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Elicitation of Water Ingestion in the Mongolian Gerbil (*Meriones unguiculatus*) by Intracranial Injections of Angiotensin II and l-Norepinephrine

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BLOCK, M. L., G. H. VALLIER AND S. E. GLICKMAN. *Elicitation of water ingestion in the Mongolian gerbil (Meriones unguiculatus) by intracranial injections of angiotensin II and l-norepinephrine.* PHARMAC. BIOCHEM. BEHAV. 2(2) 235–242, 1974. – Intracranial injections of Angiotensin II (AII) through permanent brain chemodes aimed for the lateral hypothalamic, lateral preoptic, or septal region evoked drinking of tap water from Mongolian gerbils in normal water balance. When lettuce was the only available free water source, AII injections elicited prolonged lettuce-eating responses. *l*-Norepinephrine injections did not elicit eating of food pellets but, like AII, proved to be a reliable and potent dipsogenic agent. Carbachol, a cholinergic agonist, failed to elicit any ingestive behaviors over a wide dose range. The species-typical foot-thumping behavior of the gerbil was seen during some tests with all drugs utilized. It is suggested that the dipsogenic property of AII across a wide variety of species reflects the nature of a primitive, i.e., phylogenetically old, brain mechanism shared by most mammals to deal with problems of water economy, while the organization and utilization of other central neurochemicals in thirst-related substrates may vary among species.

Angiotensin II Drinking behavior Norepinephrine Foot-thumping Carbachol Chemical brain stimulation Thirst Mongolian gerbil

INTRACRANIAL injections of the same pharmacological agent into a variety of mammalian species can elicit behavioral responses that are as varied as the animals themselves. For example, the intrahypothalamic injection of microquantities of the cholinergic stimulant carbachol can evoke or facilitate drinking or muricide in the laboratory rat (*Rattus norvegicus*) [2, 6, 10, 29], eating and foot-thumping in the albino rabbit (*Oryctolagus cuniculus*) [30], attack and sham rage in the house cat (*Felis catus*) [15,20], and can suppress ingestive responses in the restrained rhesus monkey (*Macaca mulatta*) [22].

Differences in chemically-elicited behaviors across species may be due, in part, to differences in methodology. For example, the range of doses utilized, the precise neural sites stimulated, the physiological state of the animal, and/or the prevailing environmental factors at the time of testing vary from one study to the next. Yet these differences in experimental parameters are unable, in our opinion, to completely account for the variability in responsiveness to reasonable equivalent manipulations of central neurochemical systems of different species. Thus, the variability in chemically-elicited behaviors may also reflect genuine differences among species with respect to the central neurochemical substrates underlying particular behavior patterns. Other researchers have expressed similar conclusions [5, 18, 22].

The present experiment was undertaken to assess this notion of species-characteristic neurochemical substrates with a focus on the relatively discrete and well-defined response patterns of ingestive behaviors. To date, the techniques of chemical brain stimulation have only been used with mesically-adapted species to study central neurochem-

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ical systems mediating ingestive behaviors. We chose, instead, to apply these techniques to desert (xeric)-adapted animals, which utilize rather unique and elegant combinations of physiological and behavioral mechanisms to deal with formidable problems of maintaining water economy and energy balance. By comparing the results obtained with species adapted to a variety of ecological niches and utilizing different natural diets, we hope to establish the generality of neurochemical substrates underlying mammalian behavior.

The species selected for the present study was the laboratory bred Mongolian gerbil (*Meriones unguiculatus*), a small cricetid rodent whose wild counterparts inhabit the semi-arid regions of Northern Asia. Although reports of the behavior of the Mongolian gerbil in its natural habitat are meagre, there are numerous studies of the physiology and behavior of this xerically-adapted animal in the laboratory (cf. [8, 17, 33]). The experiment described below examines the responses of the gerbil to drugs which commonly elicit ingestive behaviors in such typical laboratory species as the rat and monkey [10,22]. In addition, drug dosages and sites of stimulation were chosen on the basis of prior work in the field of chemical brain stimulation so that the behavioral outcomes might be assessed with respect to these previous studies.

