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Suppression of Conditioned Drinking by Taurine and Related Compounds

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HRUSKA, R. E., P. D. THUT, R. J. HUXTABLE AND R. BRESSLER. *Suppression of conditioned drinking by taurine and related compounds.* PHARMAC. BIOCHEM. BEHAV. 3(4) 593–599, 1975. – Mice were conditioned to respond for water reinforcements on a FR-5 schedule. Taurine, injected intraperitoneally at doses of 9.0, 13.8, and 21.3 mmole/kg, 30 min prior to the experimental session, produced a dose-related decrease in both the initial response rate and total number of reinforcements received by mice deprived of water for 24 hr. The structural analogues of taurine (aminomethanesulfonic acid, 3-aminopropanesulfonic acid, β-alanine, cysteamine, and glycine) also produced a hypodipsia. Doses of taurine which produced depression of responding for water reinforcements were used which produced no suppression of spontaneous motor activity, rotarod performance, Sidman avoidance, or shuttle-box avoidance. After intraperitoneal injection, the concentration of taurine increased in the hypothalamus and medulla, but not in other brain areas. We suggest that taurine might be acting by specifically depressing areas of the hypothalamus which stimulate drinking.

Taurine Drinking behavior Hypothalamus

TAURINE (2-aminoethanesulfonic acid) has been reported to be present in the tissues of numerous vertebrate and invertebrate species [10]. In vertebrates the highest concentrations of taurine occur in excitable tissues. Rat skeletal muscle contains 14 μmole/g taurine, while the rat heart contains about 40 μmole/g [8].

The effects of taurine on excitable tissues have been studied by applying taurine to various neurons in the spinal cord [3], cortex [2], and brainstem [6]. Spontaneous electrical activity of neurons was inhibited by the direct application of taurine in these experiments. Recently, taurine has been proposed to act endogenously as an inhibitory neurotransmitter [4,11]. It was reported that electrical impulses could enhance the efflux of taurine from rat brain cortical slices, and also that a high affinity uptake process existed for taurine [11]. However, others have failed to confirm this observation [7,12].

Despite these studies designed to determine the effects of taurine on excitable tissue, the physiological importance of taurine in vertebrates is not known. Since taurine has been reported to be involved in the osmoregulation of marine species [13, 14, 15], it was of interest to determine if taurine could alter the ability of mammals to regulate water balance. The present study has measured the effects of taurine and various related compounds on water drive in mice, which had been trained to obtain all their daily water allotment as reinforcements in a behavioral chamber. The intraperitoneal route of administration was used since intracerebral administration of taurine has been reported to decrease motor activity in the mouse [1].

METHOD

Animals

Male HaM/ICR Swiss mice, obtained from Charles River Breeding Laboratories, weighing 35 ± 4 g were used. The animals were housed in hanging cages to minimize coprophagia and access to urine. Food and water were available ad lib until 24 hr prior to drinking experiments, when the water was removed.

Drugs

Taurine (99% pure) was obtained from Sigma Chemical Co. and was recrystallized until chromatographically pure. Aminomethanesulfonic acid (AMSA), β-alanine, 3-aminopropanesulfonic acid (3APSA), cysteamine, and glycine were obtained in pure form from commercial sources. Since the highest dose of taurine (21.3 mmole/kg) was not freely soluble in water at suitable concentrations, it was prepared as a suspension in 0.5% carboxymethylcellulose (CMC). All other compounds were also dissolved or suspended in 0.5% CMC and were administered intraperitoneally in a volume of 20 ml/kg. The control solutions were made isoosmotic

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with the experimental solutions by the addition of NaCl to 0.5% CMC.

Procedure

Conditioned drinking procedure. Conditioned drinking behavior was trained in a water reinforcement mouse chamber. The liquid dipper of the apparatus delivered approximately 10 μl of tap water. The mice were allowed ad lib access only to food in their home cages. Water was available only in the experimental chamber (except between experiments when water was available ad lib). Mice, deprived of water for 24 hr, were trained to press a lever to obtain water rewards. Animals were trained on FR-5 until a stable performance was achieved during daily 20 min sessions. The trained animals showed a brisk response on FR-5, with the expected postreinforcement pauses, during which time the reward was consumed. The animals also appeared to satiate during the 20 min sessions.

