Pharmacology Biochemistry & Behavior, Vol. 18, pp. 55–59, 1983. Printed in the U.S.A.

Effects of Ethanol on Enforced Spatial Variability in the 8-Arm Radial Maze

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Received 30 July 1982

DEVENPORT, L. D., V. J. MERRIMAN AND J. A. DEVENPORT. *Effects of ethanol on enforced spatial variability in the 8-arm radial maze.* PHARMACOL BIOCHEM BEHAV **18**(1) 55–59, 1983.—Previous work has indicated that ethanol is a potent stereotypy-inducing agent. At least this is the case for spontaneously emitted instrumental behavior. The present experiments were undertaken to determine if spatial variability could be generated by drugged rats when it was enforced by reward contingencies. With a reward nonreplacement rule in force, four arms of an 8-arm radial maze were baited on every trial. Rats injected with 0, 0.75, 1.5, or 2.0 g/kg ethanol were required to run to the same set of arms from trial-to-trial and session-to-session. Efficient performance depended upon their running to the correct set of arms as well as meeting a "win-shift" demand which proscribed returning to previously visited arms during a given trial. Although all groups were eventually able to run to the correct set of arms, alcohol, especially at higher doses, promoted repetition. The inability to refrain from reentering arms prevented many alcohol-injected animals from obtaining the four rewards in the allotted time. In Phase 2 of Experiment 1, the baited arms were rotated 45°. Now the formerly empty arms contained pellets and rewards were withdrawn from the previously correct arms. Adjustment to this shift was rapid for 0 and 0.75 g/kg groups, but an increasingly severe perseveration was observed across the higher ethanol groups. Experiment 2 reproduced the results of Experiment 1 under different circumstances. While trained as before to run to a specific set of four arms in Phase 1, Phase 2 presented the rats with rewards in all eight arms of the maze. With higher doses of alcohol an increasing persistence in running to the original four arms was observed. Saline-injected animals, on the other hand, rapidly doubled the number of pellets taken. Taken together, and in view of earlier findings, the results suggest that alcohol interacts with previous training as well as recent choices with the result that spatial dispersion is restricted in spite of explicitly opposing reward contingencies.

Ethanol Alcohol Radial-arm maze Behavioral variability Spatial factors Stereotypy Perseveration

ONE of the most striking features of behavior in the radial-arm maze is its variability. Given the opportunity, rats spread their visits across most available arms before returning to previously entered ones [12,13]. They vary the sequences of these arm entries from trial-to-trial [8,12], and they punctuate their maze-running with a variety of nongoal-directed behavior (e.g., stopping, rearing, orienting, scanning, sniffing, etc., [8]).

To us, the most interesting effect of alcohol (ethyl alcohol, ethanol) is its dramatic suppression of each of these forms of behavioral variability [8]: Fewer different arms are entered, sequences become highly predictable, and behavioral topographies decline to about 35% of their undrugged level. Yet, the animals run the maze and perform at least as well as [8], and in some situations [7] better than, saline-injected controls as compared by conventional means (running time, trials-to-criterion).

However, to date the only kind of behavioral variability (BV) examined has been the sort that is spontaneously emitted—variations in behavior that are superfluous to the task at hand. For example, in our radial-maze work we have employed reward replacement procedures. In doing this, no constraint was placed upon stereotypy. Rats could run to as many or as few different arms as they chose without penalty of nonreward. Nor have we required certain levels of sequential or topographic BV. Thus, it remains to be shown whether alcohol-injected rats are incapable of expressing normal levels of BV or if they merely choose not to. The question to be examined in the present study is whether or not rats injected with alcohol can generate the necessary diversity when the situation demands it, i.e., explicitly rewards it. Or, will the relative response stereotypy of drugged rats interfere with its mastery?

More specifically, the following experiments investigate this question at two levels. In Experiment 1 we baited only the four odd-numbered arms of the 8-arm radial maze and, when these were taken, the rewards were not replaced. In Phase 2 of the experiment, all conditions remained the same except that the position of rewards were rotated 45°. Only the even-numbered arms were baited. In this way we were able to assess the degree to which rats could, on the one hand, refrain from returning to previously entered arms (Phase 1) or, on the other hand, shift away from a more enduring rule that they learned. Phase 1 and Phase 2, in other words, examine the rigidity of responses that were recently executed (within trials) and those patterns of behavior that were acquired early on and prevailed within and across trials, respectively.