GENERAL METHOD

Animals and Housing

Twelve adult, male gerbils weighing 70–100 g at the start of the experiment were housed individually in stainless steel cages (7 × 9 × 18 in.) with wire mesh fronts. Animals lived on a 2 in. gravel substrate in which they could dig. Unless noted otherwise, they had continuous access to both tap water (available from metal water spouts fed by graduated burettes) and Purina lab chow pellets. Temperature was maintained at approximately 22°C and a 12 hr light-dark cycle (light: 0600–1800 hr) was imposed for the duration of the experiment. The amounts of water and food consumed in 24 hr (to the nearest 0.1 ml and 0.1 g, respectively) were recorded periodically throughout the study. About once a week the gerbils were given white index cards for shredding and conversion to nesting material.

Surgery and Histology

Each animal was implanted unilaterally under sodium pentobarbital anesthesia (50 mg/kg) with a cannula made from 26 g (0.461 mm O.D.) stainless steel hypodermic tubing. These chemodes were aimed for the dorsal aspect of either the lateral preoptic area (LP), the medial septal nucleus (MS), or the lateral hypothalamic area (LH). Stereotaxic coordinates using bregma and the dura as landmarks, and the tooth bar set 5.0 mm above the ear bars were:

Site	Coordinates			No. of animals
	A–P	L	D–V	
LP	+2.0	1.5	6.0	4
MS	+2.0	0.0	3.0	4
LH	−0.5	1.4	5.5–6.0	4

Animals were allowed a minimum of 7 days to recover from surgery before any testing began. At the end of the experiment the animals were sacrificed with an overdose of Nembutal and perfused with saline and Formalin. Frozen sections were cut coronally at 50 μ throughout the extent of the chemode tract and every tenth section was stained with cresyl violet. Locations of the tips of the chemode tracts for each gerbil except LH 118 (whose brain was damaged during its preparation) are depicted on schematic brain sections from the gerbil atlas by Thiessen and Goar [34] in Fig. 1. Comments on relevant histological findings are discussed in later sections.

Intracranial Chemical Injection (ICI)

All tests were conducted during the light phase of the light-dark cycle. At approximately 1300 hr on the day of testing, an animal was removed from his home cage and injected rapidly through the permanent chemode with 1.0 μl of solution, utilizing the injection system described by Epstein *et al.* [4]. A length of 32 g stainless steel tubing (0.228 mm O.D.) protruding 0.1–0.2 mm beyond the tip of the implant served as the injection cannula. Approximately 15 sec after the ICI, the injector cannula was removed and the gerbil was returned to his home cage. The entire injection system was thoroughly flushed with isotonic saline and 70% alcohol both before and after its use for ICI.

The following chemicals and dosages (expressed as the base) were utilized: (1) Carbachol (carbamyl choline chloride: Carb): 1, 10, 100, and 1000 nanograms (ng); (2) Angiotensin II (in form Hypertensin® Ciba: AII): 250, 500, and 1000 ng; (3) *l*-Norepinephrine (in bitartrate form: NE): 500 and 2000 ng (prepared just prior to its injection). All drugs were dissolved in isotonic saline and stable solutions were kept refrigerated in light-resistant bottles. An isovolumetric solution of pyrogen-free normal saline (pH = 5.0–5.5) served as a control for possible volume and nonspecific effects of the ICI. The pH range of the drug solutions was 5.0–5.7, except for the 2000 ng dose of *l*-Norepinephrine (pH = 3.5).

The experiment can best be described in three sequential phases. The first phase involved microinjections at the tip of the chemode with the lower doses of the drugs and a corresponding record of the gerbils' behavior after each ICI. In the second phase, the behavioral specificity and motivational nature of the drug effects observed in the first phase were examined. In the final phase, some of the gerbils were tested with the highest dose of the drugs, and the remaining animals (unresponsive to the neurochemicals in previous tests) were reinjected with these chemicals at lower brain depths, in order to examine the anatomical specificity of the drug-induced behavior.

