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Effects of Ethanol on Locomotor Depression and Corticosterone Release Induced by Restraint-Stress: Support for a Stress-Ethanol Interaction

L-E. TRUDEAU, C. M. G. ARAGON[1] AND Z. AMIT

Center for Studies in Behavioral Neurobiology, Concordia University
1455 De Maisonneuve Boulevard West, Montreal, Quebec H3G 1M8

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TRUDEAU, L-E., C. M. G. ARAGON AND Z. AMIT. *Effects of ethanol on locomotor depression and corticosterone release induced by restraint-stress: Support for a stress-ethanol interaction.* PHARMACOL BIOCHEM BEHAV **36**(2) 273–278, 1990.—The interaction between restraint-stress and ethanol was investigated in the rat. The effects of ethanol pretreatment (0.0, 1.0, 1.5, 2.0 g/kg, 20% v/v) on locomotor depression and corticosterone release induced by restraint-stress (15, 60 min) were measured. Restraint durations of 15, 30, 90 and 120 min were found to decrease locomotor activity while animals restrained for 60 min did not differ from home cage controls. All restraint durations induced a significant increase in plasma levels of corticosterone. Locomotor activity counts of ethanol-pretreated (1.0, 1.5, 2.0 g/kg; 20% v/v) animals restrained for 15 min were not found to be lower than those of ethanol-pretreated animals remaining in home cages. Ethanol pretreatment did not differentially affect the locomotor activity of restrained or home cage animals in the 60-min condition. Plasma corticosterone levels of ethanol-pretreated animals restrained for 15 min were identical to those of ethanol-pretreated home cage controls. However, ethanol-pretreated animals restrained for 60 min demonstrated plasma corticosterone levels higher than those obtained by ethanol pretreatment or 60-min restraint alone. Blood ethanol levels were not found to be different between ethanol-control and ethanol-stress animals. These results provide support for a stress-ethanol interaction. They also suggest a differential interaction of ethanol with different intensities of stress.

Restraint stress Ethanol Corticosterone Locomotor activity Interaction Rats

AN interaction between stress and ethanol has long been thought to play a role in the etiology of alcoholism (7,29). However, in order to support the contention that organisms drink ethanol for its "antistress" effects, a stress-ethanol interaction must be observed both at a biochemical and behavioural level.

Several studies have shown that stress can significantly increase plasma levels of corticosterone (16, 20, 26, 33), norepinephrine (18, 20, 21, 26, 31), epinephrine (18, 20, 21, 26, 31), β-endorphin (28,32), and ACTH (32), as well as decrease dopamine levels (28). In the brain, significant increases in the levels of cortical DOPAC (12), as well as decreases in the levels of hypothalamic norepinephrine and β-endorphin have been found repeatedly (4, 5, 16, 28, 34). Ethanol by itself has also been shown to have effects similar to those observed with stress on most of the above variables (6, 10–12, 19, 28, 30, 32, 35). Pretreatment with ethanol, however, was shown to antagonize the respective stress-induced increases or decreases in the levels of the following variables: plasma corticosterone (6, 28, 30), norepinephrine (10,28), epinephrine (10,28), β-endorphin (28,32), ACTH (32), and dopamine (28), as well as hypothalamic norepinephrine (10,17), β-endorphin (28) and cortical DOPAC (12).

Behavioural evidence of this putative interaction between ethanol and stress has been more difficult to obtain. Despite some early studies which claimed that ethanol pretreatment could restore normal behaviour in rats placed in a conflict situation (9), other experiments addressing the effects of ethanol on escape and avoidance behaviour, conditioned suppression, and audiogenic seizures have led to equivocal and often negative results (7). It has been noted that the results of these experiments were difficult to interpret because of the particular behavioural paradigms involved, and also because of the nonspecific motor effects of ethanol (7). An example of this interpretation problem is provided by the work addressing the effects of ethanol pretreatment on the extinction of aversively controlled behaviour in the rat. In this paradigm it has usually been assumed that if ethanol had an "antistress" action, or decreased fear, it should facilitate extinction of the behaviour. However, another interpretation is possible. It has been suggested that if alcohol inhibits fear, and if fear must

[1]Requests for reprints should be addressed to C. M. G. Aragon.

be evoked in order for it to extinguish, alcohol could increase resistance to extinction of a fear-based response (7). In such paradigms it is not clear what an interaction between stress and ethanol predict.

