Evidence for a relation between salt and blood pressure (BP) has accumulated for over 50 years. Animal studies, cross-country ecological studies, epidemiologic studies of individuals, randomized trials, and meta-analyses of trials show that salt intake is directly related to BP and that lowering salt intake lowers BP.

In addition to examining group average BP responses to salt intake, researchers have reported that BPs of some individuals fall with reduction in salt intake, but BPs of others do not (ie, interindividual differences in BP response), leading to the concept of salt sensitivity in individuals. Conclusions regarding salt sensitivity have been generally based on observations of BP responses in individuals who have undergone an experimental protocol only once. These protocols varied sodium intake and/or excretion over a period of time, often for only a few days or 1 to 2 weeks, and sometimes used extreme variations in salt intake. Although one-time individual BP responses to sodium reduction have a continuous distribution, investigators have interpreted these data dichotomously, responders and nonresponders, based on arbitrarily defined cut-points. These interpretations led to suggestions that strategies for reduced sodium intake be directed at “susceptible” individuals rather than the general public.

Some studies have attempted to examine whether classification of salt sensitivity of individuals (present versus not present) is a stable attribute by repeating procedures to assess reproducibility of the BP response. Investigators have interpreted data on reproducibility as either good or poor. Several factors may account for these contrasting interpretations, including participant differences across studies, varied duration of sodium intervention and amount of sodium levels given, sample size differences, lack of control of nutrients other than sodium, or lack of consensus as to what constitutes “good” reproducibility. Alternatively, one can view the mixed results as an indication that individual BP response to salt varies, in part randomly.
Because there is considerable intraindividual random variation in blood pressure from day to day without change in salt intake, to identify an individual validly as salt-sensitive requires that intraindividual random variation in BP be taken into account. This random BP variation suggests that identifying individuals as salt-sensitive or not based on assessment of their BP response to change in salt intake only once or twice is likely to be unreliable, that is, is subject to considerable misclassification—both false-positives and false-negatives.

The Dietary Approaches to Stop Hypertension (DASH)-Sodium trial20–22 provided a special opportunity to examine range and consistency of individual BP responses to changes in salt intake in a large study sample consuming a controlled diet. This 14-week, multicenter outpatient feeding study examined effects of sodium intake on BP in participants given either a control diet, similar to what many Americans consume, or the DASH diet, each delivered at 3 different levels of sodium, fed in random order. The trial, which compared group mean changes, found that for participants consuming the control diet, a 77-mmol/d lower sodium intake (64 mmol/d versus 141 mmol/d) reduced BP by an average of 6/3.5 mm Hg.21 Mean BP was reduced in all subgroups (64 mmol/d versus 141 mmol/d) reduced BP by an average of 6/3.5 mm Hg.21

The DASH-Sodium trial compared the effects on BP of three levels of sodium intake in a large study sample consuming a controlled diet. Of these, 188 (92.2%) completed all three feeding periods. Data were analyzed comparing mean BP changes in the lower sodium diet, and salted versions were used in higher sodium diets. In addition, table salt was weighed and added to the lower range of stage 1 hypertension. The three sodium levels were 62 mmol/d (L), reflecting a possibly more favorable level of sodium intake, to identify an individual validly as salt-sensitive (or not) based on assessment of their BP response to change in salt intake only once or twice.

This report focuses on individual as opposed to group BP responses to changes in salt intake in participants who were randomly assigned to the control diet. The control diet was similar to diets of previous dietary studies on salt sensitivity. Also, participants assigned to the control diet had their BP measured on two occasions at the same sodium level while consuming the same diet, thus permitting an evaluation of reproducibility of BP response to no change in salt intake. Strengths of the trial include 30-day feeding periods of salt intake at three clinically relevant levels, control of intakes of other nutrients as well as sodium, maintenance of stable body weight, and a large sample size that included men and women, blacks and nonblacks, and older and younger individuals. This report assesses individual BP responses to changes in salt intake and consistency of these responses. Specifically, this report examines (1) systolic BP (SBP) responses of individuals after no change in salt intake (ie, natural intraindividual variability of BP); (2) SBP responses of individuals after a change in salt intake; and (3) consistency of SBP responses of individuals to change in salt intake.

