

Citation:

Schmidlin O, Forman A, Sebastian A, Morris RC Jr. Sodium-selective salt sensitivity: its occurrence in blacks. *Hypertension*. 2007 Dec; 50 (6): 1,085-1,092. Epub. 2007 Oct. 15.

PubMed ID: [17938378](#)

Study Design:

Non-Randomized Controlled Trial

Class:

C - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To test the hypothesis that the sodium (Na⁺) components of dietary sodium chloride (NaCl) can have a pressor effect apart from its capacity to complement the extracellular osmotic activity of chloride (Cl⁻) and thus plasma volume.

Inclusion Criteria:

- Black (ethnicity)
- Age 35 to 56 years
- Screening blood pressure (BP) under 160/100mmHg
- Body weight within 30% of ideal.

Exclusion Criteria:

Not specified.

Description of Study Protocol:**Recruitment**

Not specified.

Design

- 21-day study
- All participants ate a eucaloric basal metabolic diet providing:
 - 30mmol of Na⁺ and 45mmol of potassium (K⁺) per 70kg of body weight per day
 - Water, 20g per kg of body weight per day during Na⁺ restriction
 - Water, 35g per kg of body weight during Na⁺ loading

- There were three consecutive seven-day periods: Two periods of oral Na⁺ loading separated by a period of Na⁺ restriction
- All participants received placebo tablets during the second (low-salt) week
- The first standardized blood pressure measurements were obtained within approximately two hours of the subject's arrival at the General Clinical Research Center at 2:00 p.m. (considered initial or baseline BP).

Blinding Used

Participants and nurses performing BP measurements were not informed about the content of the tablets.

Intervention

- Na⁺ loading:
 - 250mmol per 70kg of body weight per day (but no more than 300mmol per day) was supplemented as NaCl during the first or third week
 - 250mmol per 70kg of body weight per day (but no more than 300mmol per day) was supplemented as sodium bicarbonate (NaHCO₃) during the first or third week
- BP was measured with an automated oscillometric device (Dinamap, Criticon Inc.) programmed to obtain five readings over a period of five minutes.

Statistical Analysis

- ANOVA
- Newman-Keuls test (supplement order)
- Paired and unpaired T-tests
- Non-parametric tests
- Linear regression
- Spearman's Rank correlation analyses
- Data are presented as mean and 95% CI. The null hypothesis was rejected at P<0.05.

Data Collection Summary:

Timing of Measurements

- Study last for 21 days total
- Three consecutive seven-day periods
- Two Na⁺ loading weeks separated by a Na⁺ restriction week.

Dependent Variables

- Assessment of Na⁺ induced pressor effects:
 - BP:
 - Measured daily every four hours (between 6:00 a.m. and 10:00 p.m.) after 10 minutes of supine rest
 - An average daily BP was calculated
 - Mean arterial pressure (MAP): The average MAP of Days Five and Six during Na⁺ restriction was subtracted from the average MAP of Days Five and Six during loading of either NaCl or Na HCO₃
 - Salt sensitivity (SS): Defined as an NaCl-induced increase in MAP of at least 5mmHg
 - Salt resistance (SR): Defined as an increase of <5mmHg

- Assessment of metabolic outcomes:
 - *Body weight*: Measured daily at 6:00 a.m.
 - *Spontaneously voided urine*: Collected daily over 24-hour periods and analyzed for Na⁺, Cl and creatinine
 - *Cumulative Na⁺ excretion (during Week Three only)*: Corrected for creatinine excretion and adjusted for 70kg of body weight
 - *Blood samples (obtained by standon the last day of each seven-day period between 9:00 a.m. and 12 noon)*: Plasma renin activity, aldosterone, hematocrit, creatinine and serum electrolytes
- Renal hemodynamics: Para-aminohippurate clearance studies were performed in 31 participants (16 SS and 15 SR subjects) on the last day of each seven-day period (using standard methods).

Independent Variables

- NaCl
- NaHCO₃.

