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Effect Of Taurine on Ethanol-Induced Sleep Time in Mice Genetically Bred for Differences in Ethanol Sensitivity[1]

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FERKO, A. P. AND E. BOBYOCK. *Effect of taurine on ethanol-induced sleep time in mice genetically bred for differences in ethanol sensitivity.* PHARMACOL BIOCHEM BEHAV 31(3) 667–673, 1988.—Long Sleep (LS) and Short Sleep (SS) mice were used in this study to investigate the interaction between ethanol and taurine. Sleep time (hypnosis) was selected as an index of ethanol-induced central nervous system depression. In order to achieve a similar degree of central nervous system depression with ethanol, SS and LS mice received 5.3 and 3.0 g/kg, IP, of ethanol, respectively. When taurine (7.5, 15 and 25 μmol/kg) was administered intracerebroventricularly (ICV) to LS and SS mice immediately after regaining the righting reflex following ethanol injection, a return to sleep time was produced. This effect of taurine was immediate in onset and occurred in a dose-dependent fashion. LS mice exhibited a greater effect from taurine administration than SS mice. In another experiment LS and SS mice were given ICV TAG, a taurine antagonist (6-aminomethyl-3-methyl-4H-1,2,4-benzothiadiazine-1,1-dioxide HCl), which significantly reduced the effect of taurine to produce a return to sleep time in the presence of ethanol. TAG did not affect ethanol-induced sleep time. In control experiments, in the absence of ethanol, neither taurine (25 μmol/kg, ICV) nor TAG (1 μmol/kg, ICV) caused a significant loss of the righting reflex (sleep time). When pentobarbital (50 mg/kg, IP) was injected instead of ethanol in the sleep time experiments, taurine (7.5, 15 and 25 μmol/kg, ICV) produced a return to sleep time in LS and SS mice that resembled the effect of taurine with ethanol in SS mice. These results indicate that taurine (ICV) can enhance the central depressant action of ethanol and pentobarbital and that the greatest effect of taurine occurred with LS mice in the presence of ethanol. It is possible that taurine may have some role in the central nervous system depressant properties of ethanol.

Ethanol Taurine Pentobarbital Sleep time Taurine antagonist Long Sleep mice Short Sleep Mice

TAURINE, a sulfur-containing amino acid, is found in the brain in high concentrations and widely, but unevenly distributed (3, 16, 44). It is suggested that taurine may function in the modulation of transmission (22,25) or as a neurotransmitter in the central nervous system (26, 40, 48). Several earlier investigations have examined the interaction between taurine and ethanol. Taurine decreases ethanol-induced sleep time when ethanol and taurine are injected by the IP route to mice (2,23). Another report, however, shows that taurine fails to alter sleep time of ethanol injection when both drugs are given by IP administration (37). Since taurine has a depressant effect in the central nervous system (4,40), recent studies indicate an interaction between taurine and ethanol when taurine is injected by the ICV route. Ethanol-induced sleep time is prolonged in a dose-dependent fashion by the ICV injection of taurine to Sprague-Dawley rats (35). In another investigation the central depressant properties of ethanol are enhanced by the ICV administration of taurine to Swiss-Webster mice (13). In addition, TAG, a taurine antagonist (6-aminomethyl-3-methyl-4H-1,2,4-benzothiadiazine-1,1-dioxide HCl), attenuates the effect of taurine to prolong ethanol-induced sleep time.

This present investigation involves a study with LS and SS mice and the interaction of ethanol with taurine alone and in combination with TAG, a taurine antagonist (48). In order to explore the possible relationship between taurine and ethanol, mice selectively bred for differential sensitivity to ethanol are used (29,30). These selectively bred mice, the so-called ethanol sensitive, LS, and the ethanol insensitive, SS, differ in the central nervous system sensitivity to the depressant effects of ethanol. The hypothesis of this study is that since LS mice are more sensitive to the depressant effect of ethanol than SS mice, the LS mice should exhibit a greater response than SS mice to the ICV administration of taurine in the presence of ethanol. In this investigation LS and SS mice are injected ICV with taurine after the administration of ethanol (IP). Sleep time is used as an index of central nervous system depression. It is the intent of this investigation to add further corroborative information on the central effect of taurine in the presence of ethanol using LS and SS mice.