Methods

Design

The DASH-Sodium trial compared the effects on BP of three levels of sodium intake and two dietary patterns among adults with nonhypertensive but higher than optimal blood pressure or at the lower range of stage 1 hypertension. The three sodium levels were defined as “higher” (H), reflecting typical US consumption, “median” (M), reflecting the upper limit of current US recommendations, and “lower” (L), reflecting a possibly more favorable level of sodium intake.

During a 2-week run-in period, participants ate a diet typical of what many Americans consume (control diet) at the higher sodium level (H run-in) and then were randomly assigned to eat one of two dietary patterns (control or DASH) for a period of 3 months (parallel group design). Participants ate their assigned diet at 3 levels of sodium, each level for 30 days, in a 3-period crossover design.

Eligibility requirements included age 22 years and older, with SBP 120 to 159 mm Hg and DBP 80 to 95 mm Hg, based on average BP measured during 3 screening visits spaced at least 1 week apart. Persons were excluded who took antihypertensive medication or any medication affecting blood pressure.20 Of 412 men and women randomly assigned into the trial, 204 were assigned to the control diet. Of these, 188 (92.2%) completed all three feeding periods. Data analyses here are based on these 188 participants.

Measurements

At each visit, technicians obtained two readings of BP 30 seconds apart, using a random-zero sphygmomanometer after the participant had been seated quietly for 5 minutes. BP during run-in was defined as the mean of 2 pairs of measurements taken once each week during the 2-week run-in period. BP at each sodium level was defined as the mean of 5 pairs of BP measurements taken during the final 9 days of each 30-day intervention feeding period. Participants provided 24-hour urinary collections once during screening and once at the end of each feeding period. Measurement staff followed a common standardized protocol and underwent centralized training annually and recertification semiannually. Throughout the study, research staff monitored quality of BP measurements. Measurement staff were masked to treatment assignment; participants and kitchen staff were masked to outcome data, including BP.

Dietary Protocol

All meals and snacks were prepared in research kitchens, and one meal per day was consumed on-site. Similar foods were used for each level of sodium; the unsalted or low-sodium varieties were used in the lower sodium diet, and salted versions were used in higher sodium diets. In addition, table salt was weighed and added to entrees, recipes, or unsalted broth for higher sodium levels. Body weights were kept constant by weighing participants each weekday, and energy levels were adjusted if necessary. Adherence was

### Table 1. Six Possible Sequences of Sodium Intake in the DASH-Sodium Trial

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Run-In†</th>
<th>Period Sequence</th>
<th>n</th>
<th>Analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H run-in</td>
<td>L M H</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>H run-in</td>
<td>L H M</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>H run-in</td>
<td>M L H</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>H run-in</td>
<td>M H L</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>H run-in</td>
<td>H L M</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>H run-in</td>
<td>H M L</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>

*Each period was 30 days, and BP was measured during the last 9 days of each feeding period; L indicates lower, 62 mmol/d; M, medium, 104 mmol/d; and H, higher sodium level, 140 mmol/d.

†Run-in, which lasted 2 weeks, always preceded each sequence, and sodium level during run-in was identical to the higher sodium level.
monitored through daily observation, attendance records, and daily logs completed by participants.

**Statistical Methods**

Although previous studies on salt sensitivity focused on change in mean arterial pressure, analyses in this report focus on SBP. SBP is most predictive of cardiovascular risk and is a number more easily interpreted and understood clinically than mean arterial pressure. In addition, as previously reported, SBP and DBP response patterns to dietary sodium changes were similar.21,22

We calculated group descriptive statistics for baseline characteristics and group average SBP change over time in response to reduced salt intake to assess whether SBP achieved stability during the 30-day period. We used histograms to display the distribution of individual SBP change with change in salt intake and the degree of natural variability in SBP change when sodium intake was not altered. We also compared standard deviations of these changes to assess how much variability in SBP response to sodium is actually caused by sodium. If most of the variability of SBP change is actually caused by sodium change, then the 2 standard deviations should be perceptibly different. On the other hand, if most variability in SBP change is due to other factors, the 2 standard deviations should be similar.