PHASE 1

Procedure

Gerbils were injected on different days (separated by a minimum interval of 48 hr) with AII (250 ng and 500 ng), Carb (1 ng, 10 ng, and 100 ng), NE (500 ng), and isotonic saline in 1 μl volumes. The amounts of water ingested 15 min and 60 min later were recorded, as well as the amount of food ingested during this 1 hr test period. All animals were initially tested with 500 ng of AII, or in some cases 250 ng, and thereafter the administration of drugs was

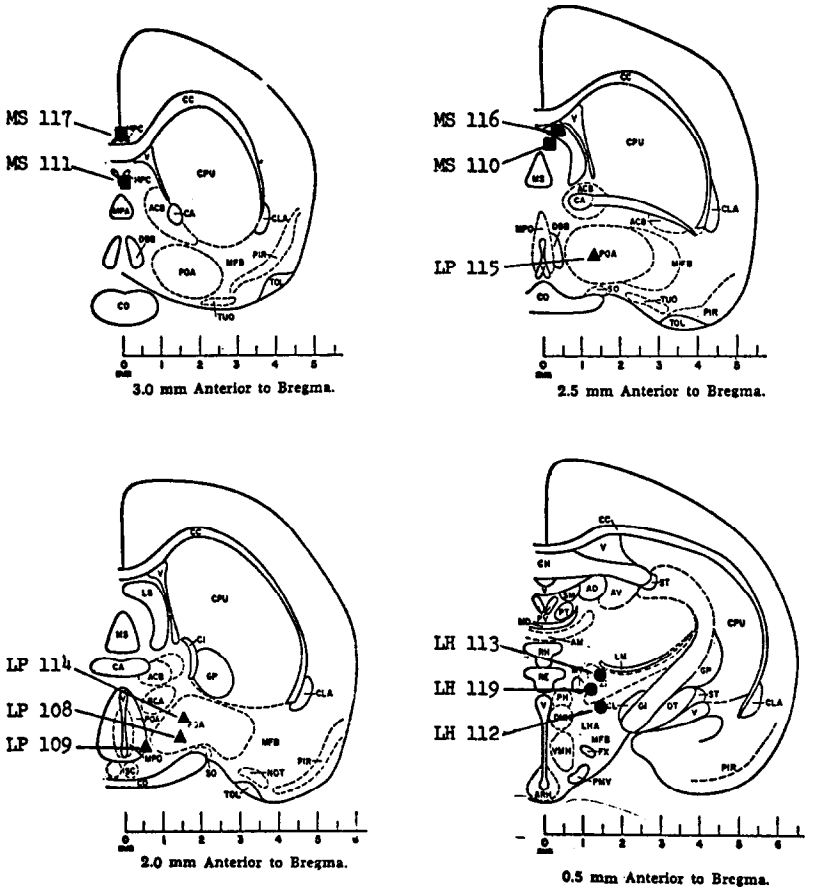

FIG. 1. Location of chemode tips for Groups LH (•), LP (▲), and MS (■), projected onto frontal sections of the gerbil atlas by Thiessen and Goar [34]. (The brain of gerbil LH 118 was lost during histology.)

randomized and balanced across animals to minimize order effects. Each animal received two injections of saline during the testing regime and a retest with AII at the end of this experimental phase. The other drugs and dosages given to each animal are presented in Table 1.

In addition to the quantitative measures of food and water intake, a continuous qualitative record of behaviors was kept during the 1 hr test periods. The behavioral events recorded were based on the motor patterns of small rodents described by Eisenberg [3].