Each experiment consisted of at least one training day, followed by a non-treated control day. The non-treated control day was followed by an experimental day on which the animals were pretreated with either an experimental compound or with an isoosmotic control solution of NaCl 30 min prior to the experimental session. The experimental day was followed by a non-treated control day. A cross-over design was used so that the behavior of each animal served as its own control. The average number of mice per drinking experiment was 11.

Two measures of response were used. First, the total number of reinforcements received by each animal was recorded, and is reported as a percentage of the number of reinforcements received on the non-treated control day. Second, the rate of responding during the first 5 min of the session was calculated. This initial response rate appeared to be linear. Initial response rates are also reported as a percentage of the non-treated control day initial response rate. Each mouse showed little variation in this parameter over many weeks of control observations. In all experiments mice responded at control rates 24 hr after injection.

Conditioned eating procedure. This was identical to the conditioned drinking procedure, except that the rewards were 20 mg food pellets and the sessions were 25 min long. In this procedure the animals did not satiate. Therefore, in order to maintain constant body weights, approximately 1.5 g of food was freely given each animal at the end of each day.

Motor activity. Spontaneous locomotor activity was measured in doughnut-shaped cages, which were 30.5 cm in diameter, with a 7.5 cm wide circular runway [21]. As a mouse traversed the runway, 4 equally-spaced floor panels were alternately depressed, thereby activating microswitches connected to counters. Animals were placed one to a cage in a dark, ventilated, sound attenuating chamber, 30 min after the injection of taurine or of the isoosmotic control solution. Motor activity was monitored at successive 15 min intervals for 2 hr by photographing the counters every 15 min automatically [22].

Rotarod. The rotarod is a wooden rod, 2.5 cm in diameter and 14 cm long, rotating at 8 rpm. The rotarod was suspended 50 cm above a foam rubber pad onto which the animals fell when they lost their position on the rotarod. Untrained mice were placed on the rotarod for 3 min and the number of falls during the session was recorded for each mouse. Animals falling during the session were immediately returned to the rotarod.

Sidman avoidance. Sidman avoidance [19] was trained in a Plexiglas chamber (12.7 X 14 X 14 cm) with an electrifiable grid floor. The response manipulandum was a 3.4 cm dia. drum mounted 1.3 cm above the floor in the center of one of the chamber's walls. Responses were registered when the drum was moved through a 30° arc. A 5 sec, 1.0 mA scrambled shock was presented to the grid floor every 10 sec unless the mouse responded. Each drum-turning response delayed the shock for 30 sec and terminated a shock being delivered. Mice were trained in 1 hr sessions for 2 weeks, at which time there was no further significant change in their day-to-day performance. Each experiment consisted of a training day, a non-treated control day, and an experimental day. On the experimental day each mouse received either taurine or an isoosmotic control solution 30 min prior to the start of the 1 hr session. A cross-over design was used so that the behavior of each animal after the isoosmotic control treatment could be compared to its behavior after the taurine treatment. Total responses, and the percentage of avoidances and escapes were calculated for each 15 min interval of the session. These parameters were then used as a percent of the non-treated control day for both isoosmotic control solutions and taurine solutions.