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METHOD

LS and SS mice (approximately 45 days old) were obtained from the Institute for Behavioral Genetics of the University of Colorado at Boulder. LS and SS mice of the 42nd, 43rd and 44th generations were used in these experiments. Animals were housed for 2 weeks prior to experimentation at 21±1°C with a light cycle from 6:00 a.m. to 6:00 p.m. The mice had free access to Purina Laboratory Chow and water. Experiments were performed at the same time period (9:00 to 11:00 a.m.) so that time of day was reduced as an experimental variable. All animals were fasted 16 hr prior to drug or saline (0.9% NaCl) injection but water was available ad lib.

Ethanol solutions for injection were prepared from 95% ethanol in saline. Taurine was purchased from Sigma Chemical Co. (St. Louis, MO). TAG, 6-aminomethyl-3-methyl-4H-1,2,4-benzothiadiazine-1,1-dioxide HCl, was a gift (Merck Sharp and Dohme Research Laboratories, Rahway, NJ). Solutions of taurine and TAG were prepared in saline and adjusted to pH 7.0 with 0.01 N NaOH solution (35). Alcohol dehydrogenase (yeast) and nicotinamide-adenine dinucleotide were purchased from Calbiochem Biochemicals, Behring Diagnostics (San Diego, CA). All other chemicals were obtained from commercial sources and were of analytical grade.

Sleep Time Experiments With Ethanol (IP) and Taurine (ICV)

Sleep time (hypnosis) was used as an index of ethanol-induced central nervous system depression and was measured as the time interval between the loss of the righting reflex. The gain of the righting reflex required that the animal be able to reright itself 3 times within 1 min, after again being placed on his back. In addition the onset of hypnosis (time interval between ethanol injection and loss of the righting reflex) was recorded.

Preliminary experiments were performed to determine the dose of ethanol for LS and SS mice that caused a sleep time of approximately 60±10 min in each strain so that the mice would exhibit a similar degree of central nervous system depression. The two doses of ethanol were used throughout the study, since assessment of the effect of another drug would be confounded by the temporal difference in sleep time caused by ethanol when the same dose was administered to LS and SS mice (6).

This experiment was designed to determine if an injection of taurine, intracerebroventricularly, could enhance the degree of central nervous system depression and return LS and SS mice to a state of hypnosis (sleep time) when taurine was given at the end of the ethanol-induced sleep time (13). Intracerebroventricular (ICV) injection of drug was administered using a previously described method (41). The procedure involved cutting the scalp of an anesthetized mouse and injecting (at depth of 3 mm) 2 mm caudal and 2 mm lateral to Bregma using a Hamilton microliter syringe with a 26 gauge needle of 3/8 inch. Drug solutions were injected slowly into the ventricle over a period of approximately 20 sec. The correct position of the injection was verified at autopsy by using trypan blue dye.

Ethanol was administered (IP) to LS and SS mice. Twenty minutes after the loss of the righting reflex a 26 gauge needle was used to enter the ventricle of the brain of the ethanol-anesthetized mouse but no saline or drug solution was given at this time, since this was the preparatory step for ICV drug administration (13). Immediately after the animals regained the righting reflex, LS or SS mice received an ICV injection of saline or taurine (7.5, 15 or 25 μmol/kg) in a volume of 5 μl. The ethanol (ETOH) sleep time was determined from the loss of the righting to the gain of the righting reflex after ethanol injection (IP). A second sleep time was recorded and called the TAU Return to Sleep Time. The TAU (taurine) return to sleep time was measured from the loss of the righting reflex to the gain of the righting reflex after taurine or saline administration (ICV). Blood samples (20 μl) were taken from the orbital sinus of LS and SS mice when they regained the righting reflex after the administration of saline or taurine. An enzymatic method (28) was used to measure blood ethanol concentrations.

The next experiments were done to determine if taurine or TAG by itself could induce a loss of the righting reflex (sleep time) in LS and SS mice. Mice were given saline (0.02 ml/g, IP) and then 50 min later the mice were lightly anesthetized with ether and injected, ICV (5 μl) as previously described (41) with saline or taurine (25 μmol/kg). In another experiment LS and SS mice were administered saline (0.02 ml/g, IP) and then 20 min later were lightly ether-anesthetized for ICV injections (5 μl) of TAG (1.0 μmol/kg) or saline. The mice were observed for 1 hr after drug administration.

