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BRIEF COMMUNICATION

Suppressed Ethanol Intake by CER Following the Sucrose-Fading Initiation Procedure[1]

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TOLLIVER, G. A., K. G. SADEGHI AND H. H. SAMSON. *Suppressed ethanol intake by CER following the sucrose-fading initiation procedure.* PHARMACOL BIOCHEM BEHAV 31(4) 949–952, 1988.—Lever responding maintained with sweetened ethanol reinforcement (3% sucrose in 10% ethanol) was initiated in food- and water-sated rats with the sucrose-fading procedure. Four tone-shock pairings, one per session, were superimposed on this behavioral baseline [conditioned emotional response (CER) paradigm]. A profound and sustained ethanol response suppression was found. Baseline levels of ethanol responding were recovered by repeating the original initiation procedure. Subsequent exposure to the CS tone alone (no shock) led to a nonsignificant reduction in ethanol responding. These results were discussed in terms of anxiolytic action of ethanol.

Ethanol initiation Sucrose-fading CER Rats

THE effects of footshock on ethanol self-administration have been studied under a variety of conditions (16). Studies looking at changes in home-cage "voluntary" ethanol intake have for the most part presented shock independent of the animal's ethanol consumption behavior. Under some of these conditions, increments in ethanol intake have been reported, occurring primarily in the postshock period (1, 6, 10, 14, 15). However, these changes are subject to the discriminability of the shock from the "no-shock" conditions as well as to the initial ethanol intake levels (3, 6, 10, 15, 18).

It is generally accepted that drugs having anxiolytic effects, i.e., benzodiazepine, barbiturates, etc., will antagonize the suppression of food and water maintained behavior by footshock. This has been demonstrated in both the direct punishment and the noncontingent Conditioned Emotional Response (CER) paradigms (13,22). Similar anxiolytic actions of ethanol have been demonstrated (4, 11, 12, 23). Thus, ethanol shows anxiolytic capabilities and in shock situations in which ethanol is self-administered, it could be hypothesized that animals might increase their ethanol intake in order to enhance the anxiolytic action.

There are a few studies in the literature which report the effects of shock on drug-maintained behavior (2, 8, 9, 17, 21). The results find a reduction in self-administration of a variety of drugs, i.e., cocaine, amphetamine, morphine and ethanol, which is directly related to the intensity of the footshock. Ethanol was the only drug in which oral self-administration was used (17), the other studies (2, 8, 9, 21) used intravenous infusions. However, food-deprived animals were used to maintain the oral ethanol baseline behavior (17). This raises the question whether ethanol was maintaining behavior as a result of its food and/or fluid properties or as a result of its physiological effect of intoxication or anxiolytic action.

Recently, procedures have been described for the development of ethanol oral self-administration as a reinforcement for lever pressing behavior in the nonfood- and nonwater-deprived rat (19). These procedures offer the opportunity to study the influence of environmental variables and behavioral history on ethanol intake under ethanol self-administration conditions independent of deprivation. As an attempt to further describe the characteristics of ethanol as a reinforcer of operant behavior, the present study assesses the influence of footshock superimposed on the ethanol self-administration operant baseline using the CER paradigm (7).

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METHOD

Animals

Four male Long Evans rats, weighing between 150–200 grams, served as subjects. The animals were housed individually in standard hanging cages with food (Purina Rat Chow) and water available at all times, except as described below. Artificial lighting was provided on a 12-hour on/off cycle (07:30 to 19:30, on). Room temperature and humidity were controlled as specified by the National Institutes of Health Animal Care Guide (23).

Apparatus

A single operant chamber was used for the study which was housed in a ventilated sound-attenuating isolation compartment. The isolation compartment (69×42×35 cm) was equipped with a fan which provided ventilation and a masking noise for the operant chamber. The operant chamber (23×20×22 cm) was equipped with a single microswitch lever mounted on the same wall with a liquid reinforcement access well and a sound source (Sonoalert, 2900 Hz). The sound source operated on 28 volts DC with an 18 kohm resistor in series to reduce the sound intensity in the test chamber. Liquid reinforcements were presented for 3 seconds by a Gerbrand Liquid Dipper mechanism (Gerbrand Mfg., Model No. G5600) fitted with a 0.1-ml cup. Two 28-volt DC lights were mounted on the chamber ceiling to provide general illumination during the operant session. The chamber floor consisted of 13 2-cm stainless steel rods mounted 1.2 cm apart. The grid bars were connected to a Grason Stadler shock source (Model No. E6070B) which was programmed to deliver a scrambled shock (0.5 mA for 1.5 seconds). The experimental conditions were programmed by relay equipment, and the number of lever responses and liquid reinforcements were recorded on electromechanical counters. Daily cumulative response records were taken (Scientific Prototype, Model CR2D) to determine the temporal distribution of lever responses.