In order to investigate the possibility that a stress-ethanol interaction does, in fact, occur at a behavioural level, the effects of restraint-stress of varying durations on simple open-field locomotor activity were studied in the rat. The consequence of pretreatment with various doses of ethanol on the behavioural effects of restraint stress was then examined. An attempt was also made to replicate the previously reported attenuation by ethanol of stress-induced increases in plasma corticosterone levels (6, 28, 30) and relate this effect to the behavioral data.

METHOD

Subjects

Naive male Long-Evans rats weighing 220–250 g when tested were purchased from Charles River Canada (St-Constant, Quebec). All subjects were individually housed with rat chow and water available ad lib. For 7 days prior to experimentation, subjects were acclimated to the colony room conditions (21°C, lights on from 0800 to 2000 hr) and handled 1–2 minutes each day to minimize the influence of human contact during the actual experimental procedures. All experiments were carried out between 0900 and 1300 hr.

Behavioural Experiments

To study the effects of varying durations of restraint stress on subsequent locomotor activity, animals were placed in a small tubular clear plastic restrainer with holes at the end to allow easy breathing. A cap allowing the passage of the tail was then screwed on at the other end thus fitting the animal snugly with only small movements of the head and tail possible. The duration of restraint was either 0, 15, 30, 60, 90, or 120 min (n = 8/group). Immediately after restraint, animals were placed in a $30 \times 30 \times 60$ cm Plexiglas open-field with a grid floor divided into four equal surfaces by two lines crossing perpendicularly at the center of the arena (13). Locomotor activity was measured for 10 min following a 5-min habituation period. Preliminary data suggested that the effect of restraint on locomotor activity is more evident following this habituation period to the open-field chamber. A count was noted by the observer each time the animal crossed a line with all four paws.

In order to examine the possible interaction of ethanol and stress and its impact on behaviour, stressed (15 or 60 min restraint) or nonstressed (15 or 60 min home cage) animals were pretreated with either 0.0, 1.0, 1.5, or 2.0 g/kg of ethanol (20% v/v, IP) immediately before restraint (n = 8/group). Locomotor activity was then measured as above. Restraint and locomotor measurements were done in the same room, under red illumination. This lighting was chosen because preliminary data indicated that the overall activity level of control animals was higher under these conditions.

Corticosterone and Blood Ethanol Determinations

An additional set of animals were restrained, as described above, for either 15, 30, 60, 90, or 120 min (n > 6/group). Immediately after, animals were transported to an adjacent room and sacrificed by decapitation. Trunk blood was collected in ice-cold glass tubes containing 200 μl of heparin (100 mg/10 ml) and shortly after, centrifuged at 1500 rpm for 5 min. Plasma was frozen at −70°C for later measurement of corticosterone (15). The entire procedure, from removal from the restrainer to decapitation, lasted less than 20 sec. The effects of ethanol on the corticosterone stress reaction was studied by pretreating stressed (15 or 60 min restraint) or nonstressed (15 or 60 min home cage) animals with either 0.0, 1.0, 1.5, or 2.0 g/kg of ethanol (20% v/v, IP) (n > 6/group). Again, blood was obtained by decapitation immediately after restraint and collected in ice-cold glass tubes containing 200 μl of heparin. Before centrifugation, 200 μl of blood were pipetted from each sample and blood ethanol levels were determined by head-space gas chromatography (3). Plasma was then obtained from each sample and frozen as above for later measurement of corticosterone (15).

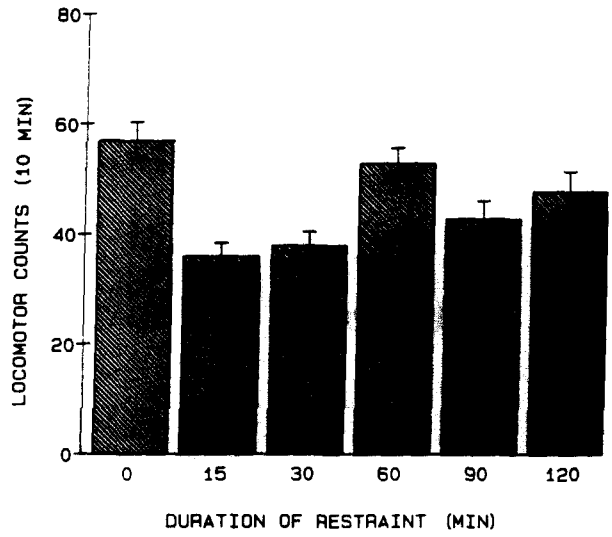

FIG. 1. Effect of different durations of restraint on open-field locomotor activity. Mean ± SEM, n = 8/group.