Experiments With Ethanol (IP), Taurine (ICV) and TAG (ICV)

In these experiments TAG, a taurine antagonist, was given to LS and SS mice to note if TAG could attenuate the effect of taurine in the presence of ethanol. The dose of TAG that was selected, did not induce any behavioral effects by itself. LS and SS mice were given ethanol, IP, and then an ICV injection (5 μl) of saline or TAG (1.0 μmol/kg) was administered 20 min after the loss of the righting reflex from ethanol administration. Upon the return of the righting reflex following ethanol administration, mice were immediately injected ICV (5 μl) with taurine (15 μmol/kg) or a taurine-TAG solution. The taurine-TAG solution contained taurine and TAG at a concentration of 15 μmol/kg and 1.0 μmol/kg, respectively. Blood samples for ethanol assay were obtained from the orbital sinus of mice when they regained the righting reflex after the administration of taurine or the taurine-TAG solution.

Experiments With Pentobarbital (IP) and Taurine (ICV)

LS and SS mice were administered pentobarbital (50 mg/kg, IP). Twenty minutes after the loss of the righting reflex a 26 gauge needle was used to enter the ventricle of the brain of the pentobarbital-anesthetized mouse but no saline or drug was given at this time, since this was the preparatory step for ICV drug injection. Immediately after the animals regained the righting reflex, LS or SS mice received an ICV injection (5 μl) of saline or taurine (7.5, 15 or 25 μmol/kg). The duration of the loss of the righting reflex after ICV injection was recorded (return to sleep time).

In the final experiment pentobarbital at a dose of 60 mg/kg, IP, was administered to LS and SS mice to determine if a higher dose of pentobarbital would show differences for pentobarbital-induced sleep time in LS and SS mice.

Statistical Analysis

Significant differences were determined by analysis of variance (ANOVA). All multiple comparisons with a control

TABLE 1

EFFECTS OF TAURINE (TAU, μmol/kg, ICV) TO PRODUCE A RETURN TO SLEEP TIME IN SHORT SLEEP AND LONG SLEEP MICE IMMEDIATELY AFTER REGAINING THE RIGHTING REFLEX FOLLOWING ETHANOL (ETOH, IP) INJECTION

Treatment	N	Onset to Sleep (sec)	ETOH Sleep Time (min)	TAU Return to Sleep Time (min)	Blood ETOH (mg/ml)
			Short Sleep Mice		
ETOH + Saline (controls)	12	101 ± 5*	49.1 ± 4.4	0.4 ± 0.2	4.50 ± 0.07
ETOH + TAU (7.5)	8	105 ± 4	52.1 ± 6.5	5.3 ± 1.1	4.46 ± 0.10
ETOH + TAU (15.0)	6	102 ± 5	46.5 ± 5.0	10.8 ± 1.9	4.37 ± 0.14
ETOH + TAU (25.0)	9	112 ± 6	46.3 ± 4.5	25.4 ± 4.7†‡	4.62 ± 0.10
			Long Sleep Mice		
ETOH + Saline (controls)	12	106 ± 3	59.0 ± 2.0	0.4 ± 0.2	2.53 ± 0.07
ETOH + TAU (7.5)	8	101 ± 2	55.6 ± 3.0	27.1 ± 3.7†§	2.49 ± 0.04
ETOH + TAU (15.0)	9	108 ± 4	48.5 ± 2.0	41.3 ± 3.6†§	2.20 ± 0.04†¶
ETOH + TAU (25.0)	9	109 ± 6	57.6 ± 3.0	95.2 ± 9.3†‡§	2.14 ± 0.07†¶

*Means ± S.E.
†Significantly different from corresponding controls ($p<0.01$).
‡Significantly different from corresponding TAU (7.5 and 15.0) groups ($p<0.05$).
§Significantly different from corresponding treatment in SS mice ($p<0.01$).
¶Significantly different from corresponding TAU (7.5) group ($p<0.05$).

and comparisons among the experimental groups were done by ANOVA followed by Scheffe's Test. In addition two-way Analysis of Variance was done on the data to determine if strain of the animal was a factor in the experimental results. Bartlett's test showed homogeneity of variance.

