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The Effect of Ethanol and Sex on Radial Arm Maze Performance in Rats

DONNA M. MAIER AND LARISSA A. POHORECKY[1]

Center of Alcohol Studies, Rutgers University, Piscataway, NJ 08854

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MAIER, D. M. AND L. A. POHORECKY. *The effect of ethanol and sex on radial arm maze performance in rats.* PHARMACOL BIOCHEM BEHAV **25**(4) 703–709, 1986.—A daily dose of 1.5 g/kg of ethanol interfered with radial arm maze performance in rats. Ethanol inhibited the acquisition of a new win-shift response to obtain a food reward, especially when a previously learned response was present. This effect was greater in females than in males. Ethanol appears to suppress flexibility in the development of optimal performance of goal-directed behavior.

Sex Ethanol Radial arm maze Rats

CHRONIC ethanol use has been found to produce a variety of neurological and functional deficits in man and animals [7,44]. Prolonged ethanol administration in rodents has resulted in hippocampal cell damage, impaired maze performance, and difficulty in the acquisition of a shuttlebox avoidance task [6, 20, 28, 35, 42, 43]. Studies in human alcoholics have shown both morphological abnormalities of the brain and a variety of cognitive deficits including impaired memory, nonverbal abstraction, and visuospatial ability [7, 18, 19, 36–38]. Acute administration of ethanol in man has also been found to result in functional deficits on a variety of tasks including Raven's Progressive Matrices (which measure nonverbal visuospatial ability), digit span and free recall tasks (which measure memory) and divided attention tasks [23, 29, 31]. The possibility of sex differences in the effect of ethanol on cognitive performance has not been adequately explored. Alcoholic women have been found to be less impaired than alcoholic men on verbal and visuospatial tasks [19,38] and also to show a different pattern of cognitive deficits than male alcoholics [36,37]. One study found that acute administration of 0.76 g/kg of ethanol produced a greater impairment on a divided attention task in females than in males. At lower doses of ethanol, no sex differences appeared [29].

Gender differences in ethanol-induced cognitive deficits have produced somewhat conflicting results. Studies in male and female alcoholics are confounded by many factors. Women generally show better verbal abilities than men, which can be a source of interference when verbal measures are used to assess cognitive performance [36]. Patterns of drinking are different between the sexes (men begin drinking at an earlier age and for different reasons than women) [5]. Physiological make-up may also influence comparisons between male and female alcoholics. Blood ethanol concentration and ethanol elimination rates have been found to be higher in women than in men after a fixed moderate dose of ethanol [15,39]. However, the lower proportion of body water in women than in men was found to explain this effect [39]. In other studies, blood ethanol concentration has not been found to be different between the sexes [25, 40, 47].

It appears that female sex steroids can modulate ethanol metabolism, thereby influencing response to ethanol. Females taking oral contraceptives have been shown to have higher blood acetaldehyde levels and decreased ethanol elimination and disappearance rates [22,24]. Studies in mice have found greater acetaldehyde levels in male C57BL mice, possibly indicating a slower ethanol metabolism in males, but no gender differences were reported in ethanol elimination rates from heterogenous stock (HS) mice [1,34]. In albino rats, ethanol elimination rates were higher in females than in males after 6 weeks of free choice drinking of 10% alcohol solution [17]. This gender difference was explained by body weight differences and greater voluntary ethanol intake in females than in males. Overall, studies of gender differences in ethanol metabolism seem to indicate that female rodents metabolize ethanol more rapidly than males [8]. In humans, sex differences are less consistent, with women metabolizing ethanol at greater or equivalent rates than men and attaining higher or similar blood ethanol concentrations. Part of this variability is undoubtedly due to menstrual cycle phase and lower body water levels in females.

