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BRIEF COMMUNICATION

Drinking Behavior in the Spiny Mouse (*Acomys cahirinus*) Following Putative Dipsogenic Challenges

DONALD A. CZECH[1] AND JENNIFER M. VANDER ZANDEN

Biopsychology Laboratory, Department of Psychology, Marquette University, Milwaukee, WI 53233

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CZECH, D. A. AND J. M. VANDER ZANDEN. *Drinking behavior in the spiny mouse* (Acomys cahirinus) *following putative dipsogenic challenges*. PHARMACOL BIOCHEM BEHAV **38**(4) 913–916, 1991.—Male spiny mice (*Acomys cahirinus*) were challenged with several putative dipsogenic stimulus conditions: hypertonic sodium chloride (NaCl), 24-h water deprivation, *d,l*-isoproterenol HCl, angiotensin II (AII) and polyethylene glycol (PEG), or control conditions, in within-subjects designs. Water intake and drinking pattern were monitored electronically in the home cage over a 2–6-h test period without food present, during the light portion of the L/D cycle. In addition, hematocrits were measured following several treatments and mean arterial blood pressure was monitored in response to several doses of AII. As expected, both water deprivation and hypertonic NaCl led to robust drinking with short latencies. PEG was also an effective dipsogen; while quite variable, latencies were often shorter than are typically reported for the rat. Isoproterenol induced a modest, but significant, dose-related drinking. Interference by AII's prominent pressor action might account, at least in part, for its relative ineffectiveness as a dipsogen. Comparisons are made with other rodent species similarly challenged.

Drinking Isoproterenol HCl Hematocrit Water intake Angiotensin II Spiny mouse Water deprivation Polyethylene glycol *Acomys cahirinus* Hypertonic NaCl Arterial blood pressure

THE ingestive behavior literature reveals an increasing interest in important issues of species diversity. Our work with the spiny mouse (*Acomys cahirinus*) has suggested that this species holds promise as a useful model for investigating aspects of fluid and energy regulation. The spiny mouse, believed to be closely related to the gerbil, has some history in investigations of diabetes and obesity (11) and of renal physiology (7), and has more recently been identified as a promising tool for a broad range of biological and neurobehavioral studies (1,8). Our laboratory has studied several aspects of feeding and drinking behavior in *Acomys*, with focus on a comparative approach, including feeding/drinking patterns and compensatory feeding (6), feeding and selected physiological responses following glucoprivic challenge (4,5), and opioid involvement in intake behavior (3). In the present study, we extended these observations in reporting on drinking behavior in *Acomys* following exposure to a number of putative dipsogenic challenges. Of particular interest were reports that a subset of mammals, including the gerbil, appears to be dipsogenically relatively insensitive to peripherally administered angiotensin (10, 14–16). It was predicted that the spiny mouse would exhibit a profile of drinking to putative dipsogenic agents similar to that of the gerbil.

METHOD

Animals

Adult spiny mice (*Acomys cahirinus*) from the colony maintained at Marquette University were individually housed in polypropylene tub-type cages in an air-conditioned room maintained on a 12/12 light/dark cycle (lights on 0700–1900 h). Deionized water and pelleted food (Wayne rodent chow) were available ad lib except on test days as indicated below.

Procedure

Water intake. At approximately 0830 on test days, male mice (N = 12–13) were weighed, food and water were removed from cages, and fresh bedding material was provided. Two hours later,

[1]Requests for reprints should be addressed to Donald A. Czech, Department of Psychology, Marquette University, Schroeder Complex 454, Milwaukee, WI 53233.