Shuttle-box avoidance. The mouse shuttle-box was similar in design to that described by Seiden [18]. Two equal compartments (12.3 X 9.3 X 15.5 cm) were divided by a Plexiglas partition reaching to 3 cm above the electrifiable grid floor. Each trial consisted of a 20 sec inter-trial interval, followed by a tone. Five sec after the tone onset, a 5 sec scrambled shock was delivered to the grids on the side of the chamber occupied by the mouse at the time the sound cue started. After the shock, the 20 sec inter-trial timer restarted. Each daily session consisted of 40 trials. An avoidance was recorded when the animal changed sides of the chamber during the sound cue but before the onset of the shock. An escape was recorded when the mouse changed sides of the chamber during the shock. A shuttle failure was recorded when the animal failed to cross during either the sound cue or shock. An avoidance or escape turned off the sound cue. However, the sound cue resumed if a recrossing was made during either the tone period or shock period. Retracing was always punished by having the shock remain on for the total 5 sec. A cross-over design was also used in this experiment so that the behavior of each animal after the isoosmotic control solution could be compared to its behavior after the taurine solution. Again, this data is presented as a percentage of the nontreated control day.

Taurine assays. Taurine assays were performed as previously described [9]. Briefly, the tissue sample was homogenized in water and trichloracetic acid was added. Protein was separated by centrifugation and trichloracetic acid was removed by ether extraction. The supernatant was taken to dryness and refluxed with HCl. The supernatant was again taken to dryness and the residue was taken up in water, which was layered on an ion-exchange column containing AG 50 H^+ cation exchange resin layered over an AG 1 Cl^- anion exchange resin. Taurine was eluted with water and determined using an amino acid analyzer.

Dissection. Taurine analyses were performed on specific areas of the mouse brain. The mice were anesthetized with ether and the body cavity opened. The descending aorta was clamped and a small slit was cut in the right ventricle of the heart. Twenty ml of 0.9% NaCl was perfused through the brain by injecting into the left ventricle of the heart.

After perfusion the brain was removed and dissected into five parts as previously described for the rat brain [5] with the modification that the hippocampus and midbrain were included with the cerebral cortex.

Statistics. Student's *t* test was used in making statistical comparisons. In experiments in which the behavior of each animal served as its own control, the paired *t* modification of Student's *t* test was used. Potency ratios and 95 percent confidence limits were performed according to the procedure of Litchfield and Wilcoxon [16].

RESULTS

Effect of Taurine and its Analogues on Water Responding

Taurine produced a dose-related decrease in both the total number of rewards obtained in the 20 min session and in the initial rate of responding during the session, as compared to the non-treated control day (Fig. 1). The rate of responding and the number of rewards received during the isoosmotic vehicle control days were either no different from the non-treated control days or were increased by those solutions which had high osmolarities. Several compounds which are analogues or homologues of taurine also reduced the initial rate and number of responses made for water by 24 hr water deprived mice. β-Alanine, the carboxyl analogue of taurine, produced a dose-related decrease which was indistinguishable in potency from the reduction produced by taurine. The estimated dose of taurine to produce a 50 percent decrease in initial response rate was 17.0 mmole/kg with 95% confidence limits of 12.6–23.0 mmole/kg, while that of β-alanine was 14.0 mmole/kg with 95 percent confidence limits of 10.5–18.6 mmole/kg. 3APSA, the three carbon homologue of taurine, was more potent than either taurine or β-alanine. The estimated dose of 3APSA required to produce a 50 percent decrease in initial response rate for water was 3.4 mmole/kg with 95 percent confidence limits of 2.0–5.8 mmole/kg. This dose is statistically lower than the doses of either taurine or β-alanine required to produce a 50 percent decrease in drinking behavior ($p<0.05$). The 2.2 mmole/kg dose of 3APSA was made hypertonic by the addition of NaCl (final molarity = 0.3479 molar).

