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Lithium Effects on Adjunctive Alcohol Consumption. III: FT-Shock as the Inducing Schedule

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HINES, G. *Lithium effects on adjunctive alcohol consumption. III: FT-shock as the inducing schedule.* PHARMACOL BIOCHEM BEHAV **34**(3) 591–593, 1989.—Under conditions in which a mild shock (0.5 mA, 200 msec) was delivered, independently of the subject's behavior, every 90 sec (an FT 90-sec shock schedule), subjects receiving chronic lithium chloride in their drinking water (25 mEq/l), showed a rapid acquisition of an adjunctive alcohol consumption, while subjects in the control groups did not. Following termination of the FT-shock condition (extinction), subjects in all groups showed an increase in alcohol consumption, relative to both baseline and adjunctive levels.

Lithium Alcohol Adjunctive drinking Shock Extinction

UNDER free-choice conditions, lithium administration produces a reduction in alcohol intake by rats (1), even when the alcohol concentration used is one which is preferred over water (13). On the other hand, when subjects under conditions of chronic lithium administration are exposed to adjunctive consumption procedures (7), they initiate adjunction alcohol drinking more rapidly than do controls, and do not (unlike controls) undergo subsequent extinction of the elevated intake levels. When Fixed Time (FT) shock administration is applied concurrently with an FT-food schedule (8), lithium subjects consume amounts equal to those shown by control subjects, and again fail to show a permanent reduction in alcohol intake under extinction conditions.

The present investigation continues the study of lithium effects on adjunctive alcohol consumption, this time utilizing a schedule of FT-shock administration as the sole inducing schedule. Shock-induced stress has generally been found to produce increased alcohol consumption by rats during the period of stress induction (3–5, 12, 15). In poststress tests, alcohol consumption is either maintained at suprabaseline levels (3, 4, 12), or shows further increases in intake level (5,15). Kinney and Schmidt (10) have suggested that there may have been a schedule-induced (adjunctive) factor to such stress-induced alcohol consumption, an interpretation that is supported by Freed's (6) observation of an increase in relative alcohol intake under adjunctive conditions utilizing shock administration.

METHOD

Subjects

The subjects were 18 male Holtzman albino rats, approximately 80 days old at the start of the experiment. One group of six subjects (Group L) received 25 mEq/l lithium chloride in their drinking water; a second group of six subjects (Group DC) received a daily ration of tap water (presented at the end of each day's test session) equal to the mean intake for the Group L subjects; and the third group of six subjects (Group NDC) had free access to tap water. Group DC served as a control for influence of thirst factors on subsequent alcohol intake. All subjects had free access to food (Purina Laboratory Chow), and were housed in standard individual stainless steel suspended cages. The rack itself was housed in an Airo Clean Engineering, Inc. Model DC-10 Airo/Neg Safety Enclosure. In order to minimize the influence of circadian drinking on lithium intake and serum levels at time of testing, 24-hour light-on conditions were maintained.

Apparatus

Testing was performed in a Coulbourn Instruments Model E10-10 modular test chamber. Alcohol (12.5%, v/v), mixed from 95% ethanol, was made available through a spout located in a niche (approx. 3.5×4.1 cm) in the center of one chamber wall, 4 cm above the floor. The test chamber was housed in a Grason-Stadler Model 1101 research chest, with an exhaust fan providing 58-dB masking noise. Shock delivery (0.5 mA, 200 msec) occurred through a Coulbourn Instruments Model E13-08 grid floor shocker, and was controlled by Coulbourn Instruments solid-state programming modules.

Procedure

Testing (5 daily sessions per week) was initiated after body weights for L and DC subjects had stabilized (ca. 12 days). For the first eight 25-min sessions, alcohol was available in the chamber, but shock was not scheduled—a period that allowed for assessment of baseline alcohol consumption levels. This was followed

by 32 daily sessions in which shock occurred, independently of the subject's behavior, every 90 seconds (an FT 90-sec schedule). Finally, shock was discontinued for 40 sessions to evaluate extinction of the adjunctive drinking behavior. Following the extinction sessions, blood was drawn from the subjects' tail veins at their usual test times, and serum lithium levels determined by flame photometry (2).