EXPERIMENT 1

METHOD

Subjects, Drug, and Apparatus

Male Sprague-Dawley rats (Simonsen Labs; Gilroy, California), 60 days of age at the beginning of the experiment were deprived of food until their free-feeding weights were reduced by 20%. This level of deprivation was subsequently maintained by supplemental refeeding adjusted from day to day in response to weight fluctuations. During the deprivation period and before behavioral training commenced, the animals were familiarized on two occasions with about 6–8 of the 45 mg precision pellets (Bioserve, Inc.) they would later find in the maze.

These rats were assigned to one of four groups (ns=6) identified by alcohol doses of 0 (saline), 0.75, 1.5, 2.0 g/kg ethanol. The drug was injected IP as a 10% (w/v) solution dissolved in 0.9% saline 13 min before sessions began. Throughout the course of the experiment, we employed an incremental dose regimen [7,8] that helped to counter the effects of tolerance. This involved increasing the prescribed base dose by 18.75 mg/kg every third session. By the end of the experiment, subjects were receiving 0, 0.86, 1.61, and 2.11 g/kg ethanol. For convenience we will refer to these groups as Saline, Low, Medium, and High.

The 8-arm radial maze was constructed of wood according to dimensions given by Olton [13]. It was elevated 73 cm from the floor, painted flat black, and positioned in a dimly lighted room with abundant extramaze cues. Two 45 mg pellets served as reward and were placed in a recepticle at the end of designated arms.

Procedure

Trials began with the placement of the animal in the central compartment of the maze with the doors to all eight arms open. The odd-numbered (i.e., 1, 3, 5, and 7) arms were previously baited and the rat was free to move from arm to arm until all the pellets were taken or until 10 min had elapsed. Running time as well as the rat's arm selections, were recorded. The session was complete after three such trials separated by 60 sec, during which the subject was confined to a holding cage and rewards were replaced. Training under these conditions continued for 12 sessions. Phase 2, which lasted for 8 sessions, differed from original training in only one respect: The baited arms were displaced by 45° such that now only even-numbered arms contained pellets; odd-numbered arms were empty. Measures and trials were as before. Data were subjected to analysis of variance followed, when appropriate, by individual comparisons (Duncan's New Multiple Range Test, $\alpha=0.05$). Trials-to-criterion data were skewed and in each case analysed by nonparametric methods (Kruskal-Wallis H-test). While the criterion analyses took into account all 12 sessions, the parametric analyses did not, as many animals were not sampling a sufficient number of arms in the allotted time to provide statistically useful data. Accordingly, and as before [8], these analyses were restricted to the last 8 sessions of Phase 1 and all 8 sessions of Phase 2.

RESULTS AND DISCUSSION

With the exception of the low dose, which slightly but nonsignificantly facilitated performance, ethanol exacted a dose-dependent impairment ranging from mild to severe, depending on the measure under consideration.

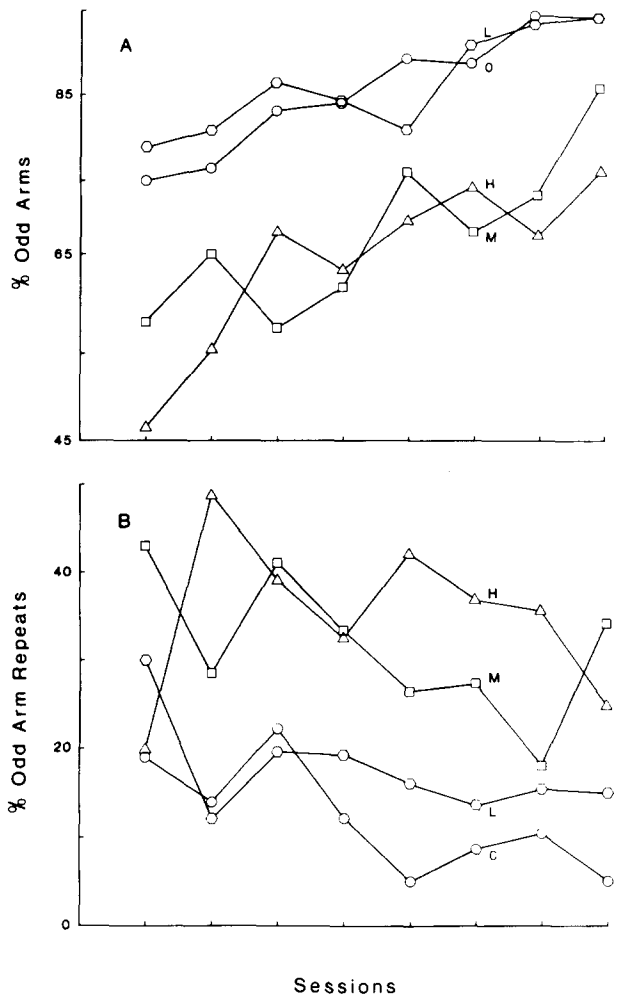

FIG. 1. Mean percent odd-arm (odd arms entered divided by total arms ×100) preference (A), and mean percent odd-arm repeat (number of odd arms reentered divided by total odd arms entered ×100) visits (B) for High, Medium, Low, and Saline (0) ethanol dose groups in Phase 1 of Experiment 1. Sessions 5–12 are illustrated.