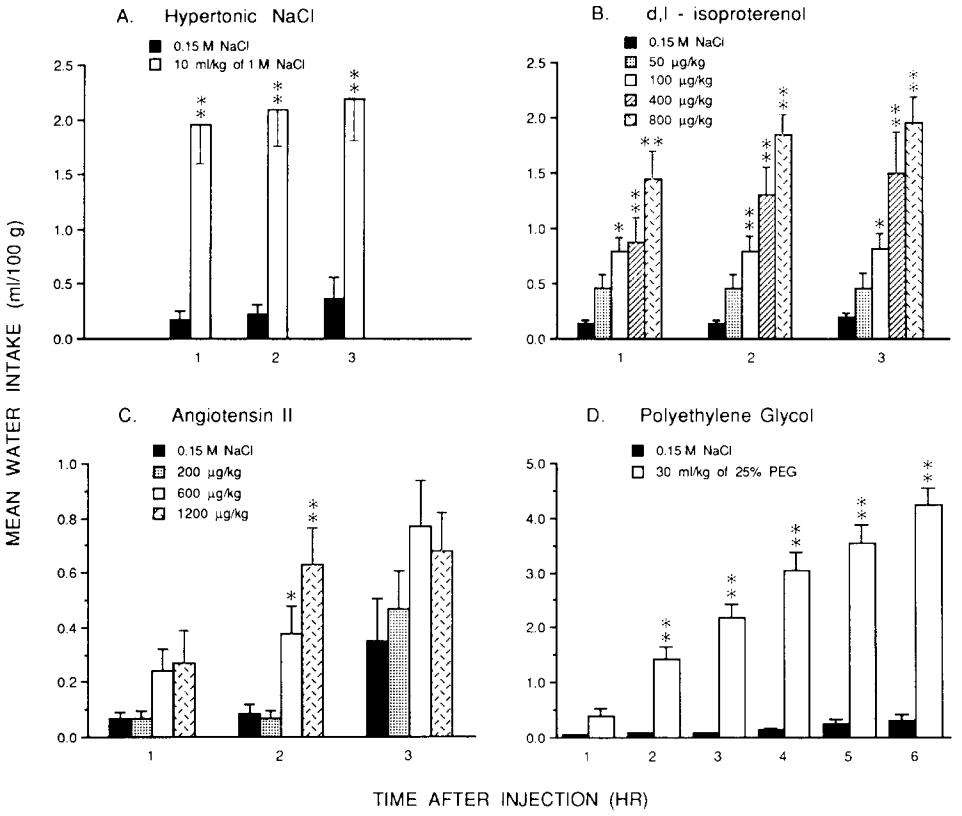

FIG. 1. Mean (±SEM) cumulative water intake at selected time intervals following peripheral injection of hypertonic NaCl (A), *d,l*-isoproterenol (B), angiotensin II (C), polyethylene glycol (D), or 0.15 M NaCl vehicle. Asterisks indicate significantly different from vehicle injection at indicated time point; $*p<0.05$, $**p<0.01$, *t*-test (A,D) or Dunnett's test (B,C), 1-tail.

they were injected SC or IP with a putative dipsogen or vehicle (0.15 M NaCl) and immediately returned to the home cage with access to deionized water provided via a leakproof drinking valve inserted into the cage wall. Thus all testing took place in the home cage and an animal always drank from the same valve. Alternatively, mice were water-deprived for 24 h. Food was unavailable during the drinking test period. Experimental treatment series were as follows, with all mice tested under all doses in a series in a within-subjects design with order of dose/treatment counterbalanced.

Hypertonic NaCl. A dose of 10 ml/kg of 1 M NaCl or vehicle was injected IP; drinking was monitored over a 3-h period.

Isoproterenol (ISOP). Doses of 50, 100, 400 and 800 µg/kg of *d,l*-isoproterenol HCl (Sigma) or vehicle were injected SC; drinking was monitored over a 3-h period.

Angiotensin II (AII). Doses of 200, 600 and 1200 µg/kg of ^{5}Ileu-AII (Sigma) or vehicle were injected SC; drinking was monitored over a 3-h period.

Polyethylene glycol (PEG). A dose of 30 ml/kg of 25% (w/v) PEG (mol.wt. ~20 K) (Sigma) or vehicle was injected SC; drinking was monitored over a 6-h period.

Water deprivation. Mice were water deprived (with food present) for 23 h. At 23 h, food was removed from cages and fresh bedding was provided. One h later, water was made available and monitored over a 2-h test period. A nondeprived condition (also with no food present during the drinking test) served as a control.

Water intake was monitored electronically with a drop sensing system, and drop counts were stored in 1–5-min time bins in a Rockwell AIM-65 microcomputer (2). Latency to first drinking response was also monitored. Drinking tests were separated by 3–4 days.

Blood pressure. Arterial blood pressure was monitored in response to SC injection of 200, 600 and 1200 µg/kg AII, or vehicle in anesthetized (Chloropent®) mice (N=5–12) of either sex via a polyethylene catheter (PE-10) inserted into the right carotid artery. The catheter, filled with heparinized (40 U/ml) 0.15 M NaCl, was connected to a Narco-Biosystems pressure transducer (Model RP 1500) coupled to a polygraph (N-B Model MK-III-S) for continuous monitoring of blood pressure.