To examine SBP response when sodium intake was not changed, we compared data from the run-in period with that of the higher sodium period on the control diet because menus and sodium levels were the same. Run-in differed from the higher sodium period only in duration (2 versus 4 weeks), number of BP measurements (average of 2 pairs versus 5 pairs), and the fact that it always preceded each sequence of the 3 sodium periods.

Since participants did not consume the medium or lower sodium level twice, we assessed consistency of SBP response to sodium by calculating Spearman rank correlations. We hypothesized that a participant who had a large SBP change with higher versus medium sodium levels, for example, probably would have a large response with medium versus lower sodium levels as well, relative to other participants (ie, would have similar SBP response rank for each change in sodium level). We avoided using the medium (or any) sodium level twice, which would have created a statistical artifact similar to that noted by Bland and Altman.25 In addition, to avoid introducing additional variability, such as carryover effects, we examined in this consistency analysis only relevant sodium periods that were consecutive. Specifically, we computed a correlation of ranks of SBP change in response to sodium level difference between run-in and L (L minus Hrun-in) versus SBP change in response to sodium level difference between H and M (M minus H) in 66 participants assigned to Hrun-inMLH or Hrun-inMLM sodium sequences (Table 1, rows 1 to 2). Similarly, we computed the rank correlation of SBP change in response to sodium level difference between run-in and M (M minus Hrun-in) versus H and L (L minus H) in 63 participants assigned to Hrun-inMLH or Hrun-inMHL sodium sequences (Table 1, rows 3 to 4). Statistical analyses were performed with the use of the Fisher z-transformed correlations.

In examining consistency of response, most published studies classified individuals categorically as sodium-sensitive, based on an arbitrary cut-point with a sodium protocol conducted twice.27 To compare our results with previous studies, we also examined consistency of response categorically. For this analysis, we identified each participant as being above or below the group median SBP change. For the (L minus Hrun-in) or (L minus H) change, the median was –6.4 (SD = 9.6) mm Hg. For the (M minus H) or (M minus Hrun-in) change, the median was –3.4 (SD = 6.6) mm Hg. We could not use the same cut-point for each occasion to define salt sensitivity because on one occasion the sodium difference was 78 mmol (L minus H or Hrun-in) and on the other occasion it was 36 mmol (M minus H or Hrun-in). The Fisher exact test was used to determine whether SBP response on one occasion was independent of SBP response on another occasion.

<p>| TABLE 2. Baseline Characteristics of Participants Consuming the Control Diet |
|---------------------------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n=188</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>49.4 (10.2)</td>
</tr>
<tr>
<td>Age &gt;45 years, %</td>
<td>64.9</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85.5 (16.2)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29.6 (4.9)</td>
</tr>
<tr>
<td>Women, %</td>
<td>54.8</td>
</tr>
<tr>
<td>Black, %</td>
<td>57.5</td>
</tr>
<tr>
<td>SBP, mm Hg†</td>
<td>135.5 (9.4)</td>
</tr>
<tr>
<td>DBP, mm Hg‡</td>
<td>85.7 (4.1)</td>
</tr>
<tr>
<td>With hypertension, % †</td>
<td>40.4</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>144.1 (7.2)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>88.1 (4.1)</td>
</tr>
<tr>
<td>Without hypertension, % †</td>
<td>59.6</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>129.7 (5.4)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>84.1 (3.2)</td>
</tr>
<tr>
<td>Mean arterial pressure §</td>
<td></td>
</tr>
<tr>
<td>With hypertension, n=76</td>
<td>102.3 (4.9)</td>
</tr>
<tr>
<td>Without hypertension, n=112</td>
<td>106.8 (3.5)</td>
</tr>
<tr>
<td>24-hour urinary sodium, mmol/d ‡</td>
<td>152.7 (73.1)</td>
</tr>
<tr>
<td>24-hour urinary potassium, mmol/d</td>
<td>52.7 (23.0)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (SD) or percentage, as indicated.

*Baseline BP is defined as average of pairs of measurements during 3 screening and 2 run-in visits.
†Hypertension is defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg averaged over 3 screening visits.
‡Indicates customary intake based on 24-hour urinary excretion obtained during screening.
§Mean arterial pressure = DBP + (SBP – DBP)/3.

