Neonatal Blood Pressure and Salt Taste Responsiveness

Stephen H. Zinner, Stephen T. McGarvey, Lewis P. Lipsitt, Bernard Rosner

Abstract—To test the association between neonatal blood pressure (BP) and salt taste response, 283 healthy hospitalized neonates were administered small drops (0.06 mL) of water and 0.1 molar (mol/L) and 0.3 mol/L NaCl solutions by means of cannulas through a nipple with a pressure transducer to record sucking responses. Neonatal and 1-month BPs were recorded by ultrasound. Mean number of sucks per burst was scored as “aversive” if the 0.3 mol/L salt minus water difference score was ≤ −10 mean sucks per burst, “preferential” if this difference was >0, and “neutral” otherwise. Babies with “preferential” responses had higher diastolic BPs than those with neutral (1.9 mm Hg) or aversive responses (3.1 mm Hg) \((P \text{ trend}=0.05)\). After adjustment for age, gender, birth weight, and activity for babies with at least one grandparent receiving antihypertensive medication, mean adjusted systolic pressure was 6.7 mm Hg higher \((P=0.003)\) \((P \text{ trend}=0.003)\) and mean adjusted diastolic pressure was 5.0 mm Hg higher \((P=0.010)\) \((P \text{ trend}=0.011)\) in neonates with preferential versus aversive salt taste responses. There was no relation of BP to sucking responses to sweet (sucrose) stimuli. Neonates can distinguish between dilute salt solutions and water. This response is related to BP and might be a potential risk factor for high BP later in life. \((\text{Hypertension. 2002;40:280-285.})\)

Key Words: risk factors ■ neonatal blood pressure ■ hypertension, essential ■ salt taste

The underlying cause of essential hypertension is unclear, but it is likely that the many factors leading to the common outcome of persistent elevation of blood pressure are represented by different subtypes within a given population. One important subtype is sodium or salt-sensitive hypertension,\(^1,2\) which may have strong genetic or familial components.\(^3\) If an appropriate measure of sodium/salt sensitivity were available early in life as a risk factor for hypertension, it might be possible to detect susceptible individuals and intervene in a timely way.

Numerous studies have demonstrated that infant blood pressures aggregate in families and are predictive of later blood pressures.\(^4-9\) Since the processes responsible for essential hypertension operate before clinical detection, it is reasonable to search for predictors of essential hypertension in infants.

This report concerns the relation of neonatal salt taste responsiveness and infant blood pressure. It is possible that early life exposure to NaCl could have developmental effects on salt taste preference and subsequently on blood pressure.

We present the details of a study of the association between neonatal blood pressure and salt taste responsiveness in a sample of infants and in subgroups categorized by family history of hypertension.

Methods
The sample was derived from normal term infants born at a major obstetric hospital in Providence, Rhode Island, over a 30-month period. The institutional review boards of the Women and Infants’ Hospital of Rhode Island and the Roger Williams General Hospital, both in Providence, approved the study protocol. A total of 283 healthy infants were enrolled after informed consent was obtained from their mothers. Prenatal recruitment took place at the prenatal clinic of the hospital and offices of a large health maintenance organization in Providence. Postnatal recruitment took place on the hospital maternity wards. There were no differences in sociodemographic characteristics between prenatally recruited participants and postnatally recruited participants.

Neonatal taste tests were performed 3 hours after the previous feeding, in the Sensory and Learning Studies Laboratory at the hospital, where the babies were 2 to 4 days of age. Neonatal taste test procedures and measurement of sucking responsiveness have been described in detail elsewhere.\(^10-12\) Briefly, several sterile cannulas opened into a rubber nipple connected to a pressure transducer that converted suction or negative pressure changes into electrical signals. The nipple cannulas delivered microdrops (0.06 mL) of the fluid taste stimuli. Signals were recorded in a microcomputer, and several sucking parameters were measured, including latency to suck, number of sucking bursts, mean sucks per burst (MSB), number of interburst intervals, and total number of sucks in the trial (total response count). These analyses are limited to mean sucks per sucking burst (MSB). The reproducibility of these tests is reported elsewhere.\(^11,13\)

In the salt taste test, 3 solutions were used to assess neonatal salt taste responsiveness: water, 0.1 molar (mol/L) NaCl, and 0.3 mol/L NaCl. After a 1-minute baseline period, the nipple was inserted and taste stimuli were presented in the following order (as seen in Table 1): 2 water trials (trials 1 and 2); 2 NaCl trials (trials 3 and 4); 2 water trials (trials 5 and 6); 2 NaCl trials (trials 7 and 8); and 2 final water trials (trials 9 and 10). At the start of each trial, 0.06 mL of each tastant was offered in a noncontingent manner (ie, without any
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**TABLE 1. Mean Sucks per Burst (MSB) in Response to Water, NaCl, and Sucrose Taste Stimuli**

