Commercial rodent diets contain more sodium than rats need

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Am J Physiol Renal Physiol 288: F428–F431, 2005; doi:10.1152/ajprenal.00310.2004.—The dietary sodium requirements for rats have been a matter of debate. Our hypothesis was that normal commercial rodent chow contains sodium in excess of dietary needs and that this could have a significant impact on cardiovascular and renal physiology. To investigate dietary sodium requirements, 3-wk-old weanling Sprague-Dawley rats were fed a custom pelleted diet containing no sodium that was isocaloric to normal commercial rodent chow. These rats were provided with two drinking bottles; one contained water, and the other contained 0.5% NaCl. Thus they could choose and consume sodium as needed. Age-matched controls received normal pelleted Harlan Teklad 22/5 rodent diet (0.5% sodium content) and water ad libitum. Body weight and fluid intake were monitored over 7 wk until the rats were 10 wk old. At the end of the study, blood pressure was recorded. Weekly sodium intake in the experimental group was only 15% of that reported for rats fed normal rodent chow beginning in the first week postweaning. Growth was identical in the two groups (7.8 ± 0.1 vs. 7.6 ± 0.1 g/day), as was the total fluid volume intake. Blood pressure was significantly lower in the experimental rats compared with controls (96 ± 4 vs. 122 ± 4 mmHg, P < 0.05). These data suggest that, when given the choice, rats will consume significantly less sodium than provided in commercial chow, without any alteration in their growth rate. Rats fed standard commercial rodent chow may consume at least seven times more sodium than is necessary. This suggests commercial rodent diets may force excess sodium to accommodate caloric intake.

Dietary sodium intake is an important element in fluid balance, renal function, and blood pressure. In the wild, the rat is a scavenger and its sodium intake is very limited, but in the domesticated or laboratory rat dietary salt is abundant. Manipulation of dietary sodium intake is an important experimental paradigm for studying renal physiology or pathophysiology. High salt intake has been found to influence a wide variety of physiological parameters in otherwise normal rats, including blood pressure (7, 11, 17, 18, 22), renin secretion (2, 20, 21), plasma aldosterone (7, 20), angiotensin receptors (20), nitric oxide synthase (2, 21), cyclooxygenase (9, 22), endothelin (18), insulin resistance (17), and vascular adaptation (22). Commercial “normal” rat chows contain 0.3–0.5% sodium, while experimental “high-salt” diets contain 2–8% sodium (2, 7, 11, 17, 18, 20–22). It has been proposed that the daily nutritional sodium requirement for normal growth and reproduction is 0.05% of dietary intake (19) and that an adult 400-g rat will consume at least 15–20 g of rat chow/day, which translates to a daily intake of 7.5–10 mg sodium. However, commercial rodent diets have been modified, altering nutritional factors to promote growth, in keeping with the guidelines for nutrient requirements published by the National Research council (NRC) (15). These guidelines push the range of sodium content in most commercial rodent diets to 0.3–0.5%. This means a normal 400-g adult laboratory rat being fed a commercial normal rodent chow is consuming 45–100 mg sodium/day, or 113–250 mg sodium/kg body wt. This contrasts with the U.S. Department of Agriculture dietary guidelines for humans (23), which recommend 2,400 mg sodium/day, or 34 mg/kg body wt for a 70-kg adult. However, estimates from the National Health and Nutrition Survey (NHANES III) based on data obtained during 1988–1991 (13, 14) suggest that the average sodium intake of American adults is well above these guidelines, closer to 4,000 mg sodium, or 57 mg·kg body wt (1·day). Even this high sodium consumption in humans is an adjusted consumption of approximately one-third to one-fifth of what laboratory rats typically receive in their commercial diet.

Adult rats tend to dislike commercial low-sodium chows, and growth is retarded when rats are fed these diets (1). However, it is not clear whether this failure to thrive is due to an acquired taste for salt from the normal chow (22), so that they do not consume the bland low-sodium chow, or whether low sodium intake actually influences growth. Studies of pregnant female rats suggest that dietary sodium content of only 0.03% can sustain normal growth and development (19), but the assumption is that on this diet caloric intake is sufficient. If so, commercial dietary sodium content may be 10-fold in excess, raising the question of what constitutes a normal sodium intake for a rat. We hypothesized that if normal National Institutes of Health-derived inbred control Sprague-Dawley rats are allowed to select their own sodium intake during weaning, they will consume less sodium than is contained in commercial rodent chow but that the reduced sodium intake will not alter growth.

METHODS

Growth and intake measurements. Thirty-two weanling male Sprague-Dawley rats (3 wk old) were purchased from Charles River Farms (Kalamazoo, MI), divided into two groups, and placed in individual cages. The experimental or “choice” group (n = 16) received a pelleted custom sodium-deficient diet (Harlan Teklad TD-90228, 0.008% NaCl) that was otherwise similar in nutritional composition and virtually isocaloric to the normal chow. These weaning rats were never fed normal chow. The choice rats were given two water bottles in their cages, one containing only water and one containing 0.5% NaCl. The volume of water and saline consumed was monitored regularly. Body weight was also monitored continuously over 7 wk, until the rats were 10 wk old.