Description of Actual Data Sample:

- *Initial N*: 35 (32 male, three female)
- *Attrition (Final N)*: 35
- *Age*: 35 to 56 (SS subjects were slightly older than SR subjects).

	SR (N=17)	SS (N=18)	sNaS (N=11)	cSS (N=7)
Age (Years)	45.2±2.7	49.6±1.8	49.0±2.5	50.7±2.3

- *Ethnicity*: Black.
- *Anthropometrics*

	SR (N=17)	SS (N=18)	sNaS (N=11)	cSS (N=7)
BMI (kg/m²)	27.2±1.4	24.8±1.3	24.5±2.7	25.3±2.1

- *Location*: General Clinical Research Center, University of California, San Francisco.

Summary of Results:

	SR	SS	sNaS	cSS	Significance
N	17(49%)	18(51%)	11(61%)	7(39%)	
Initial SBP (mean±95% CI, mmHg)	120±8	133±6*	133±7	134±11	*P<0.05
Initial DBP (mean±95% CI, mmHg)	68±4	80±4*	82±4	77±6	*P<0.05

SBP >140 or DBP >90mmHg, N (%)	2(12)	5(28)	3(27)	2(29)	
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Salt Sensitivity

- 51% (17 male, one female) were SS: Average NaCl-induced Δ MAP was 11 ± 2 mmHg
- 49% (15 male, two female) were SR: Average NaCl-induced Δ MAP was -1 ± 2 mmHg
- In SS subjects Na⁺ restriction during Week Two induced a significant hypotensive effect relative to initial BP.

Demographic Characteristics

- SS subjects had significantly higher initial BP, higher serum Na⁺ concentration and lower BMI
- Adjusted for age and BMI, the difference remained significant for DBP and MAP (not SBP).

Pressor Effects of NaHCO₃

- The sequence in which Na⁺ salts were loaded did not affect their pressor effects
- In SS, NaHCO₃ loading, compared to restriction, induced significant pressor effect. This pressor effect was significantly less than that of NaCl
- Mean values of Δ MAP adjusted for change in serum K⁺ or hematocrit were not different from unadjusted means.

Effects of NaHCO₃ and NaCl on Renal Hemodynamics

In SS, both NaHCO₃ and NaCl induced significant decreases in renal blood flow and increases in renal vascular resistance.

Metabolic Effects of NaHCO₃ and NaCl

- Both NaCl and NaHCO₃ induced similar significant increase in body weight in SS and SR
- Both NaCl and NaHCO₃ induced significant decreases in Hematocrit values in SS and SR but were significantly larger with NaCl than NaHCO₃
- NaCl-induced decrease in PRA (but not aldosterone) was slightly but significantly greater in SR than in SS
- In SS (but not SR) BP varied directly and highly significantly with the serum concentration of Na⁺.

Author Conclusion:

The current observations demonstrate that the Na⁺ component of NaCl can have pressor and renal vasoconstrictive properties apart from its capacity to complement Cl⁻ in plasma volume expansion.

Reviewer Comments:

Small sample size: Only 35 subjects; when separated by gender, only 8% (three out of 35) were women.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

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|----|---|-----|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

Validity Questions

- | | | |
|------|---|-----|
| 1. | Was the research question clearly stated? | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| 2. | Was the selection of study subjects/patients free from bias? | Yes |
| 2.1. | Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? | Yes |
| 2.2. | Were criteria applied equally to all study groups? | Yes |
| 2.3. | Were health, demographics, and other characteristics of subjects described? | Yes |
| 2.4. | Were the subjects/patients a representative sample of the relevant population? | ??? |
| 3. | Were study groups comparable? | Yes |
| 3.1. | Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT) | N/A |
| 3.2. | Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline? | Yes |
| 3.3. | Were concurrent controls used? (Concurrent preferred over historical controls.) | N/A |

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	Yes
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	Yes
5.	Was blinding used to prevent introduction of bias?	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	Yes
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	Yes
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	Are conclusions supported by results with biases and limitations taken into consideration?	No
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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