In terms of the most basic of the formal task requirements, running to the correct set of arms (as reflected by the index, number odd arms entered ÷ total arms entered × 100), Medium and High groups performed with less accuracy than other groups, $F(3,20)=38.5$, $p<0.01$. Yet as Fig. 1A indicates, all groups came to display a clear preference for the odd-numbered arms across sessions, $F(7,140)=13.9$, $p<0.01$, and no group was exceptional in its rate of improvement, $F(21,140)=1.22$, $p>0.05$.

On the other hand, the number of rats meeting criterion for each session, (Table 1) suggests a deficit more profound than that indicated in Fig. 1A. Criterion was defined as two successive sessions in which all four rewards were taken in the allotted 10 min. Although many Medium dose animals were eventually able to attain criterion, most of the High group never obtained their rewards in the allotted time.

TABLE 1

NUMBER OF SUBJECTS MEETING CRITERION DURING ACQUISITION OF THE ODD-ARM NONREPLACEMENT PROBLEM

Dose (g/kg)	Sessions 1	2	3	4	5	6	7	8	9	10	11	12
0	3	3	3	4	4	4	5	6	6	6	6	6
0.75	4	2	4	6	6	6	6	6	6	6	6	6
1.5*	0	0	1	0	1	3	2	3	5	5	5	3
2.0*	0	0	1	0	1	2	2	3	3	3	2	2

Criterion was defined as 2 successive sessions during which all 4 rewards were taken in the allotted (10 min) time. n=6/group.

*These groups differ from 0 and 0.75 by p's<0.03–0.004; 0 and 0.75 groups do not differ from each other.

TABLE 2

NUMBER OF SUBJECTS MEETING CRITERION IN PHASE 2, EXPERIMENT 1, (CHANGE FROM ODD- TO EVEN-ARM NONREPLACEMENT PROBLEM)

Dose (g/kg)	Sessions 1	2	3	4	5	6	7	8
0	6	6	6	6	6	6	6	6
0.75	6	6	6	6	6	6	6	6
1.5*	4	2	4	5	5	4	4	5
2.0*	1	2	3	2	3	3	3	3

Criterion was defined as 2 successive sessions during which all 4 rewards were taken in the allotted (10 min) time. n=6/group.

*Significantly different from 0 and 0.75, p's<0.007; 0 and 0.75 groups do not differ from each other.

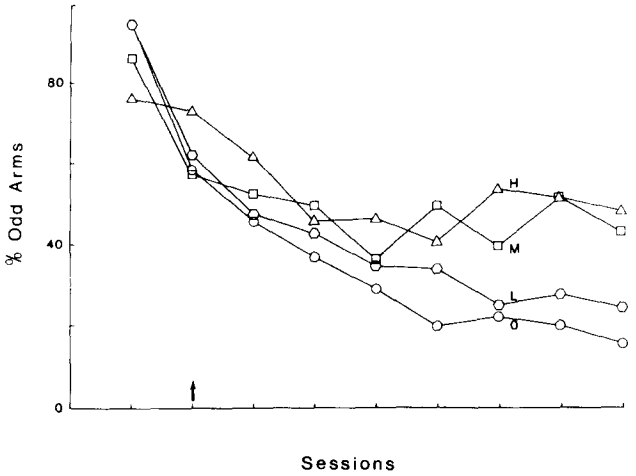

FIG. 2. Mean percent odd (unbaited) arms selected by rats in the various ethanol dose groups in Experiment 1. For reference, the last session of Phase 1 is indicated. Phase 2 begins at the arrow. Abbreviations and performance index as in caption, Fig. 1A.

These results are paralleled by mean running time differences among groups, $F(3,20)=6.71$, $p<0.01$ that, while improving across sessions, $F(7,140)=7.12$, $p<0.01$, did not do so uniformly across doses, $F(21,140)=1.81$, $p<0.05$. This latter result was principally attributable to the High dose group. Its performance was significantly poorer than each of the other groups.

The nature of the alcohol-induced deficit is plainly revealed in Fig. 1B, a depiction of the mean percent of total odd-arm visits that were repeats, returns to now-empty arms. Alcohol significantly diminished the ability to refrain from re-entry $F(3,20)=8.24$, $p<0.01$, an enduring deficit that showed no significant improvement across sessions.