RESULTS

Since it was decided in this study to produce a similar degree of central nervous system depression (sleep time) from ethanol administration in SS (less sensitive to ethanol) and LS (more sensitive to ethanol) mice, preliminary experiments were performed to determine the doses of ethanol for each group of mice which caused a sleep time of approximately 60±10 min. The doses of ethanol eventually selected were 5.3 and 3.0 g/kg, IP, for SS and LS mice, respectively. In Table 1 taurine was given at various doses by the ICV route to SS or LS mice immediately after the animals regained the righting reflex following ethanol administration. The taurine return to sleep time was determined from the loss of the righting reflex after the ICV injection of taurine in the presence of ethanol. Taurine produced a dose-dependent return to sleep time. The onset of taurine's effect occurred immediately after completion of the ICV injection. The greatest effect on the return to sleep time with the administration of taurine occurred in LS mice that received the 25 μmol/kg dose. There was a 275% increase in the return to sleep time when LS mice were compared with SS mice that were given taurine at 25 μmol/kg. Two-way Analysis of Variance indicates a significant difference ($p<0.001$) between strains (LS and SS mice) in the taurine-ethanol interaction. In addition analysis of the data by Bartlett's test shows homogeneity of variance. The highest dose of taurine produced a respiratory depressant effect that lasted for several minutes. Two SS mice died from this dose of taurine. Blood ethanol levels were determined at the end of the return to sleep time for both LS and SS mice.

The results in Table 2 show that TAG, a taurine antagonist, attenuated the effect of taurine in both SS and LS mice. TAG (1.0 μmol/kg, ICV) was given 20 min after the loss of the righting reflex following ethanol injection. At the end of the ethanol-induced sleep time control mice received taurine (15 μmol/kg, ICV) and treated mice were injected with a taurine-TAG solution. The antagonism of taurine-induced return to sleep time was 54 and 56% in SS and LS mice, respectively.

Experiments were performed to determine the effect of taurine and TAG in the absence of ethanol when these drugs were administered, ICV, to LS and SS mice. In LS mice the controls (saline), TAG group (1 μmol/kg) and taurine-treated mice (25 μmol/kg) had a sleep time of 1.7±0.4, 0.5±0.5 and 3.4±1.0 min, respectively. Similar results were obtained in SS mice in that when taurine or TAG results were compared with their appropriate controls there were no significant differences. In SS mice the controls (saline), TAG group (1 μmol/kg) and taurine-treated mice (25 μmol/kg) exhibited a

TABLE 2

EFFECT OF TAG, A TAURINE ANTAGONIST (TAG, 1 μmol/kg, ICV) ON THE RETURN TO SLEEP TIME INDUCED BY TAURINE (TAU, 15 μmol/kg, ICV) IN THE PRESENCE OF ETHANOL (ETOH, IP)

Treatment	N	Onset to Sleep (sec)	ETOH Sleep Time (min)	TAU Return to Sleep Time (min)	Blood ETOH (mg/ml)
			Short* Sleep Mice		
ETOH + Saline + TAU	6	100 ± 6‡	67.8 ± 5.2	15.3 ± 1.2	4.18 ± 0.04
ETOH + TAG + (TAU-TAG)	7	99 ± 3	72.0 ± 8.0	7.0 ± 1.4§	4.03 ± 0.08
			Long† Sleep Mice		
ETOH + Saline + TAU	7	121 ± 6	56.7 ± 1.6	43.5 ± 2.1	2.30 ± 0.03
ETOH + TAU + (TAU-TAG)	6	122 ± 5	54.3 ± 5.3	19.2 ± 2.4§	2.28 ± 0.06

*ETOH dose is 5.3 g/kg.
†ETOH dose is 3.0 g/kg.
‡Means ± S.E.
§Significantly different from corresponding controls ($p<0.01$).

sleep time of 0.3±0.3, 0.5±0.3 and 0.8±0.3 min, respectively. When the taurine data for SS mice are compared with the taurine data for LS mice there is a significant difference ($p<0.05$). For controls (saline, ICV) the sleep time results are different (SS mice=0.3±0.3; LS mice=1.7±0.4 min) and the results are different for taurine injection (SS mice=0.8±0.3; LS mice=3.4±1.0 min). Although these sleep times are statistically significant, they are so short in time, that this effect of taurine alone is not responsible for the results when taurine is injected in the presence of ethanol. Each group contained 4–5 animals. No differences in behavior were observed when taurine or TAG-treated mice were compared with controls for 1 hr postinjection.

The interaction between pentobarbital (50 mg/kg, IP) and various doses of taurine in SS and LS mice is shown in Table 3. Taurine was given, ICV, immediately after the mice regained the righting reflex following pentobarbital injection. In both SS and LS mice taurine produced a return to sleep time. When taurine at 25 μmol/kg was administered (ICV) to LS mice, the effect on return to sleep time appeared to plateau and was similar to the results (return to sleep time) that occurred with taurine at 15 μmol/kg in LS mice. The results for the 25 μmol/kg dose of taurine in LS mice were confirmed by repeating the experiment.

