Available online at www.sciencedirect.com

SciVerse ScienceDirect

www.nrjournal.com

Reductions in water and sodium intake by aged male and female rats

Denovan P. Begg[a,*], *Andrew J. Sinclair*[b], *Richard S. Weisinger*[c]

[a] *School of Medicine; University of Melbourne, Melbourne, Victoria, Australia*
[b] *School of Medicine; Deakin University, Waurn Ponds, Victoria, Australia*
[c] *School of Psychological Science; La Trobe University, Melbourne, Victoria, Australia*

ARTICLE INFO

Article history:
Received 7 November 2011
Revised 25 September 2012
Accepted 25 September 2012

Keywords:
Aging
Thirst
Sodium appetite
Renin–angiotensin system
Atrial natriuretic factor
Sex differences
Rat

ABSTRACT

Aging results in reduced water and sodium intake responses in male rats. Because sex differences exist for water and sodium ingestion of young adult animals, we hypothesized that these sex differences would protect against the diminished water and sodium ingestion of aged female rats. Water and sodium intakes were examined in male and female young adult and aged Brown Norway rats in response to dipsogenic stimuli. Aged rats of both sexes consumed less water than young adult rats in response to 24-h water deprivation, thermal dehydration and hypertonic NaCl injection, but not to peripheral angiotensin II. Aged females consumed more water than males in response to hypertonic NaCl injection. Following sodium depletion, intake of 0.5 M NaCl solution over 2 h was higher in young adult rats than in aged rats. Aged animals had reduced angiotensin receptor 1A (AT_{1A}) and atrial natriuretic peptide (ANP) mRNA expression in hypothalamic tissue with no sex differences. These data indicate that female rats are not protected from water and sodium intake deficits that occur in aging and that sex differences in sodium intake in young adult rats are eliminated with aging.

1. Introduction

Compared with young adults, elderly humans [1-4] and some strains of aging rodents [5-8] have reduced water intake in response to dipsogenic stimuli including hyperthermia. The lack of adequate water intake was a contributing factor to the estimated 30,000 deaths in the elderly during the European heat-wave of 2003 [9]. In the aged rat, reductions in water intake have been observed in response to both osmotic [5] and dehydration [10] stimuli. Despite this, day-to-day intakes of water are generally not altered with aging [6,11], and various groups have reported increased [12] or decreased [13] basal consumption.

Despite the reduced water intake observed in aging following most dipsogenic challenges, it appears that angiotensin II (ANG II)-induced drinking remains intact [6,14], although ANG II-mediated hypovolemic drinking is reduced [6]. There is a reduction in renin–angiotensin system (RAS) activity in aging [15], primarily due to a decrease in renin secretion by the kidneys with aging [16]. AT_1 receptor density is also decreased in the brains of aged rats [17], and blockade of these receptors inhibits water intake in young adult rats

Abbreviations: ACE, angiotensin-converting enzyme; ANG II, angiotensin II; ANP, atrial natriuretic peptide; AT, angiotensin receptor; NPR, natriuretic peptide receptor; OVLT, organum vasculosum of the lamina terminalis; PVN, paraventricular nucleus; RAS, renin–angiotensin system; SFO, subfornical organ.

* *Corresponding author*. Metabolic Disease Institute, University of Cincinnati, Cincinnati, OH, 45236, USA. Tel.: +1 513 558 5866; fax: +1 513 297 0966.
E-mail address: denovan.begg@uc.edu (D.P. Begg).

0271-5317/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.nutres.2012.09.014

[18]. Furthermore, the addition of a low dose of an angiotensin-converting enzyme (ACE) inhibitor to the drinking water, a stimulus that increases water intake of young adult rats by increasing brain ANG II [19], fails to increase water intake in aged rats [5]. Therefore, there is evidence to suggest that reduced central AT_{1R} activation may contribute to the reduced water intake by aged rats.

Alternatively, it has been suggested that high circulating levels of atrial natriuretic peptide (ANP), a hormone that inhibits ANG II mediated drinking, are the cause of the reduced water intake following dehydration associated with aging [6]. ANP levels are elevated in healthy aged humans [20] and aged Munich–Wistar rats [21]. The elevated levels are believed to be due to a hypo-responsiveness of the renal system in aging [22]. One argument against ANP being the primary factor in diminished water intake is the continued responsiveness to ANG II injection in aging, given that in young adult animals ANG II induced drinking is diminished by concurrent ANP infusion [23]. However, since increased ANP levels occur at a similar age as the reduction of water intake, central or circulating ANP may be involved in the reduced water intake observed in aging.

