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Spatial Aversion Conditioning with Ethanol

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CUNNINGHAM, C. L. *Spatial aversion conditioning with ethanol.* PHARMAC. BIOCHEM. BEHAV. **14**(2) 263–264, 1981.—To determine whether dose level affected ethanol's ability to establish a preference or aversion for an associated spatial location, two groups of male albino rats each received five pairings of an IP injection of ethanol (1 or 2 g/kg) with exposure to a distinctive compartment for 15 min. On alternate days, each rat was exposed to a different compartment after a saline injection. A choice test indicated that aversions were established at *both* dose levels, and thus failed to confirm a previous report of conditioned location preference at the lower dose level.

Ethanol Spatial aversion Drug reinforcement Rats

BLACK, Albiniak, Davis and Schumpert [1] reported that pairings of an injection of ethanol with placement in a distinctive compartment induced a preference for that compartment relative to a second compartment which had been associated with injections of saline. This finding, coupled with the many reports of ethanol-produced flavor aversion (e.g., [2,4]), suggests that ethanol might be both positively and negatively reinforcing, depending on the nature of the associated cue. Cunningham [3] recently attempted to provide more direct evidence for this hypothesis by combining location conditioning with taste-aversion conditioning in a single procedure (cf. [7]). However, Cunningham found that alcohol injection produced aversion to both flavor and location.

Comparison of the Black *et al.* and Cunningham studies indicates several differences that might have contributed to the discrepancy in their outcomes. Aside from differences in apparatus and deprivation state (Cunningham's rats were fluid-deprived for taste-aversion conditioning), there appear to be at least four major parametric/procedural differences that might have been important: (1) ethanol dose (volume, concentration)—1 g/kg for Black *et al.*, 1.5 g/kg for Cunningham; (2) time interval between injection and exposure to location cues—5 min for Black *et al.*, less than 30 sec for Cunningham; (3) duration of exposure to location cues—15 min for Black *et al.*, 30 min for Cunningham; and (4) pairing ethanol with the initially preferred location (Black *et al.*) vs random assignment of subjects to treatment conditions and counterbalancing of location assignment (Cunningham).

The present experiment was designed to determine whether dose level affected ethanol's ability to condition location preference or aversion. One group of rats received the dose level reported by Black *et al.* to produce location preference (i.e., 1 g/kg), whereas a second group received a dose somewhat larger than that found by Cunningham to produce location aversion (2 g/kg). The temporal parameters were those used by Black *et al.* and the rats were not deprived of food or water.

METHOD

Subjects

The subjects were 23 naive, male Holtzman albino rats, about 100 days old at the start of the experiment. All were housed individually in wire mesh cages with ad lib access to water and lab chow.

Apparatus

The apparatus was the two-compartment box described by Cunningham [3]. Each compartment measured 27.8 cm long, 12.5 cm wide and 20.0 cm deep. The left-hand compartment contained galvanized metal walls, a stainless-steel grid floor (2.3 mm rods mounted at 1.25 cm intervals), and a clear acrylic lid. The right-hand compartment consisted of unfinished hard-plywood walls covered with vertical strips of black plastic tape (1.9 cm wide, placed at 1.9 cm intervals), a wire-mesh floor (1.5 cm squares), and an acrylic lid that was also covered with black tape strips. A wooden barrier, with metal on one side and tape strips on the other, separated the compartments during conditioning. The barrier was removed for testing, and the rat's location (left vs right) was detected by pairs of photocells mounted vertically 6 cm on either side of the point where the compartments were joined. The entire apparatus was contained in a ventilated, light- and sound-attenuating enclosure (71×34×35 cm). General illumination was provided by four bulbs (No. 1819) that served as light sources for the photocell detection circuit.

Procedure

Each rat was weighed and handled for 2–3 min on each of the 2 days before the first conditioning trial. On each of the 10 conditioning days, each rat first received an IP injection in the home cage. Five minutes later, the rat was carried to the conditioning chamber and placed into one of the distinctive compartments for a period of 15 min. All rats received

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ethanol injections on odd-numbered days (1, 3, 5, 7, 9) and saline injections on even-numbered days (2, 4, 6, 8, 10). They were randomly assigned to one of four subgroups that differed in terms of ethanol dose level (1 vs 2 g/kg) and the spatial location paired with ethanol (left vs right). Ethanol dose level was varied by manipulating the volume of a 12.6% (v/v) solution of ethanol in normal saline (cf. [5]). Saline injections were given in a volume equal to each animal's ethanol injection (10 or 20 ml/kg).

Three days of location-preference testing followed the last conditioning trial. On each day, each rat was lowered by the tail into the center of the apparatus and allowed access to both compartments for a 20-min period. No injections were given during testing. The data of primary interest are the relative amounts of time spent on each side of the two-compartment box during the preference test.

TABLE 1

MEAN PERCENTAGE OF TOTAL TIME SPENT ON RIGHT SIDE OF CHOICE APPARATUS

	Side Paired with Ethanol	
Dose Level	Left	Right
1 g/kg	57.9 (n=6)	48.7 (n=6)
2 g/kg	59.3 (n=6)	43.6 (n=5)
Mean	58.6	46.1

RESULTS AND DISCUSSION

The data from the location tests are shown in Table 1 as a mean percentage of the total test period that each rat stayed on the right side of the apparatus. These data suggest that *both* doses of ethanol produced an *aversion* to the location which had been associated with ethanol. Rats that had been exposed to ethanol on the left side during conditioning spent a greater proportion of their time on the right side during testing than did rats originally exposed to ethanol on the right side. A three-way analysis of variance was applied to these data using dose, ethanol location and test days as factors. This analysis confirmed the significance of the location aversion, $F(1,19)=7.1$, $p<0.03$. There were also reliable effects due to test days, $F(2,38)=7.1$, $p<0.03$, and the interaction of test days and ethanol location, $F(2,38)=4.9$, $p<0.05$. The interaction resulted from the fact that the ethanol location factor was significant on Days 2 and 3 of testing, but not on Day 1. There were no effects of ethanol dose.

Thus, despite the use of parameters that very closely matched those used by Black *et al.* [1], the present study suggests that injection of ethanol establishes an aversion to and not a preference for an associated location. The only major procedural difference between the present study and that of Black *et al.* is that in the present study, rats were randomly assigned to drug-location conditions, whereas Black *et al.* paired ethanol with the rat's initially nonpreferred location. The present procedure was chosen over that of Black *et al.* because the latter procedure unnecessarily biases the kinds of outcomes that can be obtained (i.e., there is a greater opportunity for seeing an increase rather than a decrease in preference for the ethanol-paired location). It should also be noted that since Black *et al.* did not include an adequate control for any nonspecific (non-associative) effects that injection and exposure to alcohol might have had on initial preference, their critical outcome (a within-group increase in preference from pretest to posttest) may not really have reflected the effects of location-drug conditioning.

The question of whether alcohol is capable of producing location preference remains unresolved. Hickis, Sherman, Strub and Bradford [8] recently examined the effects of low doses of ethanol administered orally in a location conditioning paradigm. Consistent with the data of Cunningham [3] and those reported here, location conditioning resulted only in spatial aversion (at a dose of 2 g/kg). Lower doses (0.5 and 1.0 g/kg) did not produce any conditioned location effects. It may be that ethanol, unlike amphetamine and morphine, does not exert a positive reinforcing effect on associated spatial cues. Such a conclusion, however, seems inconsistent with the results of self-administration studies showing choice of ethanol based on spatial cues (e.g., [6]).

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