**Results**

**Group Results for Baseline Characteristics, Adherence, and Average SBP Over Time**

**Baseline Characteristics**

Overall, participants were middle-aged and overweight (Table 2). More than half were women, more than half were black, and 40% had hypertension. Mean 24-hour urinary sodium and potassium excretion was 152.7 and 52.7 mmol/d, respectively.

**Group Adherence**

As intended,21 mean 24-hour urinary potassium excretion was similar across sodium levels (data not shown), reflecting that dietary potassium was held constant. Body weight was similar at each sodium level (data not shown). Mean ± SD urinary excretion was 140±55, 104±42, and 62±33 mmol/d at the 3 levels of sodium.

**Group Average Pattern of SBP Over Time at Lower Sodium Intake**

To examine the length of time required for group average SBP response to stabilize after change in salt intake, we plotted weekly average (±95% CI) SBP at lower sodium level of participants (n=188) with the control diet (Figure 1). Group average SBP at the end of higher sodium level is displayed as a reference point. SBP progressively decreased
over 4 weeks, with greatest reduction after 1 week and further reductions thereafter. This pattern was similar for 66 participants assigned to Hrun-inLMH or Hrun-inLHM (L immediately after run-in) and for 61 participants assigned to Hrun-inMHL or Hrun-inHLM (L immediately after H).

Variability in SBP With No Change in Sodium Intake
To display random SBP variation within an individual and its range across individuals when the same higher level of sodium was consumed twice, we show in Figure 2 the distribution of SBP change between run-in and higher sodium levels (Hrun-in minus H). Group (n=188) average SBP change was 1.9 mm Hg (not significantly different from zero), but the range across individuals was -24 to +25 mm Hg. SBP changes at selected percentiles are shown in Table 3 (left column). Of individual responses, 22.9% had an SBP decrease $\geq 5$ mm Hg; 8.0% had a decrease $\geq 10$ mm Hg; 37.8% had an increase $\geq 5$ mm Hg; 14.9% had an increase $\geq 10$ mm Hg. These increases and decreases occurred despite consistent intake of sodium and other nutrients between the two measurements. Results were similar with analyses restricted to participants (n=61) randomly assigned to sodium sequences that went directly from higher to lower, for example, Hrun-inHLM and Hrun-inMHL (data not shown). Results were also similar with analyses restricted to nonblacks (n=80), a group that tends to show lower average BP response to salt reduction than blacks (data not shown).

Consistency in Response
We examined consistency of individual SBP responses when lower and higher levels of sodium were consumed on two occasions, with run-in as a replicate of higher sodium (Table 1). In 66 participants assigned to the Hrun-inLMH or Hrun-inLHM (ie, Hrun-in-HLM or Hrun-in-HML sequence; range, -17.1 to +23.7 mm Hg; mean±SD SBP change, 0.8±8.0 mm Hg). Results were also similar with analyses restricted to nonblacks (n=80; range, -18 to +24 mm Hg; mean±SD change, 2.5±7.8 mm Hg).

Variability in SBP Response to 77-mmol/d Difference in Sodium Intake
To display individual SBP response to change in sodium intake, we show in Figure 3 the distribution of SBP change (L minus H) in response to 78 mmol/d sodium difference (n=188). With lower sodium intake, the distribution of individual SBP responses was shifted downward (ie, to lower values of SBP) compared with the distribution in Figure 2 when sodium intake was not changed in these 188 participants. Standard deviations of the distributions in Figures 2 and 3 were similar (8.4 versus 8.6, Table 3), suggesting that much of the variability in “SBP response to sodium” is due to random factors not related to sodium change. This pattern of findings also suggests that many of the “adverse” BP responses (ie, BP increase) to sodium reduction are likely to be due to chance; otherwise, the standard deviation would have increased in the setting of sodium reduction. Group average response was -6.7 mm Hg ($P<0.0001$; range, -32 to +17 mm Hg). SBP changes at selected percentiles are shown in Table 3 (right column). About 55% of participants had SBP decrease $\geq 5$ mm Hg; 33.5% had SBP decrease $\geq 10$ mm Hg. About 6% had SBP increase $\geq 5$ mm Hg, and 2 individuals (1.1%) had SBP increase $\geq 10$ mm Hg. Results were similar with analyses restricted to participants (n=61) randomly assigned to sodium sequences that went directly from higher to lower, for example, Hrun-inHLM and Hrun-inMHL (data not shown). Results were also similar with analyses restricted to nonblacks (n=80), a group that tends to show lower average BP response to salt reduction than blacks (data not shown).
sodium sequence, the Spearman correlation coefficient for (L minus H) run-in versus (M minus H) was 0.27 (P=0.030); in 63 participants assigned to H run-in MHL or H run-in MLH sequence, the Spearman coefficient for (M minus H run-in) versus (L minus H) was 0.27 (P=0.034); the combined correlation was 0.27 (P=0.002). Figure 4 shows the scatterplot for these 129 pairs of responses.

