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Behavioral responses and fluid regulation in male rats after combined dietary sodium deficiency and water deprivation

Kimberly J. Lucia, Kathleen S. Curtis*

Department of Pharmacology and Physiology, Oklahoma State University – Center for Health Sciences, Tulsa, OK 74107, United States

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ABSTRACT

Most investigators use a single treatment such as water deprivation or dietary sodium deficiency to evaluate thirst or sodium appetite, which underlie behavioral responses to body fluid challenges. The goal of the present experiments was to assess the effects of combined treatments in driving behaviors. Therefore, we evaluated the effect of combined overnight water deprivation and dietary sodium deficiency on water intake and salt intake by adult male rats in 2-bottle (0.5 M NaCl and water) tests. Overnight water deprivation alone increased water intake, and 10 days of dietary sodium deficiency increased 0.5 M NaCl intake, with a secondary increase in water intake. During combined water deprivation and dietary sodium deficiency, water intake was enhanced and 0.5 M NaCl was reduced, but not eliminated, suggesting that physiologically relevant behavioral responses persist. Nonetheless, the pattern of fluid intake was altered by the combined treatments. We also assessed the effect of these behaviors on induced deficits in body sodium and fluid volume during combined treatments and found that, regardless of treatment, fluid ingestion partially repleted the induced deficits. Finally, we examined urine volume and sodium excretion during dietary sodium deficiency with or without overnight water deprivation and found that, whether or not rats were water deprived, and regardless of water consumption, sodium excretion was minimal. Thus, the combination of water deprivation and dietary sodium deficiency appears to arouse drives that stimulate compensatory behavioral responses. These behaviors, in conjunction with physiological adaptations to the treatments, underlie body sodium and volume repletion in the face of combined water deprivation and dietary sodium deficiency.

1. Introduction

Maintenance of the appropriate volume and concentration of body fluids within a narrow range is critical for biological processes such as neural signaling, enzymatic reactions, and tissue perfusion. Not surprisingly, then, compensatory neural, hormonal, renal, and behavioral responses are elicited to correct perturbations of body fluid volume or osmolality. Interestingly, more attention has focused on renal, neural, and hormonal responses than on the behavioral responses—sodium intake and water intake. These compensatory behaviors are goal-directed and meant to satisfy a physical need in order to maintain homeostasis, as exemplified in seminal work by Cannon and Richter in the early 1900s (e.g, [1–3]). Richter utilized a strategy in which sodium depletion was produced experimentally and the behavioral response that restores body sodium balance (i.e., sodium intake) then was observed [4]. This strategy has come to be known as the depletion-repletion model, and is frequently and broadly applied in studies of body fluid balance. In this approach, pharmacological methods often are used as challenges to body sodium or water balance (e.g., [5–16]); however, dietary sodium deficiency or water deprivation and are physiological methods that also are commonly used (e.g., [7,14,17–20]).

Water deprivation produces “thirst” by causing both intracellular and extracellular dehydration. As body fluid volume decreases, the resulting increase of solute concentration in the extracellular fluid causes osmotic movement of water from inside cells, which buffers the hyperosmolality. Water deprivation also leads to the release of vasopressin from the posterior pituitary and activation of the renin-angiotensin-aldosterone system (RAAS) which increases circulating angiotensin II (AngII). These hormonal responses conserve water and maintain blood pressure. In addition, water deprivation produces water intake by two mechanisms. First, increased body fluid concentration by as little as 1–2% [21] stimulates osmotic thirst [22–23], presumably by activating central nervous system osmo−/sodium- receptors, specialized cells that detect changes in fluid osmolality or sodium concentration [24–25]. In addition, loss of fluid volume decreases renal

* Corresponding author.
E-mail address: kath.curtis@okstate.edu (K.S. Curtis).

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perfusion and ultimately increases circulating AngII which acts at receptors in circumventricular organs [9,26–27] to stimulate volemic thirst [5]. At the same time, hypovolemia alters signaling from baroreceptors in the heart and great vessels, which terminate in the hindbrain nucleus of the solitary tract (NTS), to stimulate water intake [7,11]. Together, these hormonal, renal, and neural responses, along with osmotic and volemic thirst, correct intra- and extra-cellular dehydration and restore body fluids to optimal levels.

Dietary sodium deficiency reduces body sodium and activates the RAAS [28–29]. Increased circulating aldosterone from the adrenals promotes renal sodium retention, while elevated levels of AngII maintain blood pressure. Moreover, the induced hyponatremia is associated with "sodium appetite," which is manifested by the ingestion of salt or salt solutions that restores body sodium. Although humans typically consume adequate or excess amounts of sodium in their diet, especially in the United States where a high salt diet is common [30], sodium intake can be produced in laboratory animals by a variety of experimental methods [6,8,10–12,13–16,18–20]. In the case of dietary sodium deficiency, circulating AngII is thought to act at forebrain circumventricular organs to stimulate sodium intake [12]. Although the central site of action for aldosterone remains unclear, recent studies suggest the NTS as one possibility [14–15]. In addition, AngII and aldosterone act synergistically to stimulate sodium ingestion via central actions [6]. Finally, cardiac and arterial baroreceptors may be activated by the volume loss which occurs during dietary sodium deficiency to provide additional important signals for sodium intake [8,16]. Thus, hormonal, renal, and neural responses, along with sodium appetite, restore body sodium to optimal levels (see [31] for review).