Taken together, the results of Phase 1 indicate that for higher dose groups, while able to learn which set of arms are baited and which are not, an evidently strong tendency to return to the site of a recent reward damages their maze efficiency. Thus, even when contingencies reward spatial variability—successive new arm choices—alcohol-injected rats remain rigid.

The results of Phase 2 differed from those of Phase 1 in one respect. Whereas before, ethanol mildly impaired the ability to correctly select the set of four baited arms from among the eight possibilities, now the impairment is severe. As illustrated in Fig. 2, Medium and High dose rats run to unbaited arms almost as frequently as baited ones. Low dose and Saline animals, on the other hand, align their arm preference with the new contingency. The differences among groups are significant, $F(3,20)=18.8$, $p<0.01$, and while progressive improvement by Saline and Low dose groups led to a significant sessions effect, $F(7,140)=26.73$, $p<0.01$, the failure of the Medium and High groups to improve generated a significant Dose × Sessions interaction. $F(21,140)=2.60$, $p<0.01$. Sessions-to-criterion results (Table 2) and running time differences, $F(3,20)=8.64$, $p<0.01$ are in keeping with, and are probably chiefly due to, the failure of higher dose groups to run to the correct set of arms. Parenthetically, it might be observed that with respect to running time all groups improved across sessions, $F(7,140)=8.28$, $p<0.01$, and they improved at about the same rate. The rats with higher doses simply ran faster and faster, helping more of them to meet criterion. This adjustment occurred in the face of an unchanging arm selection accuracy.

The formal requirements of Phases 1 and 2 did not differ. It was owing only to the training in Phase 1 and the subsequent rigid perseveration induced by ethanol that the Medium and High dose groups failed to perform adequately. These findings indicate that learned strategies, whether running to a certain set of arms, or a certain recently visited arm, are repeated persistently. This suggests that the spatial variability deficit induced by alcohol is somewhat nonspecific.

EXPERIMENT 2

To what extent are some of the results of Experiment 1 attributable to nonreward? In displacing the baited set of arms 45°, Phase 2 of the preceding experiment rewarded abandonment of old patterns of behavior. But it also withdrew reward. There is evidence that alcohol retards extinction in some situations [1] and our own work [6] has convinced us of the reliability of this finding. Now it may be the case that resistence-to-extinction is merely invariability—rigid repetition and nothing more. Commonly, however, retarded extinction is taken to reflect a changed responsive-

TABLE 3

NUMBER OF SUBJECTS MEETING CRITERION IN PHASE 2, EXPERIMENT 2, (CHANGE TO ALL ARMS BAITED WITH NONREPLACEMENT)

Dose (g/kg)	Sessions 1	2	3	4	5	6	7	8
0	6	6	6	6	5	5	6	6
0.75	6	6	6	6	6	6	6	6
1.5*	3	4	3	6	5	6	6	6
2.0*	0	0	1	1	1	1	1	2

Criterion was defined as 2 successive sessions during which all 4 rewards were taken in the allotted (10 min) time. n=6/group.

*Significantly different from 0 and 0.75 groups, p's<0.06–0.002; 0 and 0.75 groups do not differ from each other.

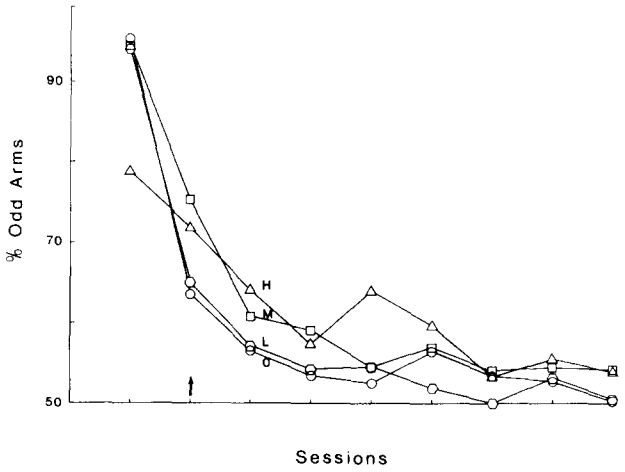

FIG. 3. Mean percent odd arms selected by rats in the various ethanol dose groups in Experiment 2. For reference, the last session of Phase 1 is indicated. Phase 2 (all arms baited) begins at the arrow. Abbreviations and performance index as in caption, Fig. 1.

ness to reward. Curiously, there are two more or less opposite conditions that are thought to lead to such a change. Either the aversiveness (or inhibitory property) of nonreward had diminshed e.g., [11]; or, the effects of nonreward have intensified such that frustration is increased and persistence redoubled (see [2] for a review). Experiment 2 is capable of testing the nonreward hypothesis, regardless of the form this hypothesis takes.