Results

Saline. The typical behavioral profile of a gerbil receiving an injection of isotonic saline was as follows. There is an initial brief grooming response (15–20 sec) when the animal is returned to its cage, and this is followed by a motor pattern consisting of alternating rearing and locomotor movements. The exploratory behaviors lasted about 15–20 min and were often interrupted by a brief period of sand digging and/or inactivity (e.g., quietly standing on rear legs). Occasionally a brief eating bout (30–160 sec) was exhibited by a few animals. About 30 min after the injection, the gerbil typically assumed a sleeping posture and remained in this position for the rest of the test hour. The amount of water ingested by any gerbil after saline injection did not exceed 0.1 cc. On a few saline tests (3/24) a gerbil was seen to ingest up to 0.5 g of food; there was, however, no demonstrable intake of food in the vast majority of these tests.

Angiotensin II. Single injections of AII into either the LP or LH caused animals in apparently normal water balance to drink water. An animal began to drink immediately or a few minutes after the injection. Drinking, once begun, usually continued for a couple of minutes, after which the animal either simply ceased drinking or began to move about his cage for a few minutes, beginning to drink again after this pause. Thus, drinking was generally seen to occur in two or three bouts, although the entire drinking response typically ceased within the first 15 min of the test hour. The amount ingested ranged from 0.3 to 3.1 ml in the 1 hr test (see Table 2). The amount of water consumed in the 24 hr period after the AII injection did not deviate from an animals's normal range of 24 hr water intake, even though the amount drunk in the 1 hr test period represented up to 58% of an animal's normal daily intake. In the few animals

TABLE 1

ADMINISTRATION OF NEUROCHEMICALS*

Area Stimulated	Gerbil	Angiotensin II			Carbachol				Norepinephrine	
		250 ng	500 ng	1000 ng	1 ng	10 ng	100 ng	1000 ng	500 ng	2000 ng
Lateral	108	X	X	X		X	X	X	X	X
Preoptic	109	X	X	X		X	X	X	X	X
	114		X		X		X	X	X	X
	115		X		X		X	X	X	X
Lateral	112		X	X		X	X	X	X	X
Hypothalamus	113		X	X		X	X	X	X	X
	118		X	X	X		X	X		X
	119		X		X		X	X	X	X
Medial	110	X	X			X	X	X	X	X
Septal	111	X	X	X		X	X	X	X	X
	116		X		X		X	X	X	X
	117		X	X	X		X	X	X	X

*X = administered drug at dose designated

tested, injections of 250 ng of AII into the LP elicited a drinking response comparable to a 500 ng injection into these same sites.

No significant amount of eating was recorded after AII injections. When compared to saline control tests, no other responses or class of responses appeared to specifically accompany AII stimulation.

Injections of AII through the chemodes aimed for the MS did not elicit any particular behavioral response. However, histological examination of these animals at the end of the experiment suggests that the injection cannula during this phase did not penetrate the corpus collosal fibers overlying the septal region (see Phase 3).

Carbachol. With the lowest dose of Carb (1.0 ng), 3 out of the 4 gerbils showed an eating episode which began 10–34 min after the injection and lasted 2–5 min; however, this response was not unlike that seen under some saline injections and the amount consumed never exceeded the range in the control tests (0.1–0.5 g/hr). No drinking was seen with this dose.

At the higher doses (10 ng and 100 ng) no eating or drinking was observed except by one animal (LH 119). He began to eat approximately 14 min after the injection of 100 ng of Carb and continued to eat for about 11 min, after which he drank 1.7 ml of water. (Unfortunately, procedural problems prevented a quantitative determination of food consumed during this particular test.) In the case of the MS gerbils, no ingestive responses were recorded with any dose of Carb.

There was no clear relationship between cholinergic stimulation and most behavioral classes; however, in several tests with the 100 ng dose some of the gerbils (LP 109, LP 115, LH 118), including one MS animal (MS 117), exhibited vigorous thumping of their hind feet. In addition, extended periods of tonic immobility (i.e., when an animal remains motionless for periods of 1–10 min and usually displays palperal ptosis) were observed during half of the carbachol tests.

l-Norepinephrine. Surprisingly, 3 of the 6 AII-induced drinkers (see Table 2) responded to 500 ng of NE with a rather strong drinking response, and in a few cases foot-thumping appeared concurrently with the drinking behavior. (It should be noted in Table 2 that the foot-thumping response was not always correlated with the ingestion of water.) The onset of drinking after NE injection was quite rapid – 1 min or less. While gerbil LP 114 did not ingest a significant amount of water when compared to saline injections, he began to drink within 1 min after noradrenergic stimulation – a response latency never observed during control tests. Injections of NE into the MS gerbils evoked no drinking response (however, see Phase 3).