Statistical Analyses

All data were analyzed by one or two-way analyses of variance (ANOVA). Post hoc testing was done using Fisher's Least Significant Difference (LSD) test. Comparisons were considered significant when $p < 0.05$.

RESULTS

Restraint-stress resulted in a significant decrease in locomotor activity, $F(5,42) = 6.94$, $p < 0.01$. As illustrated in Fig. 1, only the 60-min restraint condition did not result in a significant suppression of motor activity compared to control animals. Ethanol-pretreated (1.0, 1.5, 2.0 g/kg) animals restrained for 15 min did not show greater locomotor depression than ethanol-pretreated home cage controls (see Fig. 2). Stressed animals in the 1.5 g/kg ethanol condition were significantly more active than their home cage controls. A two (stress, no stress) by four (ethanol 0.0, 1.0, 1.5, 2.0 g/kg) ANOVA showed no overall effect of restraint, $F(1,56) = 2.53$, $p > 0.05$, a significant ethanol effect, $F(1,56) = 27.44$, $p < 0.01$, and a significant interaction between restraint and ethanol, $F(1,56) = 7.53$, $p < 0.01$. Figure 3 reveals that animals restrained for 60 min did not react differently to the ethanol injections than did home cage control animals. A two (stress, no stress) by four (ethanol 0.0, 1.0, 1.5, 2.0 g/kg) ANOVA confirmed the absence of a stress effect, $F(1,56) = 0.02$, $p > 0.05$, and of an interaction between restraint and ethanol, $F(1,56) = 0.94$,

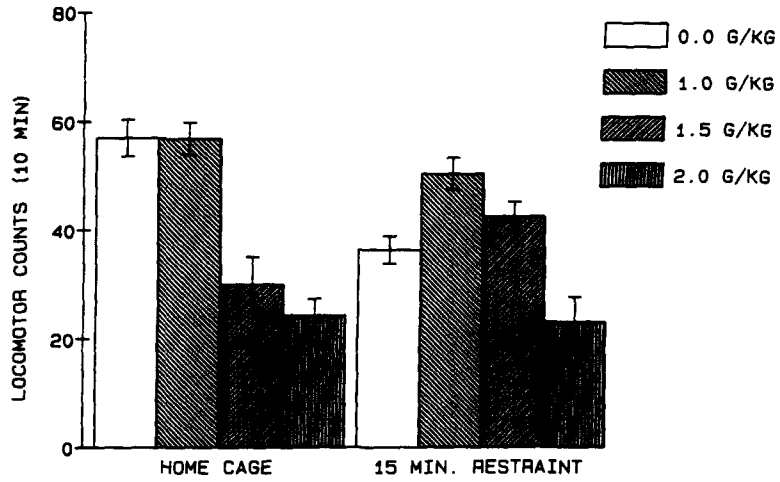

FIG. 2. Effect of ethanol pretreatment (0.0, 1.0, 1.5, 2.0 g/kg) on open-field locomotor activity for stressed or home cage rats (15 min). Mean ± SEM, n = 8/group.

$p>0.05$. However, a significant overall effect of ethanol was found on locomotor activity, $F(1,56)=35.78$, $p<0.01$.

