, inflammatory response, and urinary sodium excretion.34,35 High doses of leptin increase renal sodium excretion acutely. In contrast, chronic elevation of plasma leptin impairs renal sodium excretion.35 Salt loading to rabbits abolished the effect of leptin on sympathetic activity and cardiovascular system.36 Moreover, high salt diets induced adipocyte hypertrophy and increased leptin production in rats.1,2 Independent of dietary fat, high salt content alone could increase leptin level in rats even in the absence of obesity.2 Therefore, it is also possible that chronic high sodium intake may lead to increased leptin production or secretion, and enhanced leptin resistance, which contributes to the dysregulation of energy homeostasis and development of obesity and hypertension in humans.

In the current study, we also showed that high sodium intake is positively associated with TNF-α independent of adiposity. TNF-α is a potent proinflammatory cytokine that plays important roles in chronic inflammation and autoimmune diseases. Studies have shown that increased salt concentration significantly boosted T-cell differentiation, stimulated TNF-α expression, and led to cell death.14,37,38 Moreover, a high salt diet has been shown to trigger T-cell differentiation, promote tissue inflammation, and exacerbate autoimmune diseases in mice.14,15 TNF-α has also been implicated in salt-sensitive hypertension and renal injury. TNF-α was required for the complete expression of angiotensin II–induced salt appetite and hypertension.39 A few studies have shown that high sodium intake was associated with CRP and TNF-α in patients with hypertension and myocardial infarction.16,17 In addition, a 7-day high salt intake was found to markedly increase plasma TNF-α in normotensive salt sensitive and salt-resistant individuals, whereas no significant change in CRP was observed.40 Moreover, a 16-week dietary sodium restriction (2 g/day) was associated with a significant reduction in serum CRP, TNF-α, and interleukin-6 levels without changes in blood pressure and extracellular water in hemodialysis patients.18 Our data suggest that high sodium intake may already affect inflammatory response through TNF-α expression and production during adolescent years. Further studies are needed to validate our findings.

The major strengths of the current study include (1) the repeated collection of ≥3 24-hour dietary recalls provided more accurate dietary assessments compared with 2 recalls used in other studies11,12,28,41; (2) use of a wide range of robust measures of adiposity by dual-energy x-ray absorptiometry and by magnetic resonance imaging provided more information than by BMI alone; and (3) a relatively large, apparently healthy adolescent population with nearly equal distribution of male and female and white and African American participants. However, there are several notable limitations. First, because of our cross-sectional study design, the associations between sodium consumption and adiposity and inflammation do not prove causality. On the other hand, the Dietary Approaches to Stop Hypertension diet low in sodium, fat and high in fruits and vegetables has been associated with reduced body weight and BMI.42–44 However, it is difficult to determine whether the weight reduction is due to sodium reduction alone or combination. To the best of our knowledge, no study evaluating the effect of sodium reduction on adiposity and leptin has been conducted. Therefore, longitudinal studies or clinical trials of sodium restriction independent of energy consumption are warranted to establish the role of high sodium intake in the development of adiposity and inflammation. Second, our estimates of dietary sodium intake were based on self-reported 24-hour dietary recalls rather than on 24-hour urine collection, which is considered to be the most reliable and accurate method. Although 24-hour dietary recalls may underestimate the usual sodium intake, sodium intake from the repeated dietary recalls correlated significantly with the 24-hour urinary excretion and provided a valid method in previous association studies.11,12,28,41,45,46 In addition, the average sodium intakes in our adolescent population is comparable to the NHANES 2003–2008 data.28 Finally, our findings in white and African American adolescents might not be generalizable to other populations.

CONCLUSIONS

Despite efforts to reduce sodium intake in the United States and around the world, consumption levels remain high. Our adolescent data show that the average amount of sodium consumed by our adolescents is as high as that of adults and more than twice the AHA’s daily recommended value. In addition, our findings suggest that higher sodium consumption is associated with greater adiposity, leptin resistance, and inflammation independent of total energy intake and sugar-sweetened soft drink consumption. Longitudinal studies or clinical trials in youth are warranted to establish the role of high sodium intake in the development of adiposity, leptin resistance, and inflammation.
REFERENCES


Dietary Sodium, Adiposity, and Inflammation in Healthy Adolescents
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