No significant eating was observed. Various other kinds

TABLE 2

THE EFFECTS OF INTRACRANIAL CHEMICAL INJECTIONS (ICI) ON WATER INTAKE

Area Stimulated	Gerbil	Average 24 Hr Water Intake	1 Hr Water Intake (cc) after ICI of: Saline (1.0 μl)	Angiotensin II 500 ng	L-Norepinephrine 500 ng	L-Norepinephrine 2000 ng
Lateral	108	6.1	0.0	1.0	0.0	0.0*
Preoptic	109	4.0	0,0	2.6	1.0*	1.9*
	114	4.0	0.1	2.2	0.1*	3.1
	115	5.0	0.1	2.3	0.0	2.9*
Lateral	112	4.1	0.0	1.5	0.0	2.3
Hypothalamus	113	5.4	0.0	3.1	1.8	0.0*
	118	4.0	0.0	1.3	(NT)	0.0*
	119	9.0	0.1	2.7	3.1*	2.7*
Medial	110	5.0	0.0	2.2*	(NT)	2.9
Septal†	111	5.2	0.0	2.0	(NT)	3.0*
	116	5.1	0.0	0.6	(NT)	2.5*
	117	6.2	0.0	0.0*	(NT)	0.0

*Foot-thumping of rear leg seen during test

†All animals failed to ingest water when chemostimulation sites were 0.2–0.4 mm dorsal to the sites from which these results were obtained (see text).

NT = Not tested at this depth (see text for explanation).

of behaviors were noted during the NE tests – for example, a ventral rubbing response [cf.33] over the water spout by LP 114. However, no salient response class seemed to necessarily accompany noradrenergic stimulation, although six animals did display periods of tonic immobility not unlike those exhibited under Carb stimulation.

On the last test day, AII injections continued to evoke drinking from previously responsive neural sites while the initially unresponsive sites remained so.

PHASE 2

It is of interest to determine the motivational nature of the AII-induced drinking response observed. For example, will a gerbil appropriately change his response pattern to AII stimulation if the source of the goal-object (in this case, water) has also been changed? In order to answer this question, gerbils used in the first phase were given lettuce instead of tap water as a source of free water. With this green as their only source of free water, gerbils can maintain themselves quite well and will consume relatively large amounts of lettuce immediately after a 24 hr period of lettuce-deprivation (unpublished observations). Would these gerbils who had learned to utilize lettuce as a water resource use the motor pattern of chewing, instead of licking, to acquire water under AII stimulation? Or will the gerbil ignore the lettuce, suggesting that the AII-induced drinking response reflects the release of a relatively inflexible motor pattern?

Procedure

Animals were housed and maintained as described in Phase 1 except that fresh lettuce instead of tap water was provided daily. Approximately 1 week after the lettuce was introduced, their food intake had stabilized. Two days later all gerbils were injected with either saline or 500 ng of AII. Food intake and the amount of time spend eating the lettuce were recorded for 1 hr after the intracranial injection. A record of other behavioral responses during the test was also kept. (Attempts to directly measure the amount of lettuce ingested by weighing the lettuce before and after the test proved impractical under these experimental conditions.) Three days later the animals were again tested, but this time the type of solution which a gerbil received was reversed, i.e., those gerbils who had received saline on the

first lettuce test received AII and vice versa.