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Mean</th>
<th>SD</th>
<th>n</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Salt</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Water</td>
<td>12.7</td>
<td>9.8</td>
<td>259</td>
<td>1–45</td>
</tr>
<tr>
<td>2. Water</td>
<td>13.6</td>
<td>9.3</td>
<td>261</td>
<td>0.4–45</td>
</tr>
<tr>
<td>3. Salt, 0.1 mol/L</td>
<td>11.3</td>
<td>9.3</td>
<td>243</td>
<td>1–46</td>
</tr>
<tr>
<td>4. Salt, 0.1 mol/L</td>
<td>12.1</td>
<td>9.6</td>
<td>231</td>
<td>1–44</td>
</tr>
<tr>
<td>5. Water</td>
<td>13.2</td>
<td>10.1</td>
<td>240</td>
<td>1–51</td>
</tr>
<tr>
<td>6. Water</td>
<td>12.9</td>
<td>9.1</td>
<td>237</td>
<td>1–46</td>
</tr>
<tr>
<td>7. Salt, 0.3 mol/L</td>
<td>9.5</td>
<td>7.4</td>
<td>233</td>
<td>1–47</td>
</tr>
<tr>
<td>8. Salt, 0.3 mol/L</td>
<td>9.6</td>
<td>8.3</td>
<td>204</td>
<td>1–40</td>
</tr>
<tr>
<td>10. Water</td>
<td>12.4</td>
<td>9.5</td>
<td>232</td>
<td>1–43</td>
</tr>
<tr>
<td>Salt minus water</td>
<td>−4.0</td>
<td>7.2</td>
<td>234</td>
<td>(−28, +13.25)</td>
</tr>
<tr>
<td>(mean trials 7, 8 minus mean trials 5, 6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sucrose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Nonnutritive sucking</td>
<td>10.3</td>
<td>9.8</td>
<td>271</td>
<td>1–110</td>
</tr>
<tr>
<td>2. Water</td>
<td>23.4</td>
<td>28.6</td>
<td>270</td>
<td>1.6–179</td>
</tr>
<tr>
<td>3. Sucrose, 5%</td>
<td>30.3</td>
<td>30.1</td>
<td>270</td>
<td>1.6–176</td>
</tr>
<tr>
<td>4. Sucrose, 15%</td>
<td>31.4</td>
<td>27.6</td>
<td>270</td>
<td>1.2–169</td>
</tr>
<tr>
<td>5. Nonnutritive sucking</td>
<td>9.9</td>
<td>5.1</td>
<td>268</td>
<td>1.3–32.5</td>
</tr>
<tr>
<td>Sucrose-water</td>
<td>7.8</td>
<td>31.7</td>
<td>269</td>
<td>(−122, +158)</td>
</tr>
</tbody>
</table>

Requirement for sucking; the appropriate pump of 3 was triggered to deliver the drops of fluid. Sucking responses were recorded polygonographically for 2 minutes of each of the 10 trials. After a 20-minute wait, 270 neonates also were given a sucrose taste test with water, 5% and 15% solutions in this order11,12 but with a contingent-reinforcement procedure in which the infant’s sucking behavior triggered the pump. Because babies actually receive the water or sucrose solutions during these tests (obviously not possible for 0.3 mol/L NaCl), this procedure results in more vigorous sucking (Table 1).

Statistical analysis of the salt taste sucking responses involved several steps. First, the two trials for each separate taste were averaged. Then, difference scores were calculated between sucking responses for the mean of 2 NaCl trials minus the mean of the 2 preceding water trials (i.e., MSB for salt minus MSB for water). Newborns typically produce fewer sucks for salt than for water; hence, difference scores (salt minus water responses) are generally negative. Furthermore, difference scores close to zero correspond to less distaste for salt or relative salt taste “preference,” and difference scores further away from zero correspond to salt taste “aversive.” Sucrose taste responses were analyzed by using difference scores (MSB for sucrose minus MSB for water) in sucking responsiveness between two sucrose solutions and water; newborns produce more sucks for sucrose than for water11,14.