Based on chance only, with change in sodium intake a person’s SBP response above or below the group median on one occasion should give no information about whether that person’s response will be above or below the group median on another occasion. By chance, one quarter of the participants should be above the median both times, one quarter should be below the median both times, and half should be inconsistent responders. Based on the group median responses (ie, 2.8 and 3.4 mm Hg, respectively), 37 (29%) participants were categorized as being salt-sensitive on both occasions, whereas 36 participants (28%) were categorized as being not salt-sensitive on both occasions, for a total of 57% who were consistent. The rest were inconsistent responders: 56 (43%) participants were categorized as salt-sensitive one time (n=28) but not the other (n=28). Independence of SBP response on the two occasions could not be ruled out (P=0.16). Of these 129 participants, 75 were nonhypertensive at baseline. Of these nonhypertensive participants, 15 (20%) would be categorized as salt-sensitive and 25 (33%) as not salt-sensitive, with the remaining 35 (47%) categorized as inconsistent (P=0.81). Of the 54 hypertensive participants at baseline, 22 (41%) would be categorized as salt-sensitive and 11 (20%) as not salt-sensitive, with the remaining 21 (39%) categorized as inconsistent (P=0.26).

**Discussion**

This study showed that individual SBPs are variable over time, even when carefully measured by highly trained staff and when intake of sodium and other nutrients did not vary at all. Furthermore, rank correlations between 2 responses by the same participant (r=0.27), although statistically significant, are too weak to reliably identify individuals whose SBPs respond consistently to salt intake.

We previously showed that with sodium intake lower by 77 mmol/d, SBP is reduced by an average of 6.7 mm Hg and

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**TABLE 3. Distribution of SBP Changes in the Settings of (a) No Sodium Change and (b) 78 mmol Sodium Change**

<table>
<thead>
<tr>
<th></th>
<th>(a) No Sodium Change</th>
<th>(b) 78 mmol Sodium Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Higher run-in – Higher), n=188</td>
<td>(Lower – Higher), n=188</td>
</tr>
<tr>
<td>Quantiles</td>
<td>SBP mm Hg</td>
<td>SBP mm Hg</td>
</tr>
<tr>
<td>Maximum (Largest increase)</td>
<td>24.7</td>
<td>17.4</td>
</tr>
<tr>
<td>95th</td>
<td>15.5</td>
<td>5.4</td>
</tr>
<tr>
<td>75th</td>
<td>6.9</td>
<td>0.1</td>
</tr>
<tr>
<td>50th</td>
<td>2.8</td>
<td>-5.8</td>
</tr>
<tr>
<td>25th</td>
<td>-3.4</td>
<td>-12.7</td>
</tr>
<tr>
<td>5th</td>
<td>-11.3</td>
<td>-21.8</td>
</tr>
<tr>
<td>Minimum (Largest decrease)</td>
<td>-24.3</td>
<td>-31.5</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.9 (8.4)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-6.7 (8.6)</td>
</tr>
</tbody>
</table>

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**Figure 3.** Distribution of change in SBP in response to 78 mmol/d difference (higher versus lower) in sodium intake (n=188). Each 5-mm Hg bar is centered (eg, the 0 change bar represents the interval between -2.5 and +2.4 mm Hg).
that certain subgroups had greater average SBP responses than the overall average response (eg, 8.3 versus 5.6 mm Hg for those with hypertension compared with those nonhypertensive and 7.5 versus 5.3 mm Hg for older compared with younger adults).22 Other investigators have also reported variability in group average BP response to salt intake based on demographic and other characteristics, such as hypertension status, race, age, and gender.28–31