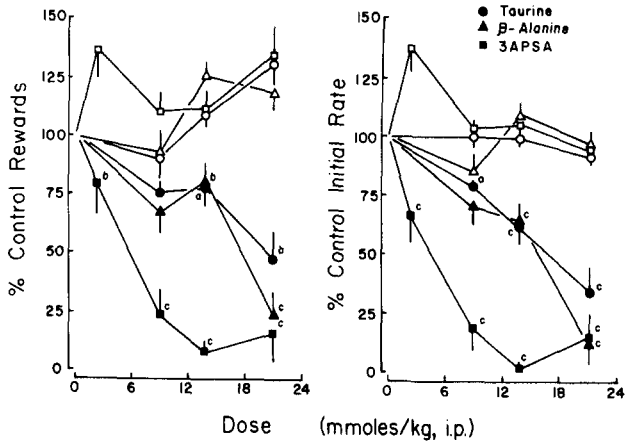

FIG. 1. The effect of taurine, β-alanine, and 3-aminopropanesulfonic acid (3APSA) on total rewards and initial rate of 24 hr water deprived mice responding on a FR-5 schedule for water reinforcements. Data are presented as a percent of the non-treated control day. Open symbols are isoosmotic control and the closed symbols are treated animals. The vertical bars represent the standard error. Mice were injected 30 min prior to the start of the 20 min session. Significance as compared to the isoosmotic control is indicated by (a) $p<0.05$, (b) $p<0.01$, and (c) $p<0.001$.

The effects of AMSA (the one carbon analogue of taurine), glycine (a putative inhibitory neurotransmitter amino acid), and cysteamine (a proposed metabolic precursor of taurine [10]) on percent control rewards and percent control initial rates are reported in Table 1. All three compounds reduced responding for water by reducing the rate of response as well as the number of total rewards received during the session. AMSA and glycine did not differ significantly from 3APSA. However, cysteamine was the most potent of the compounds tested. Cysteamine at a dose of 2.2 mmole/kg was hypotonic, and because of this hypotonicity, the control solution was observed to reduce the total number of rewards and initial response rate below non-treated control values. Therefore, when the 1.5

TABLE 1

THE EFFECTS OF TAURINE ANALOGUES ON RESPONDING FOR WATER REINFORCEMENTS IN MICE*

Drug	Dose (mmole/kg)	N	% Control Rewards		% Control Rate	
			Control	Treated	Control	Treated
AMSA†	9.0	12	92.0 ± 6.4	12.8 ± 6.7‡	103.5 ± 6.3	10.0 ± 7.6‡
Cysteamine§	2.2	12	65.9 ± 7.0	5.6 ± 4.2‡	81.1 ± 11.0	9.4 ± 7.5‡
Cysteamine[a]	1.5	6	127.4 ± 8.8	22.5 ± 6.4‡	ND[b]	ND
Glycine	21.3	18	135.3 ± 7.5	3.9 ± 1.9‡	108.1 ± 3.5	3.8 ± 2.6‡

*Data presented as mean ± standard error of the mean of the non-treated control day.
†AMSA = aminomethanesulfonic acid.
‡$p<0.001$.
§Hypotonic (0.1078 molar).
[a]Made hypertonic by the addition of NaCl (made 0.6922 molar, which is the same as for the 13.8 mmole/kg doses).
[b]ND = not determined.

mmole/kg dose was tested, the solution was made hypertonic by the addition of NaCl so that it had the same osmolarity as the 13.8 mmole/kg dose of the taurine (0.6922 molar). The animals which received the experimental compounds still showed a brisk response on FR-5, however, the postreinforcement pauses were longer. The animals also appeared to satiate, and there was no rebound effect on the non-treated control day which followed the experimental day.

The duration of the effect of taurine on water responding is illustrated in Figure 2. Both the initial response rate and total number of responses were decreased by the 21.3 mmole/kg dose of taurine within 30 min of the injection and remained depressed for 3 hr. The depressant effect of taurine on the initial response rate was no longer observed 4 hr after injection. However, the total number of reinforcements received by the taurine treated group was greater than the isoosmotic control 4 hr after the injection of taurine. The isoosmotic control solution did not affect the rate of responding during the test session at any time point, or the total number of rewards in experiments conducted 3 hr or 4 hr after the injection. However, the total number of rewards was increased above the non-treated control day at 1/2, 1, and 2 hr after injection.