Neonatal blood pressure was measured 2 to 4 days after birth in the hospital, along with length, weight, and several skinfold thicknesses. Blood pressure was recorded at a separate session from the taste testing and was measured with a Physiometrics ultrasonic device, with the use of appropriately sized upper arm cuffs. Age in days, sleep/activity status, and cuff size were recorded.8 Diastolic pressure was recorded as the 4th Korotkoff sound (muffling). Socioeconomic and family health information was obtained from the mother by interview. Family history of hypertension was determined for both parents and all grandparents, alive and deceased, with questions to the mother about physician-diagnosed high blood pressure and current use of antihypertensive medications. Neonatal blood pressures were also measured at home in 189 infants at 1 month of age by technicians who were unaware of the results of the sucking responses.

With the use of the General Linear Model (GLM) procedure of the Statistical Analysis System (SAS) for data analysis, the association between neonatal blood pressure and salt and sucrose sucking responses was determined after adjusting blood pressures for age, gender, weight, and activity status at the time of the blood pressure measurement. Data were available for 234 subjects for the analysis of salt taste difference scores and for 269 subjects for the sugar taste difference scores based on hospital blood pressure and for 189 subjects for the salt taste difference scores based on subsequent blood pressure measurements at 1 month.

**Results**

The MSB for each of the 10 stimuli with salt or water and each of the stimuli with sucrose or water are presented in Table 1. The mean difference score between both 0.3 mol/L NaCl stimuli and the 2 preceding water stimuli for 234 babies with at least 1 recorded response to water and to salt was −4.0, indicating less preference for salt than for water. The mean difference score for 15% sucrose and water for 269 babies was 7.8, indicating preference for sugar over water.

Because it appeared that the higher salt concentration produced a greater aversive response, the primary analyses in the remainder of the paper were based on difference scores for MSB, defined by the means of the two higher salt concentration (0.3 mol/L) stimuli minus the mean of the immediately preceding two water stimuli.

The distributions of the difference scores for 0.3 mol/L NaCl minus water and for 15% sucrose minus water are presented in Figures 1a and 1b. Although the range is broad, the majority of neonates have negative difference scores for salt and positive difference scores for sugar. Because of the large spreads and seemingly nonnormal distributions, these responses were further categorized.

Mean sucks per burst were scored as indicating an “aversive” (A) response if the 0.3 mol/L salt minus water difference score was ≤−10 MSB (approximating the lowest quintile); a “preferential” (P) response if this difference score was >0 (approximating the highest quintile), and “neutral” (N) if the difference score was between these two numbers (approximating the middle three quintiles). The infants were studied at a mean age of 2.4 days. Approximately 47% were male. The racial distribution was representative of the community served by this hospital at the time of the study (non-Hispanic white, 194 [83%]; black, 24 [10%]; Hispanic, 9 [4%]; other, 6 [3%]). No significant differences in age, gender, or race by salt taste response were found. No differences in salt taste responses were found for breast-fed versus formula-fed babies. Statistically significant tests for trend were found for birth weight (aversive: mean birth weight [grams] ± SEM = 3371 ± 69, n = 48; neutral: 3435 ± 46, n = 118; preferential: 3564 ± 58, n = 65, P = 0.031) and umbilical skin fold thickness (aversive: mean skin fold [millimeters] ± SEM = 2.9 ± 0.12, n = 47; neutral: 3.0 ± 0.07, n = 112; preferential: 3.2 ± 0.09, P = 0.049).

The 234 babies with recorded blood pressures and salt taste tests that could be classified as aversive, neutral, or preferential were arranged by quintile of diastolic (K4) blood pressure (Table 2). A significant χ2 test for trend (P = 0.012) was found for diastolic blood pressure and the MSB differ-
ence scores as categorized into the 3 groups. Also, as seen in Figure 2b, more babies in the highest quintile for diastolic blood pressure showed “preferential” responses to the 0.3 mol/L salt stimulus and more babies in the lowest diastolic blood pressure quintile showed “aversive” responses. Similar analyses (Figure 2a) did not show these differences for systolic blood pressures (Mantel-Haenszel \( \chi^2 = 0.93 \), 1 df, \( P = 0.34 \)).

By using MSB as a categoric variable, a regression analysis of neonatal blood pressure on the MSB score was performed for crude (unadjusted) blood pressures and for blood pressures adjusted for age in days, gender, birth weight, and activity status\(^8,9\) at the time of the blood pressure measurement (Table 3). Mean adjusted diastolic blood pressures were \( 3.1 \pm 1.6 \) mm Hg higher in babies with preferential responses to the salt taste stimulus than the babies with aversive responses (\( P = 0.05 \)). Similarly, mean adjusted systolic blood pressures were \( 3.3 \pm 1.7 \) mm Hg higher, respectively (\( P = 0.06 \)). Blood pressures were 1.9 to 2.8 mm Hg higher in babies with neutral responses than in those with aversive responses.