Ability to identify individual responders is a much more difficult task than showing the existence of groups that are more or less responsive, based on their average SBP response. Although BP response to salt reduction tends to follow a continuous distribution, some investigators have incorrectly interpreted available data based on one measurement to assert that some individuals respond to sodium reduction with a BP rise. We found that 37.8% of individuals had an SBP increase of 5 mm Hg or more and thus could have been classified as “adverse responders,” even when there was no change in sodium intake. Furthermore, the fact that the BP distribution was shifted without a change in its variability when sodium was lowered supports the idea that many adverse responses are not related to sodium reduction. The considerable variation in changes in SBP within individuals, even when sodium, weight, and diet are held constant (Figure 2 and Table 3), could be due to multiple reasons other than diet, including measurement error, inherent day-to-day BP fluctuation, environmental or behavioral stresses, and changes in physical activity. The only way to be confident about an individual’s true response to sodium is to have the individual consume different sodium levels many times and compute the average difference between higher and lower sodium intakes. This design was not used in the DASH-Sodium trial or any other study to our knowledge. The need for multiple measurements to define the relation between sodium intake and BP in individuals has been described previously.32,33

Investigations of salt sensitivity have rarely been conducted on population-based samples, and reports of “prevalence” of salt sensitivity have often been based on BP responsiveness to variations in salt intake using protocols conducted only one time. As repeat testing showed in the present study, significant proportions will be false-positives and false-negatives. With use of data from two tests and using median SBP change as the cut-point for both tests, by definition 25% of participants are classified as “salt-sensitive”; many of those are false-positives. With one test only, the proportion of positives (ie, those classified as salt-sensitive) depends on the cut-point used to define responders. Using a cut-point of −10.0 mm Hg with one test, the DASH-Sodium data show that 33.5% of participants would have been identified as salt-sensitive. Such a stringent cut-point would result in more frequently not identifying individuals who really are salt-sensitive (ie, more false-negatives). With no generally accepted definition of salt-sensitivity, cut-points are chosen arbitrarily, and resulting “prevalence” estimates are arbitrary, fail to take into account misclassification, and are not meaningful. From a public health perspective, a high false-negative rate is less desirable than a high false-positive rate, since recommendations to follow a healthy diet reduced in salt pose no harm to individuals whose BP truly does not respond to salt intake reduction (ie, false-positives).

Several studies examined reproducibility of salt-sensitivity tests using salt intake protocols conducted twice. Some investigators concluded that salt sensitivity was a reproducible phenomenon.12–16 Detailed examination of the results from these studies shows that judgment of “good” reproducibility is subjective. Although group average responses of repeated measurements may be close,12 this approach does not address whether the individual responses are highly correlated. Two studies, one using a laboratory-based challenge that varied salt intake through saline infusion and subsequent diuretic treatment on the following day in 29 individuals and the other using a dietary protocol that varied salt intake by 280 mmol/d for 7 days in 31 individuals, reported statistically significant correlation coefficients in BP response between repeat sodium protocols of 0.5613 and 0.71.14 Although of greater magnitude than the correlations we observed, even the high correlation of 0.71 still explains only 50% of the variation in BP response. Other studies reported that 75%16 and 100%15 of participants received the same classification of salt-sensitive or not based on conducting the salt-sensitivity protocol twice. These latter two studies had small sample sizes, ranging from 10 to 17. In addition, since there is no standardized criterion for establishing cut-points to define salt-sensitivity, a more stringent cut-point, for example, change of 10 mm Hg rather than 516 or 8 mm Hg,15 which was used in these studies, might have resulted in lower percentage agreement. Finally, most studies tested reproducibility of short-term response (1 to 7 days),
some of which involved extreme manipulations of sodium intake and plasma volume; consistency of short-term response may not be comparable or relevant to consistency of longer-term response and to response to more moderate sodium changes.