Procedure

Animals were trained to lever press using 20% sucrose (w/v) reinforcement. During the initial sucrose training sessions, the animals were water restricted (16 hours prior to the training session) until the lever response had been shaped. Except for these few shaping sessions (maximum of four sessions) the animals had an unlimited supply of water in the home cage. Response requirement was gradually increased to a Fixed Ratio eight schedule (FR8) over the next ten sessions. In subsequent sessions (30 minutes/five days per week), animals were given a modified sucrose fading ethanol initiation procedure (20). The liquid reinforcement was changed over sessions in the following manner: 10 sessions of 20% sucrose (w/v); 10 sessions of 10% sucrose in 5% ethanol (v/v); 10 sessions of 10% sucrose in 10% ethanol; 4 sessions of 5% sucrose in 10% ethanol; 9 sessions of 10% ethanol; 6 sessions of 1% sucrose in 10% ethanol; 8 sessions with 3% sucrose in 10% ethanol; 3 sessions with 3% sucrose in 20% ethanol; 3 sessions with 3% sucrose in 30% ethanol; 3 sessions with 3% sucrose in 40% ethanol; and finally 3% sucrose in 10% ethanol which was the solution used for the remainder of the study.

Conditioned Emotional Response training (CER). Following the establishment of the baseline conditions, each animal was run for five sessions in which the Conditioned Stimulus (CS) (tone) was presented alone at the 8th, 16th, and 24th minute of the session. This tone lasted for two minutes at each presentation. Ethanol reinforcement was available in both the tone-on and tone-off conditions.

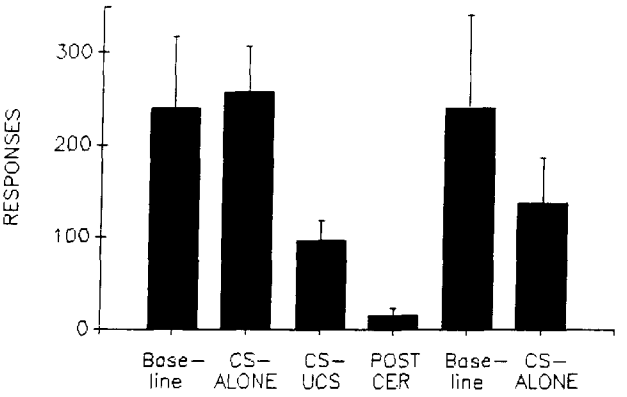

FIG. 1. Mean ethanol lever responses and standard errors for all animals in each of the six conditions of the study.

Following the five tone adaptation sessions, four sessions were run in which a single two-minute tone was presented at the 16th minute and was terminated with a single shock. In the sessions immediately following the tone-shock sessions the baseline ethanol response levels were determined without the presentation of the CS during the session. Upon recovery of the ethanol baseline responding, CS-only sessions were given to assess its influence on ethanol-reinforced behavior. As in the CS-Alone sessions given prior to the CS-shock pairing sessions, the CS was a 2-minute duration and the ethanol reinforcement conditions were in effect.

RESULTS

All animals were successfully shaped in two to four training sessions to make lever responses using 20% sucrose as the reinforcer. The animals lost an average of 15 grams (with a range from 6 to 23 grams) as a result of water restriction during these training days. This weight loss was quickly regained. Over the 6 months of the study, there was an average weight gain of 189 grams (157 to 254 grams). While the ethanol initiation procedure took a total of 70 sessions, as specified in the Procedure section, the number of sessions to complete the CER portion of the study was influenced by changes in the ethanol behavior in the postshock sessions. To summarize the number of sessions given at each phase of the CER part of the study: 5 sessions with CS-alone, followed by 4 sessions with CS-shock pairings, the next 7 sessions with no CS presentations, then 12 reinitiation sessions with no CS, followed by 5 baseline sessions with no CS, and finally 5 sessions with the CS-alone presented.