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When we discovered that the choice group was growing faster than the commercial growth nomogram (5), we set up a control group fed normal rat chow to determine whether growth of the choice rats was abnormal or in fact matched that of normally fed rats. The control group (n = 16) was fed unrestricted normal pelleted rat chow (Harlan Teklad rodent diet 8640, 0.5% Na⁺ by weight) and water by bottle. The volume of water consumed was monitored regularly. We did not try to determine the quantity of food consumed, since pelleted food creates spillage into the bedding.

Acute terminal studies. On the final day of the experiment, the rats were anesthetized by intraperitoneal injection of 125 mg/kg body wt thiobutabarbital (Inactin, Research Biochemical, Natick, MA) and placed on a heating pad to maintain constant body temperature. The rats were surgically prepared with a tracheotomy using PE-260 tubing (Fisher Scientific, Chicago, IL) for spontaneous breathing of room air. The femoral artery was catheterized with PE-50 tubing to directly monitor femoral blood pressure using a Statham pressure transducer (Viggo-Spectramed, Oxnard, CA) for determination of blood pressure and heart rate over a 10–15 period of stable pressure that commenced 30–45 min after the surgery was complete. We measured blood pressure and heart rate in 7 of the choice rats and 16 of the normal chow controls. All protocols using rats were reviewed and approved by our Institutional Animal Care and Use Committee and adhere to the guiding principals in the care and use of experimental animals. Henry Ford Hospital’s animal facility is AALAC approved.

Analysis. Comparisons over time were run using ANOVA, and post hoc testing was used with Hochberg’s method (10) to adjust the α level for multiple testing. In the terminal experiments, blood pressure and heart rate in the two groups were compared using unpaired t-tests. P < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Dietary sodium requirements to sustain normal growth in rats are controversial and ill-defined. To investigate this issue, we allowed animals to set their own sodium intake. We found that during the first week it was 0.75 ± 0.04 meq Na·wk⁻¹·rat⁻¹ (Fig. 1), while rats drank equal portions of water and saline. As they grew, sodium intake increased by 0.15 ± 0.09 meq Na·wk⁻¹·rat⁻¹ in the form of increased saline consumption, while the amount of water consumption remained constant (11.9 ± 0.6 ml/day). During the final 2 wk of the study, water intake remained unchanged (10.4 ± 1.3 ml/day), while saline intake increased to almost three times water intake (28.8 ± 0.9 ml/day; P < 0.001 vs. water). This resulted in a total sodium intake of 1.65 ± 0.12 meq Na·wk⁻¹·rat⁻¹ during the final week of the study.

We have compared sodium intake from this study against published data (1, 4, 6, 8, 12) for rats of similar age on a control diet containing normal sodium at or near 0.5% content, as shown in Fig. 2. When rats were given the opportunity to choose their own level of sodium intake, they consumed less than one-seventh of the sodium reported when rats are fed a commercial normal-sodium diet. Thus it is clear from our results that during the critical growth phase from weanling to young adult, commercial rat diets provide seven to nine times more sodium than seems necessary for normal growth and development.

While one could argue that the above comparison may not be valid because the measurements were made by different investigators at different times, several mitigating facts must be recognized. First, previously published balance studies for sodium intake in control rats of the same age are very consis-

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**Fig. 1.** Body weight (BW; g) of rats fed either a commercial rodent diet (0.5% NaCl) and water or a nominally zero-sodium diet (0.008%) with a choice of both 0.5% saline and water.

**Fig. 2.** Sodium intake (meq/wk) by rats in the present study fed a nominally zero-sodium diet (0.008%) with a choice of both 0.5% saline and water compared with intake from 5 different studies using a commercial “normal”-sodium rodent diet (at or near 0.5% Na⁺) and water. ○, Data from Ref. 1; □, data from Ref. 6; △, data from Ref. 12; □, data from Ref. 4; ♦, data from Ref. 8.

**Fig. 3.** Total fluid volume (ml water or water and 0.5% saline) consumed by rats fed either a commercial rodent diet (0.5%) and water or a nominally zero-sodium diet (0.008%) with a choice of both 0.5% saline and water.
tent (1, 4, 6, 8, 12). Second, all of these studies illustrate such a profound difference based on intake from the levels we measured in our sodium choice group (Fig. 2) that the precise difference possible in balance studies is unlikely to have any significant impact on our overall observations. It might also be argued that the ability to ingest sodium was limited by the amount of saline that could be consumed. We observed in the choice group a normal growth pattern and that a significant portion of the total fluid intake was obtained from water, suggesting that if there was a need for more sodium, there was ample opportunity for the animals to consume it. Providing dietary sodium in the fluid rather than the solid food may be problematic in that there could be a limit to the amount of saline the rats could tolerate. We cannot speculate how the rats may have chosen salt intake from a nonsaline source, but the amount our rats ingested still exceeded the published minimum requirements for normal growth (8), and these animals grew at a completely normal rate (Fig. 3). Interestingly, our present data are in keeping with historic recommendations for minimum sodium intake in rats (8, 19), which seem to have been lost in the fabrication of contemporary commercial diets.