Approximately 70% (156 of 223) of the infants had at least one grandparent who was informed of high blood pressure by a physician. About 58% (129 of 223) of the infants had at least one grandparent who used antihypertensive medications. When these regression analyses were limited to babies whose grandparents had a history of being informed by a physician that they had hypertension or were reported to be receiving medication for hypertension, the differences in blood pressures according to the babies’ salt taste responses were considerably greater (Table 4). For example, mean adjusted systolic and diastolic blood pressures in babies with any grandparent undergoing treatment for hypertension were \( 6.7 \pm 2.2 \) and \( 5.0 \pm 1.9 \) mm Hg higher in babies with preferential versus aversive responses (\( P = 0.003 \) and \( P = 0.010 \), respectively). Similar increases in both systolic and diastolic blood pressures were found in these babies when the analysis was limited to those with mother-reported history of hypertension in any grandparent (Table 4).

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### TABLE 2. Neonatal Salt Taste Responses by Quintile of Diastolic (K4) Blood Pressure (Unadjusted)

<table>
<thead>
<tr>
<th>Diastolic (K4) Blood Pressure Quintile (interval—mm Hg)</th>
<th>Aversive n (%)</th>
<th>Neutral n (%)</th>
<th>Preferential n (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>( 1 (&lt; 36) )</td>
<td>16 (36)</td>
<td>19 (42)</td>
<td>10 (22)</td>
<td>45</td>
</tr>
<tr>
<td>( 2 (36.1–39.9) )</td>
<td>8 (17)</td>
<td>26 (57)</td>
<td>12 (26)</td>
<td>46</td>
</tr>
<tr>
<td>( 3 (40.0–42.0) )</td>
<td>12 (26)</td>
<td>23 (50)</td>
<td>11 (24)</td>
<td>46</td>
</tr>
<tr>
<td>( 4 (42.1–49.9) )</td>
<td>5 (10)</td>
<td>27 (53)</td>
<td>19 (37)</td>
<td>51</td>
</tr>
<tr>
<td>( 5 (\geq 50.0) )</td>
<td>7 (15)</td>
<td>24 (52)</td>
<td>15 (33)</td>
<td>46</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>119</td>
<td>67</td>
<td>234</td>
</tr>
</tbody>
</table>

Mantel-Haenszel \( \chi^2 = 6.24 \), 1 df, \( P = 0.012 \).
Blood pressures recorded at home at 1 month of age also remained higher for babies who had preferential versus aversive responses to the neonatal salt taste. Mean adjusted 1-month systolic and diastolic blood pressures for babies with any grandparent undergoing treatment for hypertension were 3.8±2.5 and 9.6±3.4 mm Hg higher in babies with preferential versus aversive responses to the salt taste (P=0.14 and 0.006, respectively). Similar increases in 1-month blood pressure were found in these babies when the analysis was limited to reported history of hypertension in any grandparent (4.1±2.2 and 8.3±2.9 mm Hg; P=0.065 and 0.004, respectively).

Neonatal sucrose sucking responses were very similar to those found in earlier studies,15,16 with increased sucking responses from water to 5% and further increases in response to 15% sucrose (Table 1). MSB responses to sucrose were characterized as aversive (A) if the MSB difference between 15% sucrose minus water was ≤−5.0 (approximating the lowest quintile), neutral (N) if the difference score was ≥−5.0, <20.0 (approximately the middle 3 quintiles), and preferential (P) if the difference score was ≥20 (approximating the highest quintile). There were no significant relations between systolic or diastolic blood pressures and sucking response to sucrose.

### Discussion

The results of this study indicate first that neonatal sucking responses to 0.3 mol/L NaCl differ significantly from sucking responses to water. The sucking count measures show that neonates in general suck less in response to salt solutions than to water. Some controversy exists about the ability of very young infants to discriminate the taste of salt from that of water.15,16 However, in a meticulous study, Nowlis17 reported that newborns given a salt taste show facial responses similar to those after being given bitter substances, suggesting rejection. In other studies from our laboratory, neonates showed decreased sucking responses to a saline solution compared with sucrose solutions and water.14

It can be speculated that neonatal sucking responses to a salt taste stimulus might be biologically plausible proxy