When the data for the onset to sleep time and the duration of sleep time from the administration of pentobarbital (50 mg/kg, IP) to SS (n=34) and LS (n=43) mice were compared with each other, these values were significantly different (SS, onset=306±11, duration=72.9±4.0 min; LS, onset=216±5, duration=51.7±1.2 min; $p<0.01$). In addition, during the sleep time period most SS mice exhibited movements of their limbs and a whipping motion of the tail was observed in some mice. The SS mice appeared to be in a "light" sleep. None of these behavioral movements were seen in LS mice during the loss of the righting reflex following pentobarbital injection.

In SS mice taurine administration (25 μmol/kg, ICV) at the end of the pentobarbital-induced sleep time caused convulsive activity (tonic) and a rolling motion of the body that lasted approximately one minute and then produced a return to sleep time for approximately 30 min. This taurine-induced convulsive activity did not occur in LS mice, although two LS mice died from the injection of the highest dose of taurine.

In an experiment in which pentobarbital at 60 mg/kg, IP was administered to SS (n=12) and LS (n=12) mice, the onset to sleep time and the duration of sleep time were significantly different in each group. The longer onset to sleep time (sec) occurred in SS mice (SS mice=241.6±6.3; LS mice =171.6±5.4; $p<0.01$) and also a longer duration of sleep time (min) was induced by pentobarbital in SS mice (SS mice=137.7±11.4; LS mice=76.6±4.2; $p<0.01$). No unusual behavioral effects were observed in LS or SS mice with this higher dose of pentobarbital.

The data for taurine to produce a return to sleep time in the presence of ethanol (Table 1) and pentobarbital (Table 3) in LS and SS mice indicate that the greatest effect from taurine administration (7.5, 15.0 and 25.0 μmol/kg, ICV) is exhibited by LS mice in the presence of ethanol.

DISCUSSION

In this investigation taurine enhances the depressant properties of ethanol by reinstating a sleep time period in LS and SS mice. The taurine return to sleep time occurs in a dose-dependent fashion in the presence of ethanol. In Table

TABLE 3

EFFECT OF TAURINE (TAU, μmol/kg, ICV) TO INDUCE A RETURN TO SLEEP TIME IN SHORT SLEEP AND LONG SLEEP MICE IMMEDIATELY AFTER REGAINING REFLEX FOLLOWING PENTOBARBITAL (PEN, 50 mg/kg, IP) ADMINISTRATION

Treatment	N	Onset to Sleep (sec)	Pen Sleep Time (min)	TAU Return To Sleep Time (min)
		Short Sleep Mice		
PEN + Saline (controls)	8	365 ± 18*	69.1 ± 6.1	0 ± 0
PEN + TAU (7.5)	8	271 ± 13	79.9 ± 7.6	3.8 ± 0.9
PEN +TAU (15.0)	9	305 ± 26	82.2 ± 11.3	11.4 ± 2.4†
PEN + TAU (25.0)	9	295 ± 19	61.2 ± 4.2	32.1 ± 4.2‡§
		Long Sleep Mice		
PEN + Saline (controls)	11	226 ± 16	53.3 ± 2.1	0.11 ± 0.11
PEN +TAU (7.5)	8	195 ± 5	47.5 ± 3.0	10.8 ± 3.5
PEN + TAU (15.0)	8	226 ± 12	53.0 ± 1.7	20.7 ± 2.2†¶
PEN + TAU (25.0)	16	209 ± 10	51.6 ± 2.2	23.0 ± 2.6‡

*Means ± S.E.
†Significantly different from corresponding controls ($p<0.05$).
‡Significantly different from corresponding controls ($p<0.01$).
§Significantly different from corresponding TAU (7.5 and 15) groups ($p<0.05$).
¶Significantly different from corresponding treatment in SS mice ($p<0.05$).

1 the blood ethanol levels for SS mice are not significantly different for the various treatment groups because the time period is relatively short (approximately 25 min) to detect any significant changes in the biotransformation of ethanol. In the group of LS mice there is, however, a significant difference in blood ethanol levels for some of the treatment groups, since there is sufficient time for noticeable biotransformation of ethanol to occur. The disappearance of ethanol from the blood is not altered by the presence of taurine in the animals since it is reported that taurine does not affect blood ethanol levels or brain concentrations of ethanol (24).