The growth rate of the rats allowed to choose their sodium intake was continuous (Fig. 3) and surprisingly exceeded the commercial nomogram for growth by age (13) by ~30%. Therefore, we measured the growth of age-matched animals fed normal (0.5%) commercial chow but found no difference in growth rate at any time point between rats fed commercial chow and those that regulated their own sodium intake (7.6 ± 0.1 vs. 7.8 ± 0.1 g/day). It has been suggested that rats do not tolerate the sodium-restricted chows (1), which may account for reduced growth, but those studies that show attenuated growth (1, 3) also have greatly restricted sodium content below the predicted minimum required (3, 17). Thus we can say that the reduced sodium intake in our choice group had no apparent effect on growth as long as the nominally sodium-free diet was supplemented with sufficient sodium from fluids.

Collier and Johnson (6) suggested that growth is largely driven by caloric intake and that accompanying changes in salt intake are modified by renal function. Grunert et al. (8) reported that the minimum sodium content for rat diets to sustain growth was 0.05%, and as long as caloric intake was sufficient, higher levels of sodium did not enhance growth further. Brensilver et al. (3) and Beierwaltes et al. (1) found that reduced sodium content in adult rat diets at lower levels (0.018 and 0.01%, respectively) retarded growth, and Brensilver extrapolated that a minimum of 247 μeq/day should be required to sustain growth (3). Our data suggest that the problem with diets developed to contain a set sodium content is that a sodium requirement does not seem to directly increase with body weight or age, so that the difference between chosen consumption in our rats and the sodium consumed in commercial diets became greater as the rats grew and consumed more. This suggests that the need for sodium, as a percentage of total intake, seems to be greater in younger rats (<7–8 wk of age) than in mature, growing rats. Also, it is important to note that the growth rate of both of our groups was accelerated compared with the standard published growth nomograms found in the catalogues of the major rodent suppliers (5). For instance, our male rats on either diet at 9 wk of age (day 42 of the study) weighed ~385–400 g compared with a mean of only 300 g predicted by the nomogram for 9-wk-old male rats. A broad perusal of the literature suggests rats at given ages are much larger now than some 20 years ago. There is also a difference in age and size of the same strain depending on the source of the supplier since different breeders have different criteria for selecting breeding stock (18). The reason for these differences is unclear but could be the result of environmental conditions, a more sedentary existence, or more likely the fact that these nomograms were produced decades ago and dietary improvements in chow have enhanced the growth curves. Interestingly, if one relies on the current nomograms and purchases a 300-g rat, assuming it is 9 wk old, our data would suggest the rat might actually be only 7 wk old.

To investigate whether the decrease in sodium intake caused any differences in cardiovascular parameters, we measured mean systemic blood pressure and heart rate. In Inactin-anesthetized rats, we found that mean blood pressure of rats fed the normal commercial diet was 122 ± 4 mmHg. However, in rats that chose their sodium intake, blood pressure was significantly lower (P < 0.001) at only 96 ± 4 mmHg. In contrast to blood pressure, there was no difference in heart rate between controls (366 ± 11 beats/min) and the sodium choice group (369 ± 9 beats/min). Note that barbiturates like Inactin may elevate blood pressure, and this effect may be different as a consequence of the type of diet. This difference we observed is much greater than we would have expected, and serial measurements in conscious animals would be more convincing.

It has been reported that chronic increased sodium intake may increase blood pressure (11, 22), and reducing sodium is thought to reduce blood pressure although few studies actually demonstrate this. The inability of investigators to show reductions in blood pressure due to reduced sodium intake may reflect permanent changes in the cardiovascular and renal systems that are caused by obligatory feeding of excess sodium after weaning. Our study may indicate that this issue is more significant than we first thought.

In summary, the sodium intake from normal commercial rodent chows appears to be about sevenfold higher than rats require for normal growth, and this difference may be even greater in older animals. Additionally, if a low-sodium diet is started at weaning, before the rats become accustomed to the high salt in normal chow, they eat it and grow normally, suggesting that the preference for high-salt commercial diets is an acquired taste. We found that rats with chronically reduced sodium intake had lower blood pressure compared with those on regular chow. We believe that if rats are allowed to choose their own diet, they will ingest much less salt than is forced on them by the so-called normal chows. The forced sodium excess in commercial diets could compromise control values for basal cardiorenal function in experimental rat models. The impact of these differences on any study using these diets should be carefully considered.

GRANTS

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REFERENCES

2. Bosse HM, Bohm R, Resch S, and Bachmann S. Parallel regulation of constitutive NO synthase and renin in JGA of rat kidney under various