The results were collapsed into mean volume consumption levels (ml) for successive 4-session blocks, and subjected to statistical analysis using a Treatment × Session mixed-design ANOVA. To separate the effects of adjunctive control from extinction processes, separate ANOVA's were performed for each experimental condition.

RESULTS

While Group L subjects consumed an average of 32.7 ± 4.3 ml of lithium solution per day (DC subjects were given 33 ml/day; NDC subjects consumed 38.6 ± 3.9 ml per day), their body weights (as well as those of the Group DC control subjects) gained steadily throughout the experiment. Nonetheless, the weights for both these groups were lower than those of the NDC subjects: L = 523 ± 20.8; DC = 531 ± 22.2; and NDC = 602 ± 24.1 g. Serum lithium levels for Group L subjects averaged 1.23 ± 0.37 mEq/l. That this concentration is considerably lower than that expected from the observations of Trautner *et al.* (14) is not surprising in light of the considerable amount of alcohol consumed in the test apparatus.

Mean alcohol consumption values (± SEM) across sessions are shown in Fig. 1. Analysis of the last four days of baseline consumption (the first four days were characterized by a great deal of within-subject variability) by a one-way ANOVA indicated a significant Treatment effect, $F(2,15) = 5.41$, $p<0.05$. This was clearly the result of the low consumption values evidenced by the NDC subjects (there was no overlap in the volumes for these subjects with those for the subjects in the other two groups), since the differences between Group L and Group DC consumptions were negligible.

Lithium had a clear effect on alcohol consumption while the FT shock schedule was in effect. Group L subjects increased their consumption volumes by an average 3.51 × their baseline values across the 32 adjunctive sessions. In contrast, neither the DC nor the NDC subjects showed any consistent or significant change in their alcohol consumption. By the end of the adjunctive phase, all six Group L subjects were consuming more than their baseline intake, while only one DC subject and two NDC subjects were doing so (Table 1). This difference was substantiated by the ANOVA, which showed a significant Treatment effect, $F(1,10) = 5.41$, $p<0.05$, a significant Sessions effect, $F(7,70) = 9.22$, $p<0.01$, and a significant Treatment × Sessions interaction, $F(7,70) = 7.19$, $p<0.01$.

With the discontinuation of the FT-shock presentation (extinction), all subjects produced an increase in their alcohol consumption across sessions—exceeding, by the end of the 40 extinction sessions, not only their baseline intakes, but generally drinking more than was evident under the FT-shock conditions. All six NDC, DC, and L subjects had alcohol intakes that were greater than their baseline volumes; and six NDC, five DC, and four L subjects ended at consumption levels that were higher than their terminal FT-shock values (the one DC and two L subjects that did not exceed FT values matched them—no subject was drinking less at the end of the extinction phase than it had at the end of the adjunctive phase). There was no overlap in consumption volumes between the members of the three groups by the end of the extinction phase. The ANOVA supported this observation, showing significant Sessions and Treatment effects, but no significant interaction effect, $F(9,90) = 5.50$, $p<0.01$; $F(1,10) = 5.03$, $p<0.05$; and $F(9,90) = 1.36$, $p>0.05$, respectively.

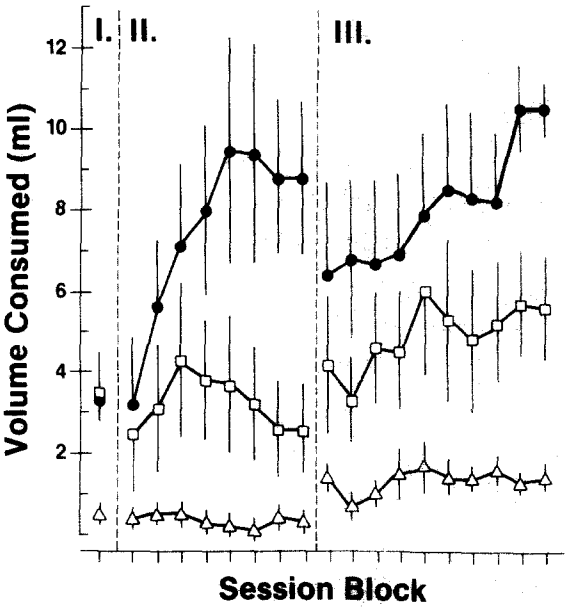

FIG. 1. Mean (± S.E.M.) volume of alcohol consumed over 4-session blocks under baseline (I), adjunctive (II), and extinction (III) conditions. Closed circles = Lithium; open squares = Control; open triangles = NDC.