Results

All gerbils with LH implants responded to AII stimulation with prolonged lettuce-eating responses – 4–6.5 min. With injections of isotonic saline, 3 of the animals showed no lettuce eating, and the fourth animal (LH 119) spent only 30 sec in the hour nibbling at the lettuce. In the case of the LP gerbils, 2 animals showed significant responses under AII stimulation (3–4 min) while the remaining two animals (LP 108 and LP 114) showed little if any ingestive responses with the dipsogenic agent (0–30 sec). Saline injections had no effect on the consummatory behaviors of these gerbils. When AII or saline was injected in the MS, these rodents showed no ingestive responses; however, the experiments to be described in Phase 3 demonstrate that these animals can be induced to ingest lettuce when the injection cannula reaches a site from which AII-induced drinking of tap water can also be elicited.

The kinds of response patterns seen under the present lettuce experiment did not differ from those observed under previous tests with AII and saline. However, a few of the LH gerbils did show a noticeable increase in the amount of adjunctive behaviors (e.g., gathering material, foraging, carrying food pellets, and digging) during this AII stimulation as compared to previous AII tests when only tap water was available. No eating of food pellets was observed during these chemostimulation tests.

PHASE 3

In this phase of the experiment, all LP and LH gerbils were given ICI with higher doses of NE (2000 ng) and/or Carb (1000 ng). At the end of testing, all these animals were given a final test with 500 ng of AII to determine the viability of these chemostimulation sites following the rather large number of injections to which they were subjected. In addition, the MS gerbils were tested with AII and NE at new brain depths by extending the length of the stimulation cannula by 0.2–0.4 mm.

Results

Under the test conditions described in Phase 1, 1000 ng of Carb failed to elicit any consummatory response. The most common response (7 of 8 gerbils) was a tonic immobility characterized by postural rigidity and ptosis; however, these animals could easily be aroused by tactile or auditory stimuli. Increasing the dose of NE to 2000 ng produced an increase in the number of gerbils from which drinking could be elicited by this putative neurotransmitter. Five of the 8 LH and LP placements gave robust drinking responses (1.9–2.9 cc) which were accompanied by foot-thumping in most cases (see Table 2). However, since two of the eight gerbils (LH 118 and LP 108) failed to respond to AII on the final ICI, the data gathered on these 2 animals during this phase are difficult to interpret. Of the 6 gerbils who remained positive to AII, 5 could be induced to drink with this dose of NE, while the sixth animal was unresponsive, although he did drink to the 500 ng dose of NE.

When the stimulation cannula was lowered in the MS animals, 3 of the 4 gerbils ingested relatively large amounts of water under AII and NE stimulation (see Table 2). Unlike the tests with AII in the LH and LP gerbils, a few animals also exhibited foot-thumping responses. The histological analysis of the one MS gerbil (MS 117) who failed to respond to either dipsogen showed that injection cannula failed to reach the septal area, while the cannula tips of the other gerbils did lie within the dorsal aspects of the septal region (see Fig. 1).

These same MS animals were then given a lettuce test as described in Phase 2 with injections of AII (500 ng). All the positive tap water drinkers showed a rather prolonged lettuce eating response (range: 5.5–6.5 min), while the one negative animal remained unresponsive in this test. Although not quantified, injections of NE (2000 ng) also evoked extended bouts of lettuce eating. No ingestion of food pellets was observed during these tests with either drug.