<table>
<thead>
<tr>
<th>Type of Blood Pressure</th>
<th>Regression Coefficient±SE</th>
<th>P</th>
<th>Regression Coefficient±SE</th>
<th>P</th>
<th>Test for Trend† P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>2.4±1.6</td>
<td>0.13</td>
<td>1.5±1.8</td>
<td>0.39</td>
<td>0.48</td>
</tr>
<tr>
<td>Adjusted§</td>
<td>2.8±1.5</td>
<td>0.06</td>
<td>3.3±1.7</td>
<td>0.06</td>
<td>0.07</td>
</tr>
<tr>
<td>Diastolic BP (K4), mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>1.9±1.4</td>
<td>0.17</td>
<td>2.6±1.5</td>
<td>0.09</td>
<td>0.10</td>
</tr>
<tr>
<td>Adjusted§</td>
<td>1.9±1.4</td>
<td>0.16</td>
<td>3.1±1.6</td>
<td>0.05</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*MSBN refers to estimated mean difference in blood pressures in babies in the “Neutral” salt taste response group minus those in the “Aversive” response group.
†MSBP refers to estimated mean difference in blood pressure in babies in the “Preferential” salt taste response group minus those in the “Aversive” response group.
‡Based on a score variable 1 if aversive, 2 if neutral, and 3 if preferential.
§Adjusted for age in days, gender, birth weight, and activity status.
measures for inborn sodium/salt sensitivity. Early studies of salt taste preference and neural responses in animal models support the concept of sodium-specific salt taste response.18–21 Neural responses to an NaCl salt taste appear to be specific to sodium and distinguishable from those to potassium salt (KCl), based on in vitro studies with lingual epithelia from different animals.20,22 These results from animal studies suggest that salt taste responses might be specific to NaCl and even to sodium itself and thus might provide a reasonable proxy measure for salt or sodium sensitivity. Several recent reports have examined early nutritional and other prenatal or neonatal factors on later blood pressure,22–25 and a study by Weinberger and colleagues supports a relation between salt sensitivity and death. However, most studies reported from older children and adults do not support a direct link between taste for salt and blood pressure.27 These studies probably were performed long after any fetal or early life programming that might be reflected in the current data. Regardless of the physiological pathways linking salt taste to blood pressure variability, the current study showed significant associations between salt taste responses and blood pressure but not with sweet taste responses and blood pressure. In the total group of newborns studied, there was an association between relative salt taste preference (or less aversion) and higher systolic and diastolic blood pressures. Although the variability in blood pressures in newborns as well as older children is considerable,9,28 the salt taste responses were different in babies with higher blood pressures (Tables 2 and 3 and Figure 2).

In newborns categorized according to various definitions of positive family history for hypertension, the significant associations of blood pressure and salt taste responses were stronger and more consistent. Newborns with a positive family history of hypertension showed a strong relation between relative preference for the salt taste and higher blood pressures and those measured at 1 month of age were 5 to 9 mm Hg higher in babies with a grandparent undergoing antihypertensive treatment if they showed a preferential rather than an aversive response to the salt taste stimulus (Table 4). Conversely, when the analysis was limited to infants with no grandparental history of hypertension, there was no association between salt taste response and blood pressure. No relation was found for sweet taste responsiveness and blood pressure. As previous work has demonstrated blood pressure “tracking” in infants,8 these results suggest that the salt taste response might be predictive of later life blood pressure. Further follow-up of these children is required to support this hypothesis.

Positive family history of hypertension might identify subgroups of infants who are most susceptible to subsequent blood pressure elevations. Positive family history of hypertension has been linked with sodium/salt intake and sensitivity and with various other measures of cardiovascular sensitivity and reactivity.3,29,30 If family history of hypertension is linked with the pathophysiologic mechanisms underlying sodium/salt sensitivity, it might be expected that neonatal salt taste response and blood pressure associations would be stronger in such subgroups. Because only 10% of participants in this study were black (reflecting the composition of the population at the time the study was initiated), the sample was too small to show any racial differences in these responses if they exist.

Little is known about the precise role of salt taste early in life in relation to salt/sodium intake and their potential long-term interrelations with infant and later childhood blood pressure. The Dutch newborn study showed that a low sodium diet was associated with lower blood pressures initially and at 15-year follow-up, but salt taste was not assessed.23 Also, the determinants of salt taste responsiveness are incompletely understood. For example, amniotic fluid sodium concentrations might condition these responses.31 It is possible that variation in salt taste responses might predict blood pressure directly or indirectly through dietary intake.

Perspectives

The data presented in this report suggest an early life relation of the sucking response to a salt taste stimulus and blood pressure that persists at least to 1 month of age. Although there are no data linking neonatal salt taste responsiveness and human sodium sensitivity, it is intriguing to consider such a hypothesis, given sodium-specific animal data and lingual epithelial in vitro studies.18–21 Although more research is needed to understand the biology of the underlying relations of neonatal blood pressure, salt taste response, and sodium/salt sensitivity, it is possible that salt taste responses might relate in some way to blood pressure regulation and could form part of a risk factor profile for higher blood pressures later in life.

Acknowledgments

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References


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