Blood sampling. Blood was sampled by retro-orbital puncture technique under light ether anesthesia at designated times (see Table 1) following SC injection of 30 ml/kg of 25% PEG, 200 and 1200 µg/kg of AII, 400 µg/kg of ISOP, or equivalent volume of 0.15 M NaCl vehicle; and following either 23-h water deprivation (food present) or in a nondeprived state. Capillary tubes were immediately centrifuged and the hematocrit was read directly. With PEG, AII and ISOP, food and water were unavailable during the presampling (postinjection) period. Male mice were used in the PEG series; all other conditions used both males and females (N=8–10). Within-subjects counterbalanced designs were again used, with a 7-day interval between treatment conditions.

Analysis

Cumulative water intakes, adjusted for body weight, were evaluated with repeated measures ANOVAs, and Dunnett's and

t-test procedures. Hematocrits and blood pressure changes were analyzed with ANOVA and/or *t*-tests. Minimally acceptable significance level was set at $p<0.05$.

RESULTS AND DISCUSSION

Both 24-h water deprivation and hypertonic saline injections stimulated vigorous drinking in *Acomys*. With a single exception, 24-h water-deprived mice began drinking immediately or within five min of being given access to water, ingesting at least 90% of their intake within the first 10–15 min. By the end of the first h, mean water intakes were 3.53 (±0.26) and 0.07 (±0.02) ml/100 g, respectively, for deprived and control conditions. Ad lib water intake of spiny mice observed in our laboratory is about seven ml over the 24-h period (~15.5 ml/100 g, based on mice with an average weight of 45 g). *Acomys*' response to hypertonic NaCl is shown in Fig. 1A, with 12 of 13 mice consuming over 80% of their total intake within the first hour. Latencies to first drink ranged from 5–50 min, with 11 of 13 mice exhibiting latencies under 25 min. In these respects, *Acomys*' behavior is similar to that of a wide variety of mammals, including the rat.

Isoproterenol stimulated a significant, although modest, intake at doses from 100 μg/kg, and did so in a clearly dose-related manner (Fig. 1B). While latencies were somewhat variable, most of the drinking occurred within the first h at all but the two highest doses. It thus appears that isoproterenol is a more effective dipsogen in *Acomys* than in some other mice (14), as well as in several strains of hamsters (15,18) and in the degu (18). The dose required, however, is considerably higher than typically reported for the rat. Differences, however, have been observed among rat strains as well; Rowland and Fregly (13) have recently reported a weak drinking response to isoproterenol in Fischer 344 rats.

Angiotensin II (Fig. 1C) was a comparatively weak or ineffective dipsogen in *Acomys*. A relatively large dose (600 μg/kg) was needed to stimulate intake significantly greater than vehicle condition at h 2. Further, this modest effect was sustained only as long as baseline control intake was close to zero. If the spiny mouse possesses a functional AII-activated drinking mechanism, it appears not to be a very efficient one or it is somehow being compromised. Failure to stimulate drinking with peripherally injected AII has been reported for other species as well (10, 14–16). Kobayashi et al. (10) note insensitivity to AII as a dipsogen in carnivorous avian species which ordinarily drink little water, deriving most of their ingested water from meat, and/or in various nonavian species that live in or are derived from populations from arid habitats and drink little water in nature. These authors suggest that an angiotensin-thirst mechanism might have been attenuated or lost during the evolutionary adaptive process in such species. *Acomys* derives from arid desert regions of Northeast Africa and the Middle East, and obtains its water from feeding on snails and succulent vegetation, thereby certainly falling into a similar ecological niche (7). Alternatively, a pressor action of AII might have interfered with a drinking response (12,16). It has been reported that the gerbil drinks in response to centrally administered AIII (17) and that its pressor response to peripheral AII is more pronounced than it is to AIII (16). Further, Robinson and Evered (12) have shown that exogenous AII (IV infusion) is a substantially more potent dipsogen in the rat when its pressor action is attenuated with a vasodilator. To address this issue, we monitored arterial blood pressure in anesthetized mice injected with the same doses of AII as were used in drinking tests. These data are presented in Table 1.