In its first phase it is identical to Experiment 1 with odd but not even arms baited. Where it differs is in Phase 2, all eight arms now being baited. The results showed that while Saline and Low dose groups rapidly took advantage of the increased bounty, the other alcohol groups continued to favor the original four arms they were trained to run to.

METHOD

Rats of the same age and sex of those in Experiment 1 were randomly assigned to the same ethanol dose groups (ns=6) as before and were trained in twelve sessions to run to the set of odd-numbered arms. In Phase 2, all eight arms were baited and the animals' performance under these circumstances was observed. Trial length, measures, and statistics were as before.

RESULTS AND DISCUSSION

The results of Phase 1 exactly paralleled the corresponding phase of Experiment 2. There were significant dose, $F(3,20)=11.5$, $p<0.01$, and session $F(21,140)=9.02$, $p<0.01$ influences in the percent selection of odd arms, and percent odd-arm repetition was significantly dose-related, $F(3,20)=3.12$, $p<0.05$, Together, these factors contributed to the disparate trials-to-criterion $H(3)=12.6$, $p<0.01$, and running time, $F(3,20)=9.6$, $p<0.02$, across groups.

In Phase 2, ethanol, especially at the highest dose, significantly promoted perseveration of the old habit, $F(3,20)=5.10$, $p<0.01$. This is depicted in Fig. 3 as a more enduring preference for odd arms, even though all were baited. As Table 3 indicates, Medium dose rats were eventually able to secure all eight rewards, but the High dose animals never performed well. This was owing not only to their reluctance to abandon the odd-numbered set of arms but also because, regardless of where animals ran, they were increasingly more likely to return to a previously visited arm as alcohol dose increased, $F(3,20)=6.18$, $p<0.01$.

Although the pattern of results was similar, comparisons between Fig. 2 and Fig. 3 suggest that the adjustment to the conditions of Phase 2, Experiment 2 was more rapid. This, we suspect, was in part owing to an unavoidable cue that may have promoted exploration. This cue was contained in the circumstance that, having obtained four rewards, the rats' customary removal by the experimenter was discontinued. This novelty may have aided in the discovery of the new rewards. The elimination of nonreward in this experiment may also have been contributory. In any case, a clear facilitation of perseveration prevailed here in the absence of extinction procedures.

GENERAL DISCUSSION

Earlier [8] we found that the spontaneous behavioral variability of rats was markedly narrowed by alcohol, and speculated that the drug would impair performance on tasks that required variability for their mastery. The present experiments were designed with this question in mind and the prediction has been borne-out. Except at the lowest dose employed, we found alcohol to severely impair a rat's adjustment to spatial rule changes, even when the change is without penalty of nonreward. Moreover, rats injected with ethanol are strongly inclined to return to the baited arms from which they recently exited. Thus, alcohol promotes the repetition of long-term habits maintained over several sessions (running to a certain set of arms) and "within-trial," recently executed responses (arm repetitions).

These findings add to the growing and apparently consistent literature (reviewed in [5]) that implicates alcohol as an agent of behavioral stereotypy. This drug narrows the variability of operant [4] and instrumental [6] response rates, operant [4] and instrumental [8] response sequences, and it narrows the diversity of topographies emitted in the straight-alley [7] and radial maze [8]. Finally, the spontaneous degree of spatial dispersion in two choice [3] and radial [8] mazes is considerably contracted by alcohol. The present study has now shown that the variability deficit can be extended beyond that emitted spontaneously. Even when

enforced by reward contingencies, stereotypy persists at higher doses. However, with this report, only the spatial dimension has been subjected to analysis. Whether ethanol exacts a similar stereotypy of performance across other reinforced dimensions remains to be seen.

The degree to which alcohol mimics the effects of hippocampectomy (e.g., [10,14]) and scopolamine (e.g., [9,10]) can be striking and bears mention here. We are tempted to propose the hippocampus as one of the more important targets of ethanol action. Our previous work [7], however, has indicated that the range of behaviors affected by alcohol's impairment of hippocampal function may be rather restricted. Our current radial-arm maze work combines hippocampal lesions with alcohol administration. To date, we find the manipulations to be independent and additive, not interactive. Thus, the neural basis of the results reported here and elsewhere [8] remains undiscovered.

ACKNOWLEDGEMENT

This study was supported by USPHS grant 7R01 AA05699-01 to L. D. D.

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