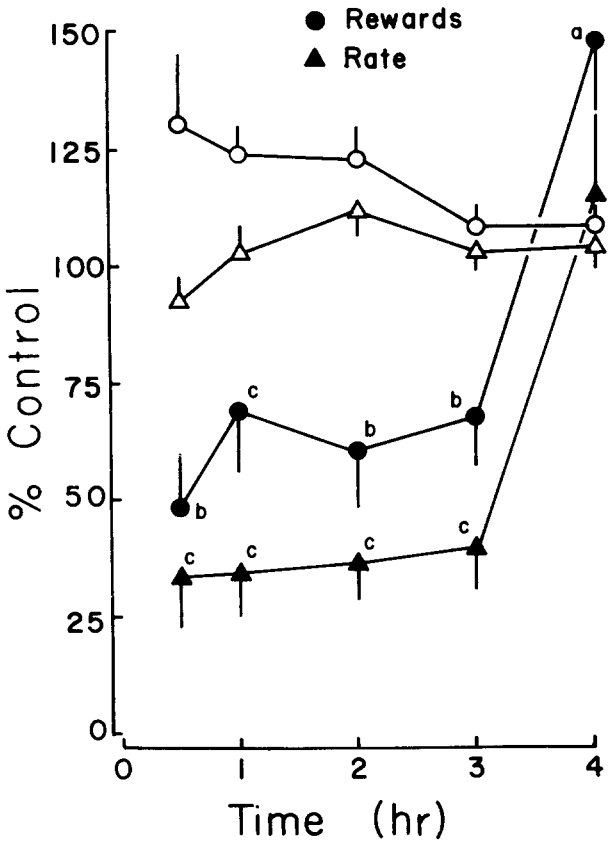

FIG. 2. The effect of taurine (21.3 mmole/kg) as compared to the non-treated control day as a function of pretreatment time on total water rewards and initial response rate. Open symbols are isoosmotic controls and closed symbols are taurine treated. Vertical bars represent the standard error. Significance as compared to the isoosmotic control is indicated by (a) $p<0.05$, (b) $p<0.01$, and (c) $p<0.001$.

The isoosmotic controls for taurine (21.3 mmole/kg), 3APSA (21.3 mmole/kg), β-alanine (13.8 mmole/kg), and cysteamine (1.5 mmole/kg) increased the total number of rewards above those obtained in the non-treated control day. The initial response rate was only increased by one treatment, the isoosmotic control for the 2.2 mmole/kg dose of 3APSA. The initial response rate is, therefore, a very stable parameter.

Effect of Taurine on Responding for Food

At one-half after injection, the 21.3 mmole/kg dose of taurine depressed conditioned eating rate to 50% ± 9% of control, while the 9.0 mmole/kg dose did not depress conditioned eating rate (102% ± 7% of control).

Effect of Taurine and some of its Analogues on General Behavior

Spontaneous locomotor activity. Taurine (21.3 mmole/kg) injected 30 min prior to the start of the 2 hr session depressed motor activity in the period between 15 min and 60 min when compared to the motor activity of the isoosmotic control animals (Fig. 3). There was no significant depression for the first 15 min, during which time the initial rate of responding for water was significantly depressed. At a dose of 13.8 mmole/kg, taurine produced no depression of motor activity over the 2 hr period (Fig. 3). This dose of taurine, however, was effective in reducing both the initial response rate and total number of rewards received in the drinking experiment. The 9.0 mmole/kg dose of taurine also did not affect motor activity, but did decrease water responding.

Cysteamine produced a dose-related decrease in motor activity which was an order of magnitude more potent than that produced by taurine. Even the lowest dose used (1.5 mmole/kg) produced a significant depression of 2 hr cumulative motor activity to less than 67 percent of control. The 2.2 mmole/kg dose of cysteamine reduced the 2 hr cumulative motor activity to 41 percent of control. Therefore, it was not possible to dissociate the general motor depressant effects of cysteamine from its ability to reduce responding for water rewards.

Rotarod. The highest dose of taurine used in these experiments (21.3 mmole/kg) did not affect the ability of rotarod-naive mice to maintain their position on the rotarod either 20 min after injection or when they were retested 40 min after injection. The average number of falls in 3 min for the isoosmotic control group (N = 16) was 0.6 ± 0.2 (mean ± SE) at 20 min and 0.1 ± 0.1 at 40 min after injection. The taurine treated group (N = 16) had an average of 0.2 ± 0.1 falls at 20 min and 0.1 ± 0.1 falls at 40 min.