Most investigations of body fluid homeostasis utilize a single treatment (e.g., water deprivation or dietary sodium deficiency), particularly when examining related behavioral responses (thirst or sodium appetite, respectively). However, some researchers have focused on volume challenges and sodium intake. For example, a series of studies by De Luca and colleagues (e.g [32–34].) used a water deprivation-partial repletion protocol to determine whether water deprivation caused both thirst and sodium appetite. They found that sodium appetite emerged when rats were permitted to first correct their water loss, and concluded that thirst masked the sodium appetite that also was stimulated by water deprivation. In other studies, Stricker and colleagues [35] demonstrated that rats would consume concentrated sodium solutions after overnight water deprivation if those were the only fluids available (see also, [36]). Their goal was to determine whether rats could correct the induced dehydration under these conditions and, indeed, rats consumed hypertonic saline and then excreted the ingested sodium in small volumes of highly concentrated urine that allowed the water deficit to be repaired. Together, these studies using water deprivation to examine signals that cause sodium ingestion or to assess the effectiveness of compensatory responses provided useful and interesting information about mechanisms that underlie thirst and sodium appetite, and about the importance of those behaviors in body fluid regulation, more generally.

Nevertheless, understanding of these behaviors and their role in body fluid homeostasis is incomplete. This is, perhaps, not surprising, given the overlap both in hormonal and neural signals produced by water deprivation and dietary sodium deficiency, and in the contribution of those signals to both thirst and sodium appetite. Here, we take a different approach and study these compensatory behaviors together using combined treatments that disrupt body fluid balance. We used adult male rats to evaluate the effect of combined overnight water deprivation and dietary sodium deficiency on water intake and salt intake in order to obtain information about how these treatments may interact to drive behavior. We also examined plasma volume and plasma Na^+ to determine if behavioral compensation of induced deficits in body sodium and fluid volume are altered by combined treatments. Finally, we assessed urinary sodium and volume excretion during dietary sodium deficiency with or without overnight water deprivation to determine how renal mechanisms contribute to the responses.

2. Methods

2.1. Animals

Adult male Sprague-Dawley rats (Harlan) weighing 335–525 g at the beginning of the experiments were housed individually in plastic cages in a temperature-controlled room (21–25 °C) on a 12:12 h light/dark cycle with lights on at 7:00 A.M. for at least seven days prior to experiments. Rats were given free access to standard rodent chow and water except where noted. All methods were approved by the Oklahoma State University - Center for Health Sciences Animal Care and Use Committee and conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

2.2. Experimental procedures

All rats were given ad libitum access to 0.5 M NaCl in graduated tubes, along with water, for 2–3 days to adapt to the availability of the solution. After adaptation, 0.5 M NaCl was removed from the cages and rats were randomly assigned to one of four conditions:

Control - rats were maintained on a standard sodium diet (NaR; Harlan) with ad libitum access to water throughout the experiment.

Overnight water deprivation (Dep) - rats were maintained on NaR throughout the experiment and, on day 10, were water deprived overnight (water bottles removed from cages until the next day; approximately 22 h).

Dietary sodium deficiency (NaD10) – rats were given only sodium-deficient rodent chow (NaD; background sodium approximately 0.01–0.02%; Harlan) throughout the experiment with ad libitum access to water.

NaD + Dep - rats were given only NaD throughout the experiment and on day 10 were water deprived overnight.

Separate groups of rats were used in each of the three following protocols. Testing began at approximately 7:30 A.M. on day 11.

2.2.1. Protocol 1. Behavioral responses

Rats were assigned to one of the four experimental conditions (Control – n = 6; Dep – n = 6; NaD10 – n = 8; NaD + Dep – n = 8) in this protocol, which was designed to assess the time course of behavioral responses to combined dietary sodium deficiency and overnight water deprivation using two-bottle (water and 0.5 M NaCl) intake tests. Preliminary assessment of beginning body weights using 1-way ANOVA showed no differences among the four groups.

All rats were weighed on day 1, 10, and 11; subsets were weighed at additional time points throughout the 11-day experiment. After rats were weighed on the test day (day 11), food and water were removed from cages and rats were given both water and 0.5 M NaCl in 50 mL graduated tubes. Intakes of each solution (mL) were recorded after 5, 10, 15, 30, 45, and 60 min, and then hourly for a total of 7 h.

2.2.1.1. Statistical analyses. All data are reported as means +/− standard errors.

Body weight of rats in each of the experimental conditions on day 10 and 11 were expressed as change from weight on day 1 and analyzed using a 3-way, repeated measures analysis of variance (rm ANOVA) with diet (NaD or NaR), water deprivation (Dep or no dep), and day (day 10, day 11) as factors, repeated for day.

Cumulative water intake and cumulative 0.5 M NaCl intake during hours 1–7 were analyzed using separate 3-way rm. ANOVA with diet (NaD or NaR), water deprivation (Dep or no dep), and time as the factors, repeated for time. In addition, cumulative water and 0.5 M NaCl intake during the first hour were analyzed for each experimental condition separately using 2-way rm. ANOVAs with solution (water or