Figure 1 presents lever responding for all experimental conditions. The response levels between the baseline conditions and the CS-alone sessions were unaffected by CS presentations. The average session (30 minutes) ethanol intake for the baseline conditions was 0.49±0.15 g/kg (mean ±SEM). Data from individual animals indicated that 3 of the 4 rats had a slight, but nonsignificant, increase in ethanol responses during the CS-alone sessions when compared to their baseline sessions.

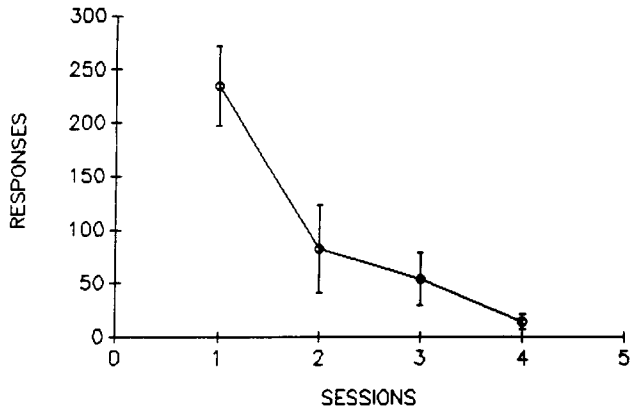

FIG. 2. Mean ethanol lever responses and standard errors for all animals in each of the four tone-shock sessions of the study.

Ethanol responding was significantly reduced in the CS-shock sessions ($t=5.12, p<0.05$). Figure 2 presents the average ethanol responses during each of the four CS-shock sessions. While the response patterns for the individual animals were slightly different across these four sessions, the effect of the shock sessions was to reduce ethanol responding to near zero for all of the rats.

Over the next seven sessions in which no CS presentations were given, the animals' ethanol responses continued to decline to levels below the CS-shock sessions (see Post CER sessions, Fig. 1). In order to reestablish ethanol responding it was necessary to implement the original initiation procedures with no CS present. The first retraining session was run with the animals 16-hours water-deprived using 10% sucrose/10% ethanol as the reinforcer. Lever responding was reestablished in all of the animals with this single water restriction session. As in the original initiation procedure, the sucrose level was gradually decreased to 3% over eleven sessions while the ethanol concentration remained at 10%. The baseline response levels were reestablished over five sessions as indicated in Fig. 1. While no overall difference was found between the original baseline response levels and the reestablished baselines, one animal increased its responses for ethanol and two rats responded at a lower level. All animals demonstrated a reduced ethanol response rate of approximately 32% over the five sessions in which the CS-alone was reintroduced, however this reduction was not statistically significant.

DISCUSSION

The effect of a tone-shock pairing on ethanol self-administration under the conditions of the present study was the gradual and almost complete disruption of ethanol responding after just four tone-shock pairings using 0.5 mA shock. The failure of the animals to adapt to the test conditions in the seven "no-tone" sessions following the tone-shock pairings prevented testing the effects of the tone-alone on ethanol intake. Following the reestablishment of the ethanol baseline by the reintroduction of the original initiation procedure, effects of the tone-alone could be assessed. Tone presentations at this time, one month after the last tone shock pairing, resulted in a nonsignificant reduction in ethanol responses.

These results are consistent with those studies which found reduced ethanol drinking in the environment where a shock schedule was in effect (5,25). Thus, contrary to the expected increase in ethanol intake under the conditions of a signalled inescapable shock (10,15), the aversive conditions used here reduced the animals' ethanol intake despite a substantial history of oral self-administration of 10% ethanol. These findings are in keeping with the effects of shock on self-administration of other drugs, such as cocaine, amphetamine, and morphine (2, 8, 9, 21).

One assumption that was explored in this study was that if the anxiolytic properties of ethanol are part of the reinforcing aspects of ethanol, it could be hypothesized that the self-selection of ethanol should be increased following the introduction of the CER procedures. The failure of the animals to maintain or to increase ethanol consumption under these conditions argues against the notion that ethanol self-administration behavior was reinforced by ethanol's anxiolytic properties.

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