DISCUSSION

Intracranial injections of AII proved to be a reliable dipsogenic agent in the gerbil. Since the same drinking response has been elicited by AII in a wide variety of species in which it has been tried [1, 4, 26, 32], it would appear that this phenomenon reflects the workings of a primitive, i.e., phylogenetically old, brain mechanism utilized by mammals to deal with problems of water economy. The ability of a gerbil to switch motor responses (licking to chewing) in order to accomodate a change in free water source (from tap water to lettuce) under AII stimulation suggests that the drinking behavior induced in this manner is quite similar to that which occurs normally. Recently, Graeff *et al.* [9] and Rolls *et al.* [24] have demonstrated that intracranial injections of AII in sated rats will elicit a previously learned bar pressing response that produces drinking water. Thus, not only can consummatory patterns be altered in response to a change in the source of the goal object under AII stimulation, but the nature of the appetitive response patterns elicited by this dipsogenic agent also seem to be flexible and adaptive. It is interesting to note that the flexibility in response patterns demonstrated with the gerbil under AII stimulation is unlike that exhibited by rats when drinking is elicited by electrical stimulation of the hypothalamus. In the latter case, a rat will exhibit a learned behavior (instrumental response) to obtain water while receiving electrical brain stimulation, but it has great difficulty in switching its consummatory response pattern when water is available from a dish instead of a drinking tube [36]. It would appear, therefore, that the motivational state induced by AII is better able to mimic the natural drive state induced, for example, by a period of water deprivation than is the condition obtained with electrical brain stimulation (see also [38]).

The naturalness of the AII-induced drinking response is also underscored by our observations in several animals that when water is removed from the test cage after an injection of this dipsogenic agent, no other oral responses emerged (e.g., eating or gnawing) but there was persistent searching behavior directed toward the area of the cage from which the water is normally available.

Carb stimulation of these same brain sites failed to elicit any ingestive responses in the dose range utilized (1–1000 ng). The only clear-cut effects of Carb were tonic immobility that was often accompanied by postural rigidity and foot-thumping of the rear leg. Similar effects in the Mongolian gerbil with the crystalline form of carbachol have also been observed (Spatz, Glickman, Ellesman and Leavitt, unpublished manuscript). Furthermore, intrahypothalamic injections of this cholinergic stimulant in the

rabbit can evoke the species-typical foot-thumping response [30].

Recent work by Myer *et al.* [23] with the rhesus monkey suggests that a nicotinic-type of cholinergic receptor might be involved in the mediation of the drinking response of species other than the rat, in which the muscarinic-type of synaptic mechanism seems to play an important role [31]. Since Carb activates both types of cholinergic receptors, it is possible that the muscarinic effects are masking or counteracting a nicotinic mechanism that is normally involved in the gerbil's drinking behavior. Furthermore, this simultaneous activation of functionally separate cholinergic receptors might lead to the behavioral paralysis seen under Carb stimulation. In a preliminary attempt to test this hypothesis, four different gerbils bearing LH implants received injections of nicotine tartrate (2000 ng of the base/0.5 μl) into AII drinking sites. No ingestive responses were recorded with nicotine injections; however, every animal showed a foot-thumping response and exhibited sustained periods of activity that were never observed with Carb stimulation. While these preliminary data fail to support the nicotinic-drinking hypothesis, they do suggest that the foot-thumping seen under Carb stimulation may be due to the activation of nicotinic receptors. (Tests combining Carb with muscarinic blocking agents like atropine should put this latter notion to a critical test.)

The most provocative finding in the present study is the substantial drinking response evoked by central injections of NE. While there have been reports of a mild dipsogenic action of centrally administered adrenergic stimulants in the rat [21, 27, 28], this study demonstrates that the reliable and primary effect of intracranial injections of NE in the gerbil (under the present testing conditions) is water ingestion, and not the food ingestion response typically seen in other mammalian species that have been tested.

There are a number of problems involved in the interpretation of this NE-induced drinking response. Two of these problems stem from potential non-specific effects of the testing methods employed in the present study. First, there is the rather lengthy testing procedure which involved numerous injections of various drugs. Warnings of repeated central drug treatments have been issued [25] and it is possible that the neural tissue at the site of stimulation may develop a nonspecific sensitivity to all kinds of drugs following repeated injections. In addition, the low pH of the NE solution (3.5) may non-specifically stimulate neural tissue, or at least contribute in some way to the behavioral effects observed after NE injections. In order to control for these potential experimental artifacts, four additional gerbils were implanted with LH chemodes. When a positive response to AII (500 ng) could be obtained, the next 2 tests involved injections of NE (2000 ng) and a 0.9% acidic saline solution (pH adjusted to 3.5) given in an order which counterbalanced across animals. The low pH saline solution failed to elicit any ingestive responses, although hyperactivity in the form of locomotor behavior was seen in a few of the tests. Three of the 4 gerbils who responded to AII with drinking also ingested substantial amounts of tap water (0.9–3.6 cc) after NE injections into these same brain sites. The fourth gerbil did not respond to either AII or NE. While not systematically or quantitatively studied, the three responsive animals could also be induced to eat lettuce under adrenergic stimulation when lettuce provided the only source of free water. The results obtained with these additional gerbils suggest that neither pH factors nor the repeated testing procedure used in the present study could account for the NE-induced drinking behavior observed.