Plasma levels of corticosterone were significantly increased by restraint-stress, $F(5,32)=11.53$, $p<0.01$. As seen in Fig. 4 the biggest increase was obtained after 30 min of restraint. Restraint durations of 15 and 60 min produced corticosterone levels significantly lower than those obtained after 30 min of restraint. Restraint durations of 90 and 120 min, however, did not result in corticosterone levels significantly lower than those obtained after 30 min. Plasma corticosterone levels of the ethanol-pretreated (0.0, 1.0, 1.5, 2.0 g/kg) animals restrained for 15 min were identical to those of ethanol-pretreated animals remaining in home cages (see Fig. 5). A two (15 min restraint, 15 min home cage) by four (ethanol 0.0, 1.0, 1.5, 2.0 g/kg) ANOVA revealed a significant effect of restraint, $F(1,50)=11.22$, $p<0.01$, and of ethanol, $F(1,50)=16.83$, $p<0.01$, and a significant interaction between restraint and ethanol, $F(1,50)=3.50$, $p<0.05$. Figure 6 illustrates that ethanol-pretreated animals restrained for 60 min showed a significantly bigger increase in plasma corticosterone levels than their respective ethanol-pretreated home cage controls at every ethanol dose. A two (60 min restraint, 60 min home cage) by four (ethanol 0.0, 1.0, 1.5, 2.0 g/kg) ANOVA revealed a significant effect of restraint, $F(1,48)=37.80$, $p<0.01$, and of ethanol, $F(1,48)=9.70$, $p<0.01$, but no significant interaction between stress and ethanol, $F(1,48)=0.17$, $p>0.05$.

No differences were found in blood ethanol levels (immediately after the end of the treatment) between restraint (15 or 60 min) or home cage (15 or 60 min) control animals at all ethanol doses (see Table 1). A two (15 min restraint, 15 min home cage) by three (ethanol 1.0, 1.5, 2.0 g/kg) ANOVA revealed no effect of restraint, $F(1,35)=7.29$, $p>0.05$, and effect of ethanol, $F(1,35)=15.36$, $p<0.01$, and no interaction between restraint and ethanol,

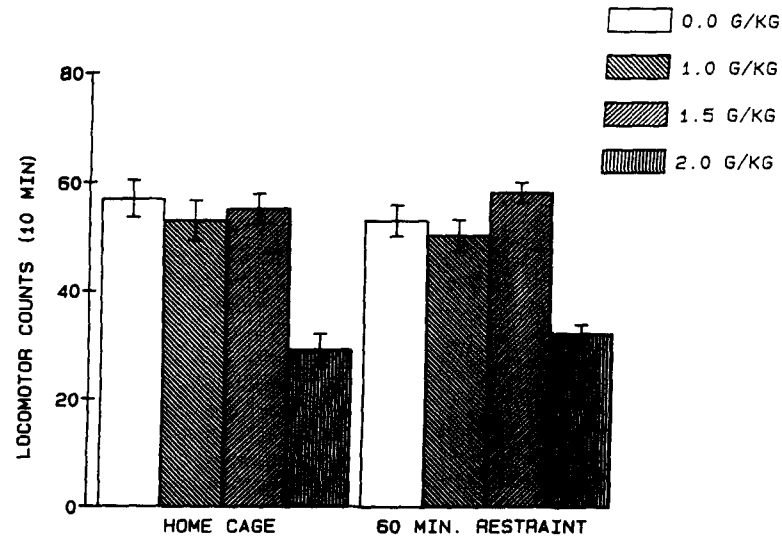

FIG. 3. Effect of ethanol pretreatment (0.0, 1.0, 1.5, 2.0 g/kg) on open-field locomotor activity for stressed or home cage rats (60 min). Mean ± SEM, n = 8/group.

TABLE 1

EFFECT OF RESTRAINT-STRESS (15 AND 60 MIN) ON MEAN (mg/ml) PLASMA ETHANOL LEVELS ± S.E.M., n=8/GROUP

	Ethanol Dose (g/kg)		
	1.0	1.5	2.0
15 Min Home Cage	1.13 ± 0.08	1.48 ± 0.11	1.68 ± 0.12
15 Min Restraint	1.08 ± 0.09	1.42 ± 0.12	1.77 ± 0.14
60 Min Home Cage	0.73 ± 0.04	1.10 ± 0.10	1.56 ± 0.04
60 Min Restraint	0.67 ± 0.03	1.07 ± 0.02	1.58 ± 0.04

$F(1,35)=0.27$, $p>0.05$. A two (60 min restraint, 60 min home cage) by three (ethanol 1.0, 1.5, 2.0 g/kg) ANOVA also revealed no effect of restraint, $F(1,35)=0.45$, $p>0.05$.

A nonsignificant Pearson Correlation ($r=-.39$) was found between the corticosterone level and the locomotor activity score of all respective conditions, $t(16)=1.69$, $p>0.05$.