DISCUSSION

Under conditions of FT-shock presentation, alcohol consumption by control subjects did not show any tendency to increase across sessions; that is, there was no evidence of adjunctive alcohol consumption by either Group DC or Group NDC animals. While this result is contrary to the outcomes of shock-induced stress cited above, the differences may have resulted from the greater palatability of the alcohol solutions utilized in the earlier studies (5–10% vs. 12.5%), the greater shock intensity utilized (1.0–1.5 mA, 1.0–2.0 sec duration vs. 0.5 mA, 200 msec duration), or a combination of both factors. While deprivation status did influence baseline consumption (producing greater intake by DC subjects than by NDC subjects) and level of drinking during FT-shock conditions, it was not a factor in terms of response to the FT schedule: neither control group increased their level of alcohol intake under these conditions. Subjects receiving chronic lithium, on the other hand, did show clear evidence of the acquisition of adjunctive alcohol consumption when FT shock is used as the inducing schedule. Since Group L baseline intake was virtually identical with that for Group DC, this difference is not likely to be the result of differences in thirst motivation: rather, Group L subjects appear to be more responsive to those factors producing adjunctive drinking than are their Control counterparts. In this regard, the differences are similar to those reported earlier (7,8) when FT food delivery is used as the inducing schedule. The relatively low level of shock employed, combined with the reduction in reactivity to this level of shock noted by Hines and Poling (9), may have contributed to the effect by producing a reduction in subjective shock intensity to a level that was less aversive than that perceived by the two control groups.

Removal of the FT-shock condition (extinction) produced an effect in all three groups that was entirely consistent with the earlier studies cited. All three groups increased their intake to

TABLE 1

TERMINAL CONSUMPTION COMPARISONS: NUMBER OF SUBJECTS IN EACH GROUP FOR WHICH CONSUMPTION UNDER ONE EXPERIMENTAL CONDITION WAS LESS THAN, EQUAL TO, AND GREATER THAN CONSUMPTION UNDER ANOTHER EXPERIMENTAL CONDITION

	Adjunctive:Baseline			Extinction:Baseline			Extinction:Adjunctive		
	A<B	A=B	A>B	E<B	E=B	E>B	E<A	E=A	E>A
Group L	0	0	6	0	0	6	0	2	4
Group DC	5	0	1	0	0	6	0	1	5
Group NDC	3	1	2	0	0	6	0	0	6

A = adjunctive; B = baseline; E = extinction.

levels that were in all instances greater than their baseline levels, and generally greater than those observed during the FT-shock phase. That two of the six Group L subjects failed to increase their intake relative to adjunctive levels is likely the result of the magnitude of their intake (16.0 and 12.5 ml in 25 min) during the adjunctive phase, rather than to a failure to respond to the poststress conditions, since these two subjects had the highest levels of alcohol intake of all 18 subjects. Thus, the only differences appeared to be quantitative ones, with L, DC, and NDC subjects all producing the same quantitative response to the extinction phase: an increase in alcohol consumption.

Chronic lithium administration thus appears to increase susceptibility to adjunctive alcohol consumption independently of the nature of the inducing schedule, without greatly influencing the nature of the poststress increase in alcohol consumption. These results, thus, suggest caution with respect to alcohol consumption by individuals who are receiving lithium on a therapeutic basis, but do not necessarily speak to the issue of lithium's putative effectiveness as a treatment for alcoholism (11,16). Under the latter application the administration of lithium is not established until after the excessive alcohol intake has been established, and under conditions in which the intake-inducing conditions are, if not eliminated, at least undergoing modifications aimed at reducing their influence. That is, a more proper evaluation of lithium as a therapeutic agent in the treatment of alcoholism would involve the administration of lithium only after adjunctive drinking had been established during the extinction phase.

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