The mechanism by which NE elicits water ingestion in the gerbil can only be conjectured at this time. It has been reported that the AII-induced drinking response in the rat seems to be mediated by central catecholaminergic mechanisms [7], suggesting a possible dependent relationship between the dipsogenic properties of AII and NE in the present study. In this regard, mediation by central beta-adrenergic systems is a possibility [13,14]; however, we have been unable in a few tests that we have conducted (n = 6) to evoke a drinking response with central injections of isoproterenol (5000 ng) into LH, LP, or MS areas that were positive to NE stimulation.

The tests that we have performed so far do not rule out the possibility that the drinking response seen with NE (or AII) could be a secondary response to changes in local blood flow. A local hormone action of NE in the control of cerebral blood flow has been proposed [11,19], and the fact that the non-dipsogenic agents Carb and isoproterenol have a vasodilating action while the dipsogenic agents AII and NE are vasoconstrictors would suggest that a non-neuronal hypothesis deserves further study.

In addition, since all testing was carried out during the light phase of the illumination cycle, we do not know to what extent our behavioral results might be due to possible underlying circadian rhythms in neural substrates related to ingestive behaviors [16]. Nevertheless, the chemospecific and goal-directed nature of the water ingestion behavior observed in the present experiments suggest that the gerbil may utilize not only the universal mammalian dipsogen angiotensin II for controlling its water intake, but that central catecholaminergic mechanisms are also involved in the neural substrate of thirst.

Other than water ingestion, foot-thumping was the only response which was frequently observed. It has been suggested that the foot-thumping response of the Mongolian gerbil is an arousal-mediated and not necessarily goal-directed behavior [8]. This conceptualization would appear to fit the data in the present study in view of the fact that this behavior was elicited at one time or another by all the drugs utilized and was not limited to stimulation in any specific area.

It has been proposed that basic, species-typical behaviors such as eating, copulation, and drinking are outgrowths of central states of arousal [12, 35, 37]. From this point of view, centrally elicited behaviors are derived from the channeling of a relatively nonspecific state of arousal into specific, prepotent motor patterns by interactions with environmental stimuli. To the extent that foot-thumping may serve as an indicator of central arousing processes, the possibility that the AII- or NE-induced drinking response is due solely to a general arousal phenomenon seems unlikely since elicited foot-thumping and drinking were not always correlated with each other.

The histological data in the present study are too meager to suggest a possible anatomical locus for the action of these dipsogenic agents. Before the effective neuroanatomical substrates for consummatory responses in the gerbil can be more accurately localized and characterized, more extensive and refined mapping studies of brain sites from which ingestive behaviors can be altered by a variety of techniques will have to be done. Perhaps with a more extended dose range of NE, for example, one might be able

to tap into hunger-related adrenergic neurons within the same sites stimulated in the present study, or there may be catecholamine neurons specifically involved in a central eating substrate that are located in, or project to, other brain loci.

Finally, it might be the case that the relative distribution and/or contribution of central catecholamine neurons to eating and drinking behavior may vary among species belonging to different taxonomic groups, or adapted to different habitats, in such a way that the neurochemical substrates underlying basic motivated behaviors are species-characteristic. We are presently pursuing this hypothesis by utilizing similar chemostimulation techniques with other members of the cricetid family which occupy different ecological niches.

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