DISCUSSION

Restraint-stress reduced subsequently measured locomotor activity as compared to unrestrained animals. This effect was dependent on the duration of the restraint period. While 15- or 30-min restraint depressed locomotor activity significantly, 60-min restraint produced no effect. Longer durations of stress (90 and 120 min) also depressed locomotor activity. Pretreatment with ethanol was shown to protect subjects from the locomotor depressant effect of 15-min restraint. At the 1.5 g/kg ethanol dose (a dose which depressed activity by itself), stressed animals were actually more active than their home cage controls (Fig. 2). These data may provide some behavioural support for a stress-ethanol interaction.

A marked increase in plasma levels of corticosterone was also found to be induced by all durations of restraint. These data confirm the results of other studies (6, 16, 20, 28, 30). While both 15- and 60-min restraint resulted in similar levels of corticosterone at the end of the manipulation, they did not demonstrate the same levels of corticosterone after ethanol pretreatment (Figs. 5 and 6). In the 15-min condition, stressed animals receiving ethanol did not present higher plasma levels of corticosterone than their home cage ethanol counterparts. This finding was not seen in the 60-min restraint condition, where at every ethanol dose tested, stressed animals receiving ethanol had higher corticosterone levels than home cage ethanol controls. These data suggest that stress and ethanol have additive effects in the 60-min condition but not in the 15-min condition. As in the behavioural paradigm, it thus appears that the occurrence of a stress-ethanol interaction was dependent on the duration of restraint-stress. Although these data seem to support the conclusions of previous studies (6,28) proposing that stress and ethanol interact in their effects on plasma corticosterone, it was nevertheless not possible to confirm that ethanol-pretreated stressed animals had corticosterone levels which were actually lower than those found in stressed animals not pretreated with ethanol. The reason for this difference remains unclear, but differences in experimental procedures may have played a role. In one of those previous studies (28), ethanol-pretreated animals (3 g/kg, 20% v/v) were restrained for 30 min, but decapitation was carried out only 60 min after the end of restraint. In the other (6), animals were restrained for 90 min and ethanol (0.5 g/kg, 20% v/v) was injected after 60 min. Decapitation in this case was carried out immediately after the end of the 90-min restraint period.

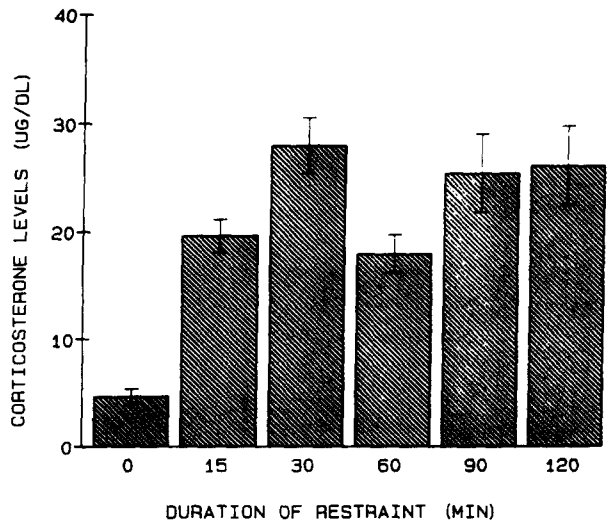

FIG. 4. Effect of different durations of restraint on plasma corticosterone levels. Mean ± SEM, n>6/group.

The observed interactions between stress and ethanol cannot be explained by a simple effect of restraint on peripheral ethanol metabolism. Although previous studies have shown that repeated immobilization over a course of 14 days could result in an increased rate of ethanol metabolism, a single immobilization was never found to have an effect (22,23). As demonstrated previously (28), animals receiving ethanol and stress and control animals receiving ethanol alone did not differ in their blood ethanol levels in all ethanol doses tested and in both restraint durations (see Table 1).