Devenport's group, in a series of studies, found a highly significant effect of moderate doses of ethanol (1.5 to 2.0 g/kg IP) on radial arm maze response in male rats while low doses (0.75 g/kg) had no effect. Ethanol-treated rats showed de-

[1]Requests for reprints should be addressed to Dr. L. A. Pohorecky.

creased behavioral variability in the radial arm maze which was expressed as fewer entries into different arms and fewer incidences of nongoal-directed behavior [13]. When food reward was contingent upon running to a specified subset of four of the maze's eight arms, ethanol-treated rats performed with less accuracy. They made more re-entry errors (re-entering an arm from which they had already removed the food reward). When the rewards were placed in previously unrewarded arms (reversal), requiring the rats to learn a new and competing response, ethanol-treated rats continued to enter the previously rewarded arms and failed to learn the new response [14]. Even when rewards were placed in all eight arms of the maze, ethanol-treated rats persisted in running to the originally baited arms, and avoiding the newly baited arms [14]. Saline-injected rats when subjected to extinction in the maze expanded the number of arms they visited, while ethanol-treated rats did not [10]. Devenport's work has shown that 1.5 to 2.0 g/kg of ethanol administered IP every other day results in a decreased ability to learn a maze task for food reward. While the ethanol-treated rats generally learned the task, their overall responding was less accurate, less flexible, and more disorganized [9].

A recent study found that a daily injection of 1.25 g/kg of ethanol interposed between a rat's fourth and fifth arm selections in an eight-arm radial maze (all arms rewarded) increased the number of re-entry arm errors and the time taken by the animals to obtain the remaining four food rewards [21]. Over the 10 days of treatment, the ethanol-treated rats took progressively more time to get the first four rewards which were obtained prior to the ethanol injection. This effect was possibly due to a conditioned aversion to the maze as a result of the unpleasant effects of ethanol treatment [21].

Ethanol appears to increase repeat errors in animals acquiring a maze response for food, and to interfere with the acquisition of an optimal strategy to obtain the food rewards [14,21]. Once the maze response has been acquired, ethanol appears to interfere with the learning of a new possibly competing response [10,14]. Animals with hippocampal damage also show perseverative and inflexible behavior and the effect of ethanol on behavior may be linked to hippocampal damage [9, 11, 12, 45]. Anticholinergic drugs such as scopolamine, also have been found to interfere with radial arm maze performance, usually by increasing the number of re-entry errors. Re-entry errors are generally interpreted to involve a deficit in working memory [4].

Two previous studies have found slightly better radial arm maze performance in male than in female rats [16,41]. However, in these studies, the animals were provided with enriched vs. impoverished environments, or were reared in the dark. One of these could not be replicated [3]. So, their findings require further support. Other studies using Hebb-Williams and Lashley III mazes have found superior male performance [23]. In these studies, though, the mazes were very similar to open fields, in which female rodents are normally more active and hence, more prone to maze errors [2,3]. A recent study by Beatty using a procedure similar to Devenport's in which some arms were consistently baited while others were not, found that female rats made more re-entry errors than male rats, and slightly more entries into never-baited arms than males [3].

The purpose of the present study was to extend Devenport's and Beatty's findings especially in regard to sex differences. In this study the subject was required to learn a new set of reward contingencies while under drug treatment. Only certain arms of the maze were baited with food rewards. The effect of acute ethanol on a well-learned radial-arm maze response and the rate of recovery from daily ethanol treatment were also investigated. It was hypothesized that ethanol would interfere with the acquisition of a new response in a previously learned task. The additional factor of sex was considered as previous studies have been conducted only with male animals.

STUDY 1

METHOD

Animals

Subjects were eight male (171.8±9.3 g) and 10 female (123.2±7.3 g) 41- to 49-day-old rats (from three litters) bred in our laboratory from Holtzmann Sprague Dawley parents (Charles River Co., Wilmington, MA). Subjects were partially food deprived; they received only one to three pellets of Purina rodent chow per day, depending on body weight loss during the preceding 24 hours. This was sufficient to maintain body weight with moderate weight gain. Mean body weight at the conclusion of the experiment was 250.4±9.7 g for the males and 204.6±7.1 g for the females. Subjects were pair-housed in standard stainless steel cages in a colony room (lights on 0800 to 2000 hours).