Sidman avoidance performance. The effect of taurine on Sidman avoidance performance did not appear to be dose-related (Table 2). The only effect on wheel turning responses was produced by the lowest dose of taurine (9.0 mmole/kg) in the first 30 min and in the total 1 hr session. This effect was not observed after the higher doses of taurine. This apparent statistical effect may have resulted from the stimulation produced by the isoosmotic control solution for the lowest dose instead of from a depression produced by taurine. Also, there were no effects of taurine on Sidman avoidance during the first 15 min, when the initial rate of water responding was depressed. The percent

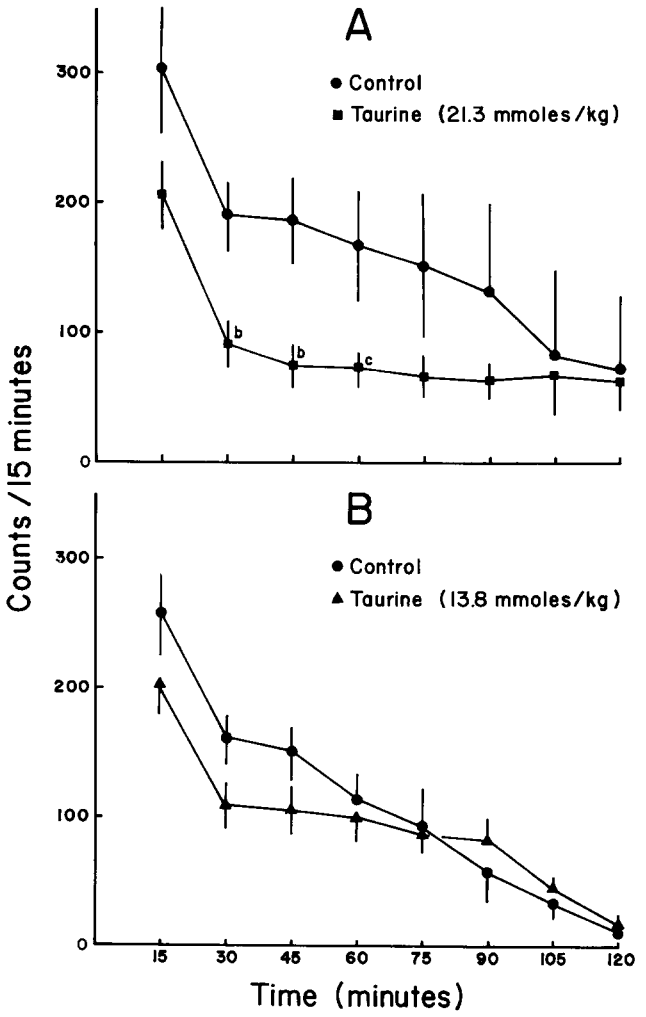

FIG. 3. The effect of two doses of taurine and their isoosmotic controls on spontaneous locomotor activity in mice. Animals were injected 30 min before being placed in the chambers. Twelve mice are in each group. Vertical lines represent the standard error. Significance is indicated by (b) $p<0.01$ and (c) $p<0.05$.

avoidances are also affected, but not in a dose-related fashion. In general, as the dose of taurine was increased, the avoidance performance improved instead of worsening. This effect was opposite to the result expected if there had been a general dose-related behavioral depression produced by taurine. The percent escapes was not affected by taurine at any dose and this result indicates that the animals were capable of responding to this aversive stimulus (i.e. shock).