Overall, corticosterone plasma levels and locomotor activity were found not to be linearly related. The assumption that a relationship may exist between stress-induced locomotor depression and plasma corticosterone levels was based on a report addressing the relationship between locomotor activity and corticosterone release induced by various temperatures of hot-plate stress (14). In this study, it was shown that a gradation of hot-plate temperatures able to affect locomotor activity in a way best represented by an inverted U-shaped curve, was accompanied by plasma corticosterone levels describing an upright U-shaped curve. In the present study, although a stress-ethanol interaction was found both in locomotor activity and in plasma corticosterone, the data suggest that the two phenomenon are not causally related. The increase in plasma corticosterone induced by stress does not appear to have directly caused the locomotor depression also induced by stress. After 90 and 120 min of restraint, for example, locomotor activity was not as depressed as after 15 min even though corticosterone levels were not significantly different between these conditions. This conclusion, however, does not preclude the possibility that both interactions result from a common mechanism. A cursory glance at Figs. 1 and 4, however, reveals that for the lower restraint durations (15, 30, 60 min), a U-shaped curve and an inverted U-shaped curve can be observed for locomotor activity and plasma corticosterone levels, respectively. A relationship between plasma corticosterone levels and locomotor activity induced by restraint-stress is thus observed within a restricted range of stress intensities, in a way similar to

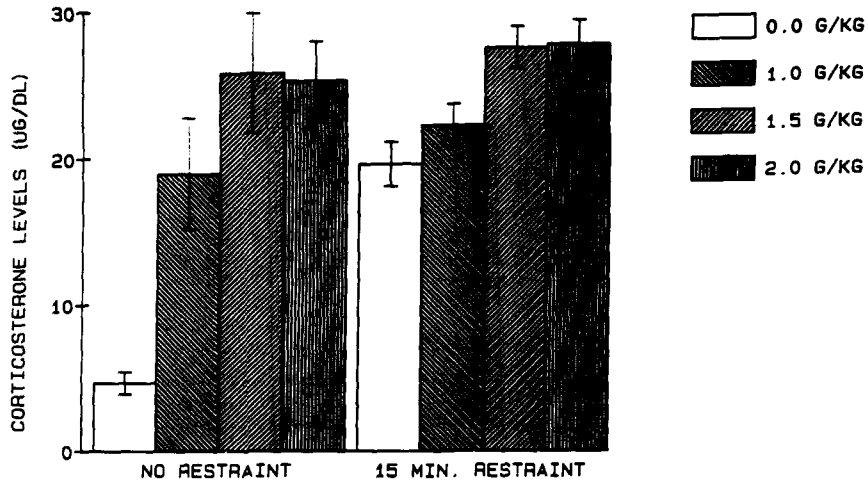

FIG. 5. Effect of ethanol pretreatment (0.0, 1.0, 1.5, 2.0 g/kg) on plasma corticosterone levels for stressed or home cage rats (15 min) Mean ± SEM, n>6/group.

that found in the above-mentioned study using hot-plate stress (14). It may be hypothesized that had these authors used a wider range of stress intensities, the observed relationship between locomotor activity and plasma corticosterone levels might not have been found.

A locus of interaction between stress and ethanol cannot be deduced from the results obtained in the present study. However, the differential interaction of ethanol with different durations of restraint stress (15 versus 60 min) suggests that the effects of these two stress durations may be mediated by different mechanisms. In the stress-induced analgesia literature (1,2) stressors have commonly been distinguished as either being opioid or nonopioid mediated. The possibility exists that the various durations of restraint used in the present study may be differentiated in the same way. If this proves to be right, one might be able to determine whether the interaction between stress and ethanol is mediated through an opioid or a nonopioid mechanism. Experiments are underway in our laboratory to examine this possibility.

The suggestion that stress and ethanol interacted differentially depending on the duration of restraint may be an important observation. It could help explain the contradictory results obtained by researchers attempting to demonstrate that stress is a factor influencing the voluntary consumption of ethanol in rats (8, 24, 25, 27). Indeed, the various characteristics of stressors such as type, duration and/or intensity (as well as the time at which the dependent variables are measured) are probably crucial in providing the conditions necessary for an interaction with ethanol to be possible.

In conclusion, the results obtained in this study show that pretreatment with ethanol may indeed attenuate both a behavioural and a biochemical reaction to a stressor. These data support the existence of an interaction between stress and ethanol.