Maximum changes in mean pressure shown in Table 1 (right-hand column) reflect increases of 38.5, 59.5 and 80.7%, respectively, for 200, 600 and 1200 μg/kg AII. Differences in doses of

TABLE 1

HEMATOCRIT AND MEAN ARTERIAL BLOOD PRESSURE (MAP) RESPONSES TO VARIOUS PUTATIVE DIPSOGENIC CHALLENGES (MEAN ± SEM)

Treatment	Hematocrit (%)	Baseline MAP (mmHg)	Max Δ MAP (mmHg)
0.15 M NaCl	45.3 ± 0.9	—	—
PEG (30 ml/kg 25%)	56.2 ± 0.7†	—	—
0.15 M NaCl	48.4 ± 0.5	83.5 ± 2.8	2.3 ± 0.4
AII (200 μg/kg)	49.0 ± 0.6‡	83.7 ± 2.8	32.2 ± 2.5†
AII (600 μg/kg)	—	87.0 ± 2.7	51.4 ± 3.0†
AII (1200 μg/kg)	53.3 ± 0.6†	81.4 ± 3.8	65.0 ± 3.7†
0.15 M NaCl	48.3 ± 0.5	—	—
ISOP (400 μg/kg)	46.7 ± 0.6*	—	—
Water-dep (23-h)	54.1 ± 0.3†	—	—
Nondep control	48.7 ± 0.8	—	—

Postinjection delay of 3 h for PEG and ~30 min for AII and ISOP.
*$p<0.05$, †$p<0.001$, compared to appropriate vehicle/control.
‡$p<0.01$, compared to 1200 μg/kg AII.

AII used in the present study and those used by Wright et al. (100 and 1000 μg/kg) preclude direct comparison; however, it is apparent that percent increases in mean arterial pressure in the spiny mouse were generally higher than were reported for the gerbil (16), e.g., 1000 μg/kg AII was needed to produce a 45% increase in mean pressure in the gerbil, whereas 600 μg/kg produced a 59% increase in mean pressure in the spiny mouse. Further, percent increases in pressure in *Acomys* in response to 200 and 600 μg/kg AII are comparable to increases reported to be associated with attenuation of drinking in rats following IV infusion of AII (12). Our data are thus consistent with an hypothesis that pressor action of AII is likely to have interfered with a drinking system/response in *Acomys*. Further work will need to also consider the time course of both pressor action and drinking following AII administration, and might well include other species reported to be dipsogenically insensitive to exogenous AII.

In sharp contrast, polyethylene glycol induced very robust drinking in *Acomys* (Fig. 1D), although considerable variability was observed in latency to first drink. Seven of 13 mice drank within 60 min; all drank within 3 h and mean latency was 85 min. Compared to the rat, drinking in these animals appeared relatively soon after PEG injection. Early drinking following PEG has also been reported for *Mus musculus*, with about 80% of intake occurring within 2 h (14). As Rowland and Fregly point out in reference to the common house mouse, such a robust drinking response to PEG in a species that is unresponsive (or perhaps only weakly responsive) to exogenous AII raises an issue of coupling between endogenous AII and hypovolemia-related drinking/thirst (14). Pressor effects might, however, have masked such linkage. Curiously, these investigators did not find a significant difference in the hematocrit two h after PEG versus sham injection in *Mus musculus*, an observation also reported for both degu and gerbil (18). At four h, however, PEG-treated gerbils had elevated hematocrits, and both degus and gerbils drank significantly more water within four h than did their control groups. It is not clear whether an increase in water intake at two h was significant. In light of these observations, we also measured hematocrits following several challenge treatments/doses. As indicated in Table 1, the hematocrit in *Acomys* was significantly higher in the PEG condition than it was following vehicle injection ($p<0.001$). The hematocrit was also significantly elevated at the highest dose

of AII (1200 μg/kg), a dose which effectively stimulated drinking at h 2. Haefeli and Peters (9) earlier reported elevated hematocrits following intravenous infusion of AII in rats, estimating loss of plasma volume large enough to stimulate drinking. This hypovolemic effect was determined to be a pharmacological consequence of increased vascular permeability and marked elevation of blood pressure.

The present study extends our work toward characterizing aspects of ingestive behaviors in the spiny mouse, a species beginning to attract considerable attention for use in behavioral/biological research. *Acomys*' profile of drinking behavior is similar in part to that of the gerbil for several putative dipsogens, differing from a number of other rodent species in that it also responded in a significant dose-related manner to the beta-adrenergic agonist, isoproterenol. Future research will need to include further examining physiological responses to angiotensin(s), and documenting drinking behavior following additional pharmacologic manipulations.

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