Shuttle-box performance. Taurine did not produce any disruption of shuttle-box performance at any dose studied, as compared to the isoosmotic control solution, when the taurine was administered 30 min prior to the start of a 40 trial session. The percent performance of the isoosmotic control solution treated group (N = 7) as compared to their non-treated control day was 97.5 ± 8.1 (mean ± SE) for total shuttles, 135.2 ± 37.0 for inter-trial shuttles, 134.7 ± 20.2 for percent avoidance, and 100.0 ± 0.0 for percent escapes. The percent performance of the taurine treated group (21.3 mmole/kg, N = 7) as compared to the non-treated control day was 99.0 ± 7.0 for total shuttles, 117.1 ± 34.2 for inter-trial shuttles, 87.2 ± 12.5 for percent avoidance, and 100.0 ± 0.0 for percent escapes. The 9.0 and 13.8 mmole/kg doses of taurine were similarly without effect as compared to their isoosmotic controls.

Taurine Concentration in Various Areas of the Brain

The 21.3 mmole/kg dose of taurine increased taurine levels only in the hypothalamus and medulla 30 min after the intraperitoneal injection (Table 3). The taurine levels in the other brain areas, the cerebellum, striatum, and cerebral cortex, were not affected by this dose of taurine 30 min after injection.

DISCUSSION

Taurine has been proposed as an osmotically active substance of importance in the osmoregulation of marine invertebrates, such as the mussel and echinoderms [13,14], and in two species of fish, the flounder and the three-spined stickleback [15]. In the mussel, taurine appears to be sequestered by cells to increase the osmolarity needed for normal cell size and thus spare other amino acids from this role. In the other invertebrates and fish, taurine appears to be released from cells to reduce their osmolarity and maintain normal cell size and keep the functional amino acids at normal levels.

This function of taurine appears inappropriate for non-marine vertebrates that do not have to maintain an osmotic balance with their surroundings. Indeed, the increase of osmotically active particles in the blood would increase thirst, not decrease it. However, in vertebrates other effects of taurine have been shown which may resolve this paradox. The microiontophoretic application of taurine and related substances to neurons in the spinal cord [3], brainstem [6], and cortex [2] decreases their spontaneous firing rate and may cause a hyperpolarization of these neurons [3].

In vertebrates, certain of the control mechanisms for body fluid balance appear to reside in the hypothalamus, and a drinking circuit has been proposed that includes various hypothalamic areas [17,20]. If taurine depressed the neuronal activity of these hypothalamic circuits which promote drinking, then the hypodipsic effects of taurine would be predicted from this model. Since the hypothalamus would regulate thirst stimulation, a depression in this area would negate the hyperosmotic stimulation of the injected solution [17]. Furthermore, the intraperitoneal administration of taurine leads to increases in the concentration of taurine only in the hypothalamus and medulla, but not in the other brain areas. The significance of the increase in the medulla is not known. However, these results suggest that intraperitoneal injections of taurine, which selectively increase hypothalamic taurine concentration, might result in changes only in those behaviors which are mediated by the hypothalamus. In this light, it is not surprising that under the same experimental design there is also a depression by taurine of conditioned eating. However, taurine does not depress conditioned eating behavior to the same extent as drinking behavior. This implies a partial separation of the effects of taurine on conditioned drinking and eating. After the intraperitoneal taurine administration, there is no increase in the taurine concentrations of areas of the brain which are involved with motor

TABLE 2

THE EFFECT OF TAURINE, INJECTED 30 MIN PRIOR TO THE START OF A 60 MIN SESSION, ON SIDMAN AVOIDANCE PERFORMANCE IN MICE. PERCENTAGE CHANGE AS COMPARED TO NON-TREATED CONTROL DAY.*