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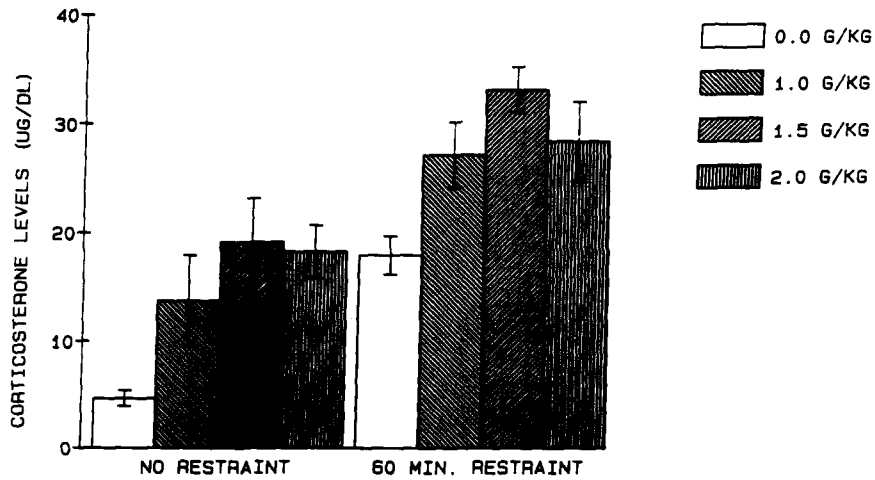

FIG. 6. Effect of ethanol pretreatment (0.0, 1.0, 1.5, 2.0 g/kg) on plasma corticosterone levels for stressed or home cage rats (60 min) Mean ± SEM, n>6/group.