This study supports other works in which an ethanol-taurine interaction is demonstrated after ICV injection of taurine in Sprague-Dawley rats (35) and Swiss Webster mice (13). Also, TAG, a taurine antagonist, attenuates the effect of taurine to produce a return to sleep time (13,35). The mechanism by which TAG antagonizes the effect of taurine appears to be noncompetitive in nature (13).

LS and SS mice were selected for this research project because of their differences in sensitivity to the central nervous system effects of ethanol (29,35). The metabolism of ethanol in LS and SS mice does not appear to be responsible for the behavioral differences observed in these mice (17,19). Several studies show that various neurotransmitters and other substances when injected into LS and SS mice in the presence of ethanol produce quantitatively different effects (9, 33, 34, 38). For example, Masserano and Weiner (34) suggest that the neurochemical mechanisms mediating differences in ethanol sensitivity in LS and SS mice are due to differences in the catecholaminergic and possibly the cholinergic neuronal systems. Although their work with gamma-aminobutyric acid and picrotoxin does not indicate any differences in responses between LS and SS mice resulting from the administration of these drugs, other investigators have shown some evidence for the involvement of the GABAergic system (33). From their work with LS and SS mice, Martz *et al.* (33) suggest that increased GABA sensitivity and enhanced ethanol sensitivity may be casually related. The reason for lack of effects observed in LS and SS mice with GABA drugs and ethanol in the other study (34) may be related to insufficient dosage of GABA and the use of only one dose of picrotoxin (33).

Evidence suggests that ethanol enhances GABA receptor-mediated chloride transport in rat synaptoneurosomes (47) and this action of ethanol is antagonized by Ro15-4513, an imidazobenzodiazepine derivative that is a benzodiazepine receptor inverse agonist (46). In a recent study muscimol-stimulated chloride uptake into brain vesicles derived from LS and SS mice shows that muscimol is more potent in stimulating chloride uptake in LS mice as compared with SS mice (1). It is suggested that genetic differences in LS and SS mice to ethanol-induced sleep time may be related to differences in the GABA receptor-mediated chloride transport.

Pentobarbital was the other central nervous system depressant that was used in this study. Our work shows that SS mice exhibit the greater response to the administration of pentobarbital, particularly at the higher dose. Most other investigators also report that SS mice are more sensitive to pentobarbital (7, 39, 45). Even the original work of Erwin *et al.* (8) which demonstrates no significant difference in sleep time between LS and SS mice, does show that SS mice have a longer sleep time when the data are reanalyzed (31). When muscimol-stimulated chloride uptake into brain vesicles derived from LS and SS mice is examined in the presence of pentobarbital, the results indicate a similar effect of pentobarbital on chloride flux in both LS and SS mice (1). Although it appears that SS mice are more sensitive to pentobarbital-induced sleep time, the difference in sleep time is probably related to differences in the biotransformation of pentobarbital (7,19).

Taurine can produce hypothermia in animals (20) and its hypothermic effect should be considered in the interpretation of the results that are presented. It is reported that hypothermia may be a factor in the biochemical effects attributed to ethanol (15) and that changes in body temperature alters the pharmacological effects of ethanol (27,42). Although it has been indicated that ethanol-induced hypothermia may influence the effects of ethanol, other results in the literature show that hypothermia appears to be an independent effect. Hypothermia is without effect on 1) reducing the hyperglycemic response to ethanol (49), 2) behavioral performance due to ethanol (32), 3) central nervous system depression from ethanol administration (18), 4) the rate of ethanol disappearance from the blood (10,11), and 5) ethanol-induced reduction of cerebellar cGMP (12). In addition, brain sensitivity to ethanol increases as body temperature is elevated (14). The induction of hypothermia by taurine would therefore reduce sleep time in animals and not

extend it, if the sole pharmacological effect of taurine involved hypothermia. However, the pharmacological effects of taurine appear to be more complex.

This present investigation shows that taurine can interact with ethanol to enhance the central nervous system depressant properties of ethanol and the greater effect occurs in LS mice. Although the exact mechanism of the ethanol-taurine interaction is unknown, some evidence suggests that it may have a possible relationship to the GABAergic system (5, 36, 43). In addition the effect of taurine on membranes may also be considered, since the physicochemical properties of taurine suggest that it interacts with phospholipids (21). Future experiments along these lines may provide further information about the pharmacologic effects of this unique amino acid.

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