Similar to water intake, consumption of sodium-containing fluids can be diminished in aging. For example, young adult rats treated with an ACE inhibitor drink hypertonic sodium solutions in preference to water [19]. However, with aging this sodium preference is reduced in Fischer 344, Sprague–Dawley and Brown Norway rats [5,17]. This reduction may be associated with the decrease in AT_1 binding in the organum vasculosum of the lamina terminalis (OVLT) and paraventricular nucleus (PVN) in aged rats [17].

There are sex differences in ad libitum [24,25] and diuretic-induced [26] sodium intake in the rat, with greater intake generally observed in females. The one study that examined possible sex differences in sodium intake in aging rats found reduced stimulated sodium ingestion in male and female Sprague–Dawley, and in male but not female aged Fischer 344 rats [17]. The conflicting data in the Fischer 344 strain may, however, be related to the sodium-avoiding behavior previously observed in Fischer 344 rats [27]. It therefore remains unclear whether the differences in basal sodium intake between adult male and female rats are present in aged animals of other strains.

In this experiment water intake in aged male and female Brown Norway rats challenged by hyperosmotic injection, dehydration and ANG II was examined. Salt consumption at baseline and following sodium depletion was also investigated. It was hypothesized that female rats would not experience the diminished water and sodium intake characteristic of aged male rats. Given that the mechanism underlying the decreased water intake response in aging remains unknown, hypothalamic mRNA of angiotensin, natriuretic peptide receptors and ANP were examined as possible mechanisms for the reduced water intake.

2. Methods and materials

2.1. Animals

Brown Norway rats were bred in the central animal house, La Trobe University. Animals were tested either at 4 (young adult: n = 18 male [Initial body weight; 301.6 ± 5.1 g] and n = 18 female [244.7 ± 4.8 g]) or 30 months of age (aged animals; n = 16 male [386.3 ± 8.2 g] and n = 17 female [288.9 ± 6.6 g]). Standard laboratory rat chow and water were available ad libitum except during challenges, as noted. Animals were singly housed for the duration of the experiment and were maintained on a 12/12-h light/dark cycle; challenges and sacrifice were performed at the mid-point of the light cycle. All fluid intakes were measured by weight-on/weight-off measurement of syringes fixed with glass sippers. All animals tested received each experimental challenge with a minimum one-week washout between challenges and one week between the final challenge and sacrifice. The animal procedures were approved by the La Trobe University Animal Ethics Committee.

2.2. Challenges

2.2.1. 24-h water deprivation

Baseline water intake (2 h in the middle of the light) was determined two days before the challenge. The day after baseline, water was removed from the cages and returned 24 h later and intake recorded after 2 h. 24-h urine output was determined both at baseline and during the dehydration challenge using custom metabolic cages described previously [28]. Food was present during the challenge.

2.2.2. Thermal challenge

As above, 2-h baseline water intake was recorded on the day before the challenge. On the test day, rats were moved, in their home cages, to a temperature-controlled room heated to 40 ± 1°C for 1 h. During this time, they had no access to water (food was present). The animals were then removed from the heated room and returned to their standard room (25 ± 2°C). At this time water was returned and water intake was recorded after 2 h. Body weights were measured prior to and following the thermal challenge, see [29].

2.2.3. Peripheral administration of NaCl and angiotensin II

Animals were subcutaneously injected, one week apart, with (a) isotonic NaCl injection (control), (b) hypertonic (1 M) NaCl solution (1 mL/100 g body weight) and (c) 100 μg/kg angiotensin II (100 μL/100 g body weight). Following injection, water consumption was measured over a 2-h period, as previously described [5,6].

2.2.4. Furosemide injection

Rats were provided access to a 0.5 M NaCl solution, water and food for three days prior to sodium depletion as previously described [30] to establish baseline intakes. On the day of sodium depletion, 0.5 M NaCl solution and food were removed, access to water remained, and animals were administered furosemide (20 mg/kg I.P.; Apex Laboratories, Australia). Twenty-four hours after furosemide injection, the 0.5 M NaCl solution was returned and intake was determined over 2 h. After the 2 h, food was returned. Intakes of 0.5 M NaCl and water were again determined at 24 h. Two-hour urine output was determined both at baseline and following furosemide injection.