REFERENCES

1. Amit, Z.; Galina, Z. H. Stress-induced analgesia: Adaptive pain suppression. Physiol. Behav. 66:1091–1120; 1986.
2. Amit, Z.; Galina, Z. H. Stress-induced analgesia plays an adaptive role in the organization of behavioural responding. Brain Res. Bull. 21:955–958; 1988.
3. Aragon, C. M. G.; Spivak, K.; Amit, Z. Effects of 3-amino-1,2,4-triazole on ethanol induced open-field activity: evidence for brain catalase mediation of ethanol's effects. Alcohol.: Clin. Exp. Res. 13:104–108; 1989.
4. Barta, A.; Yashpal, K. Regional distribution of endorphin in the rat brain: effects of stress. Prog. Neuropsychol. Biol. Psychiatry 5: 595–598; 1981.
5. Bliss, E. L.; Ailion, J.; Zwanziger, J. Metabolism of norepinephrine, serotonin and dopamine in rat brain with stress. J. Pharmacol. Exp. Ther. 161:122–133; 1968.
6. Brick, J.; Pohorecky, L. A. Ethanol-stress interaction: biochemical findings. Psychopharmacology (Berlin) 77:81–84; 1982.
7. Cappel, H.; Herman, C. P. Alcohol and tension reduction: a review. Q. J. Stud. Alcohol 33:33–64; 1972.
8. Cicero, T. J.; Myers, R. D.; Black, W. C. Increase in volitional ethanol consumption following interference with a learned avoidance response. Physiol. Behav. 3:657–660; 1968.
9. Conger, J. J. The effects of alcohol on conflict behaviour in the albino rat. Q. J. Stud. Alcohol 12:1–29; 1961.
10. DeTurck, K. H.; Vogel, W. H. Effects of acute ethanol on plasma and brain catecholamine levels in stressed and unstressed rats: evidence for an ethanol-stress interaction. J. Pharmacol. Exp. Ther. 233:348–354; 1982.
11. Ellis, F. W. Effect of ethanol on plasma corticosterone levels. J. Pharmacol. Exp. Ther. 153:121–127; 1966.
12. Fadda, F.; Mosca, E.; Niffoi, T.; Colombo, G.; Gessa, G. L. Ethanol prevents stress-induced increase in cortical DOPAC: Reversal by RO 15-4513. Physiol. Behav. 40:383–385; 1987.
13. Galina, Z. H.; Amit, Z.; van Ree, J. M. Behavioral support for an ACTH receptor in the CNS. Peptides 6:285–291; 1985.
14. Galina Z. H.; Sutherland, C. J.; Amit, Z. Effects of heat stress on behavior and pituitary adrenal axis in rats. Pharmacol. Biochem. Behav. 19:251–256; 1983.
15. Glick, D.; von Redlich, D.; Levine, S. Fluorometric determination of corticosterone and cortisol in 0.02–0.05 milliliters of plasma or submilligram samples of arenal tissue. Endocrinology 74:653–655; 1964.
16. Keim, K. L.; Sigg, E. B. Physiological and biochemical concomitants of restraint stress in rats. Pharmacol. Biochem. Behav. 4:289–297; 1976.
17. Kuriyama, K.; Kanmori, K.; Yoneda, Y. Preventive effect of ethanol against stress-induced alteration in content of monoamines in brain and adrenal gland. Neuropharmacology 23:649–654; 1984.
18. Kvetnansky, R.; Sun, C. L.; Lake, C. R.; Thoa, N.; Torda, T.; Kopin, I. J. Effect of handling and forced immobilization on rat plasma levels of epinephrine, norepinephrine, and dopamine-hydroxylase. Endocrinology 103:1868–1874; 1978.
19. Livezey, G. T.; Balabkins, N.; Vogel, W. H. The effect of ethanol (alcohol) and stress on plasma catecholamine levels in individual female and male rats. Neuropsychobiology 17:193–198; 1987.
20. Livezey, G. T.; Miller, J. M.; Vogel, W. H. Plasma norepinephrine, epinephrine, and corticosterone stress responses to restraint in individual male and female rats, and their correlations. Neurosci. Lett. 62:51–56; 1985.
21. McCarty, R.; Kopin, I. J. Sympatho-adrenal medullary activity and behavior during exposure to footshock stress: A comparison of 7 rat strains. Physiol. Behav. 21:567–572; 1978.
22. Mezey, E. Effects of stress on ethanol metabolism. In: Pohorecky, L. A.; Brick, J., eds. Stress and alcohol use. Proceedings of the first international symposium on stress and alcohol use. Amsterdam: Elsevier-North Holland; 1983:421–427.
23. Mezey, E.; Potter, J. J.; Kvetnansky, R. Effect of stress by repeated immobilization on hepatic alcohol deshydrogenase activity and ethanol metabolism. Biochem. Pharmacol. 28:657–663; 1979.
24. Myers, R. D.; Holman, R. B. Failure of stress of electric shock to increase ethanol intake in rats. Q. J. Stud. Alcohol 27:132–137; 1967.
25. Nash, J. F.; Maickel, R. P. The role of the hypothalamic-pituitary-adrenocortical axis in post-stress induced ethanol consumption in rats. Prog. Neuropsychopharmacol. Biol. Psychiatry 12:653–671; 1988.
26. Natelson, B. H.; Tapp, W. N.; Adamus, J. E.; Mittler, J. C.; Levin, B. E. Humoral indices of stress in rats. Physiol. Behav. 26:1049–1054; 1981.
27. Ng Cheong Ton, M. J.; Brown, Z.; Michalakeas, A.; Amit, Z. Stress induced suppression of maintenance but not of acquisition of ethanol consumption in rats. Pharmacol. Biochem. Behav. 18:141–144; 1983.
28. Patel, V. A.; Pohorecky, L. A. Interaction of stress and ethanol: effect on β-endorphin and catecholamines. Alcohol.: Clin. Exp. Res. 161:122–133; 1988.
29. Pohorecky, L. A. The interaction of ethanol and stress: A review. Neurosci. Biobehav. Rev. 5:209–229; 1981.
30. Pohorecky, L. A.; Rassi, E.; Weiss, J. M.; Michalak, V. Biochemical evidence for an interaction of ethanol and stress: preliminary studies. Alcohol.: Clin. Exp. Res. 4:423–426; 1980.
31. Popper, C. W.; Chiueh, C. C.; Kopin, I. J. Plasma catecholamine concentrations in unanesthetized rats during sleep, wakefulness, immobilization and after decapitation. J. Pharmacol. Exp. Ther. 202:144–148; 1977.
32. Rivier, C.; Vale, W. Interaction between ethanol and stress on ACTH and β-endorphin secretion. Alcohol.: Clin. Exp. Res. 12:206–210; 1988.
33. Selye, H. The physiology and pathology of exposure to stress. Montreal: Acta Medical; 1950.
34. Tanaka, M.; Khono, Y.; Tsuda, A.; Nakagawa, R.; Ida, Y.; Iimori, K.; Hoaki, Y.; Nagazaki, N. Differential effects of morphine on nonadrenaline release in brain regions of stressed and non-stressed rats. Brain Res. 275:105–115; 1983.
35. Vogel, W. H.; DeTurck, K.; Miller, J. M. Differential effects of ethanol on plasma catecholamine levels in rats. Biochem. Pharmacol. 35:3983–3987; 1986.