Time (min)	Dose† (mmole/kg)	Wheel Turning Responses		% Avoidances		% Escapes	
		Isoosmotic	Taurine	Isoosmotic	Taurine	Isoosmotic	Taurine
15	9.0	138.5 ± 16.1	98.3 ± 13.7	106.3 ± 7.6	87.0 ± 5.8	101.7 ± 1.7	100.0 ± 0
	13.8	93.1 ± 13.2	98.3 ± 19.0	99.1 ± 1.6	91.3 ± 3.8‡	100.0 ± 0.0	100.0 ± 0
	21.3	87.5 ± 17.8	76.3 ± 18.6	98.8 ± 0.7	92.4 ± 5.8	100.0 ± 0.0	100.0 ± 0
30	9.0	139.3 ± 14.6	85.8 ± 13.6‡	102.5 ± 4.1	87.3 ± 5.0	101.2 ± 1.2	100.0 ± 0
	13.8	98.7 ± 14.9	100.1 ± 23.6	99.9 ± 1.0	93.7 ± 2.8‡	95.8 ± 4.2	100.0 ± 0
	21.3	94.9 ± 10.2	78.2 ± 13.8	99.5 ± 0.6	94.4 ± 3.4	100.0 ± 0.0	100.0 ± 0
60	9.0	136.2 ± 12.8	89.7 ± 14.0‡	101.0 ± 1.9	92.7 ± 3.3	101.2 ± 1.2	100.0 ± 0
	13.8	94.5 ± 13.7	77.8 ± 12.9	99.9 ± 0.7	96.6 ± 1.5‡	96.9 ± 3.1	100.0 ± 0
	21.3	99.2 ± 9.7	74.0 ± 9.9	100.0 ± 0.4	96.4 ± 1.6‡	100.0 ± 0.0	100.0 ± 0

*Data is presented as mean ± standard error.
†Eight animals were used at each dose.
‡$p<0.05$ as compared to the isoosmotic control day.

TABLE 3

TAURINE LEVELS (μmole/g wet wt)* IN VARIOUS REGIONS OF THE MOUSE BRAIN 30 MIN AFTER INTRAPERITONEAL INJECTION

Brain Region	Control†	Taurine‡	*p* Value
Cerebellum	9.05 ± 0.36	8.77 ± 0.15	NS§
Medulla	5.33 ± 0.26	6.18 ± 0.23	<0.05
Hypothalamus	4.76 ± 0.07	5.62 ± 0.13	<0.005
Striatum	11.92 ± 0.73	12.32 ± 0.45	NS
Cerebral Cortex	9.95 ± 0.42	9.16 ± 0.28	NS

*Four samples per value ± standard error.
†Control (0.5% CMC).
‡Taurine (21.3 mmole/kg).
§NS = not significant, $p>0.05$.

control and other behavioral functions. The present study shows that doses of taurine which affected drinking did not produce a general behavioral depression. The 9.0 and 13.8 mmole/kg doses of taurine produced no disruption of spontaneous locomotor activity (Fig. 3) or shuttle-box performance. The highest dose of taurine used in this study (21.3 mmole/kg) only depressed spontaneous motor activity in a consistant manner (Fig. 3). This dose was without effect on rotarod performance and shuttle-box avoidance. The effect of taurine on Sidman avoidance performance (Table 2) was not dose-related and was not consistently produced on any one of the parameters measured. For example, escape responding was not affected, while wheel turning and avoidance responding were variably reduced.

To solve this discrepancy, another active avoidance performance was also measured. Shuttle-box avoidance is more difficult for the animal to learn and is a more sensitive measure of behavior than Sidman avoidance. If taurine caused a general behavioral depression in the Sidman avoidance procedure that was partially hidden, this depression should become more apparent in shuttle-box avoidance. However, there was no effect of taurine on shuttle-box performance at any dose used. It would appear that the possible general behavioral depression effects of taurine are separable from the depression of responding for water reinforcements in mice, if the compound is administered intraperitoneally. With cysteamine the general behavioral depressant effect was impossible to separate from the depression of drinking.

The observation that the intracerebroventricular administration of taurine caused a general disruption of behavior in mice [1], lends further support for the hypothesis that the specificity of the action of taurine on the hypothalamus may be related to its differential brain permeability.

After intraperitoneal administration taurine selectively increases in concentration in the hypothalamus and decreases responding for water without affecting other general behaviors. Since taurine has been shown to depress various neurons in the brain [2, 3, 6], we postulate that taurine depresses the hypothalamic centers necessary to stimulate drinking behavior.

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