Other investigators who conducted a salt-sensitivity protocol on two occasions have concluded that salt sensitivity is not a highly reproducible phenomenon in individuals. Consistency in response was interpreted as poor, with intraclass correlation coefficients between two responses of 0.13 for ambulatory BP and 0.45 for clinic-measured mean arterial pressure. Similarly, Gerdts et al reported a nonsignificant correlation of 0.26 for casual and 0.02 for average 24-hour ambulatory BP when 30 participants underwent a salt-sensitivity protocol twice. Other investigators reported weak κ statistics ranging from 0.24 to 0.38 when correlating the classifications of salt sensitivity and no salt sensitivity after conducting their protocol twice. Using a cut-point of ≥5 mm Hg change in mean arterial pressure, Mattes et al reported that only 54% of 25 participants were consistently classified as salt-sensitive or not. Although our results were similar to those of Mattes, these percentages are highly dependent on cut-points chosen.

Unlike our correlational analyses, our categorical analyses, which used cut-points to define responders, did not achieve statistical significance (P = 0.002 versus P = 0.16). In part, this lack of significance reflects the reduced power for analyzing categorical versus continuous data. Assuming that the observed consistency was indeed the true consistency, our power for rejecting the null hypothesis of independence of response on the two occasions with only 129 individuals was 0.30. Previous studies of consistency in BP response to salt intake changes typically had sample sizes less than 30, indicating that they were underpowered for categorical analyses.

Based on published results from protocols conducted thus far, no evidence has been provided that the characterization of salt sensitivity of individuals is a stable attribute. In the present study, with participants broadly representative of about 50% of the US population, with a relatively robust sample size of 129 to test for consistency of response, and with all aspects of diet controlled and blood pressure carefully measured, even 4 weeks of a sodium feeding period were not sufficient to produce high rank correlation coefficients. Categorical analyses, with use of group median response as a cut-point, showed only slightly more than one quarter of participants (i.e., 29%) could be classified as consistently salt-sensitive when by chance 25% would be expected to be so classified. Our study design did not include exact duplicate protocols, as the run-in condition lasted only 2 weeks with 2 pairs of BP measurements, whereas the higher sodium period lasted 4 weeks with 5 pairs of BP measurements, which could have contributed to higher variability than in studies that had exact duplicate protocols and more BP measurements. Nevertheless, both sodium periods had the same menus with the same sodium levels, and ranks relative to other participants should have been consistent.

Of interest is the time course of group average SBP response to lower sodium levels. Group average SBP of participants on lower sodium progressively declined throughout the 4 weeks. Although the greatest decline occurred after 1 week, the lower sodium level had not yet exerted its full blood pressure–lowering effect by 4 weeks.

We conclude that to identify individuals as salt-sensitive or not, a different study design than what has been used thus far is necessary. Such a study design would require an individual to undergo variations in salt intake several times, is costly and inefficient, and may not lead to clinically useful methods to identify responders. Perhaps in the future, individuals will be more reliably identified as responders on the basis of other yet-to-be-identified characteristics. Until then, current recommendations for lower salt intake directed at the general public rather than targeted solely to unidentifiable “susceptible” individuals should continue as one of several strategies to prevent and control adverse BP levels widely prevalent in the adult population.

Perspectives

These study results show that because BP varies so much from day to day within individuals, it is very difficult to characterize individuals as being greater or lesser responders to salt intake changes. This conclusion implies that the model of targeting sodium-lowering interventions to individuals identified as salt-sensitive would not be worthwhile. Thus, the more appropriate approach is a public health one that targets its message to the general public without any effort to identify individuals whose BP would be most likely to respond. The value of this strategy is underscored by the fact that because BP (especially SBP) rises with age, a majority of the population is at risk of developing high blood pressure. After age 60 years, more than 50% of US adults have high BP, and reducing life-long exposure to high salt intake may prevent this BP rise. In addition, population-wide reduction to moderate salt levels could best be accomplished by reducing the amount of salt added during food processing and preparation, thereby returning the US food supply to sodium levels that existed before widespread use of highly processed food and foods prepared outside the home. Both the currently recommended sodium limit of 100 mmol/d and the level (65 mmol/d) the DASH results suggest may be preferable, are moderate, and still are much higher than physiological requirements of ~20 mmol/d. For patients receiving drug therapy, individual adjustment, either of sodium intake or medication usage, or both, may be needed for their hypertension treatment. As with other widely prevalent diseases, public health recommendations directed to the general public are the best means for preventing high BP.

Appendix

The DASH-Sodium Collaborative Research Group

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