Apparatus

An eight-arm radial arm maze was constructed of plywood and painted a glossy black [30]. The central portion of the maze was an octagon 43 cm in diameter. The arms were 86 cm long and 12.5 cm wide. The maze was 56 cm in height and was located in the center of the colony room. Animal racks, the door, and other articles of furniture in the room provided many extramaze cues. A small food cup at the end of each arm was baited with a chocolate chip (Foodtown, Inc., Edison, NJ). The arms were numbered and only the four odd-numbered or even-numbered arms were baited at any one time, depending on the phase of the experiment. Chocolate chips were located at several locations of the colony room near the maze to prevent the animal from being guided to the correct arms by odor cues.

Procedure

Testing was always conducted during the light portion of the diurnal cycle. The appropriate four arms (odd or even-numbered) were baited with a chocolate chip and the animal was placed in the center of the maze. The animal received two 3 minute trials per day separated by a 1 minute intertrial interval which was spent in a holding cage. Between trials, the maze was washed with a 70% ethanol solution and chocolate chips were replaced in the food cups. Injections were given intraperitoneally 12 or 15 minutes prior to the first trial and consisted of a 1.5 g/kg dose of 10% w/v ethanol or saline. This dose was chosen because it was found by Devenport to induce deficits in maze responding and because it does not produce depression of motor behavior (for an overview see [32]). Subjects were weighed daily and received their food ration at the end of the day. The following observations were made on each trial: time required by the animal to obtain all four rewards (time to criterion), number of even and odd arms visited before obtaining all four rewards (pre-criterion), and number of even and odd arms visited after obtaining all four rewards (post-criterion). Since time to obtain all four

TABLE 1

TIME TO CRITERION (MINUTES) AFTER A 1.5 g/kg INJECTION OF ETHANOL OR SALINE WITH ODD ARMS BAITED (STUDY 1-PHASE 2)

	Females	Males
Ethanol	3.0 ± 0.40	1.9 ± 0.41
Saline	1.8 ± 0.22	1.5 ± 0.22

rewards is obviously an important factor to a food-deprived animal, it was postulated that the optimal strategy would be to obtain the food rewards in as short a time as possible with the minimum amount of work (arm visits). The experiment was divided into four phases.

Phase 1—odd arm training. Only the odd-numbered arms were baited. The animal was required to run to the odd-numbered arms and obtain all four chips in 3 minutes or less (criterion). This initial training phase lasted 16 days, by which time all animals had reached criterion and were performing consistently to criterion on each trial.

Phase 2—ethanol given post-acquisition. Only the odd-numbered arms were baited. Each animal received one injection each of 1.5 g/kg of ethanol or saline on two separate days 15 minutes prior to the testing trials. The purpose of this phase was to see if acute ethanol administration would disrupt the previously acquired maze response.

Phase 3—ethanol given during reversal. Only the even-numbered arms were baited in this phase. The animals were divided into four groups: female-ethanol, female-saline, male-ethanol, and male-saline. Each animal received a 1.5 g/kg dose of ethanol or saline daily 12 minutes before the first maze trial. The animals were required to learn to run to the even-numbered arms and obtain all four rewards in 3 minutes or less. This phase lasted for 12 days. Due to a sluggishness on the part of ethanol-treated animals, they were given 5 minute instead of 3 minute trials.

Phase 4—no ethanol. Only the even-numbered arms were baited. Daily injections were ended so the animal was drug-free. The purpose of this phase was to assess if the animal could reach criterion on the maze task when the stress of the injection and the effect of the drug were removed. This phase lasted 1 day in the saline-treated animals and 3 days in the ethanol-treated animals. The saline-treated animals received two, 3 minute trials, while the ethanol-treated animals received two, 5 minute trials.

The data were analyzed using a repeated measures (two-way) analysis of variance with drug and sex as the between subjects (one-way) factors [25].

RESULTS

Phase 1—Odd Arm Training

Every subject acquired the odd-arm response to criterion. There were no significant sex differences. Once animals learned to go to the odd arms, their performance was rapid and consistent. On the last day of Phase 1 subjects obtained all four rewards in a mean time of 1.6±0.12 minutes. A distinct preference was displayed for the odd arms (7.7±0.40 total odd arm visits/trial vs. 3.1±0.28 total even arm visits/trial). The animals visited the odd arms almost exclusively prior to criterion and visited the even arms mostly after they had eaten the four chips from the odd arms. Prior to drug

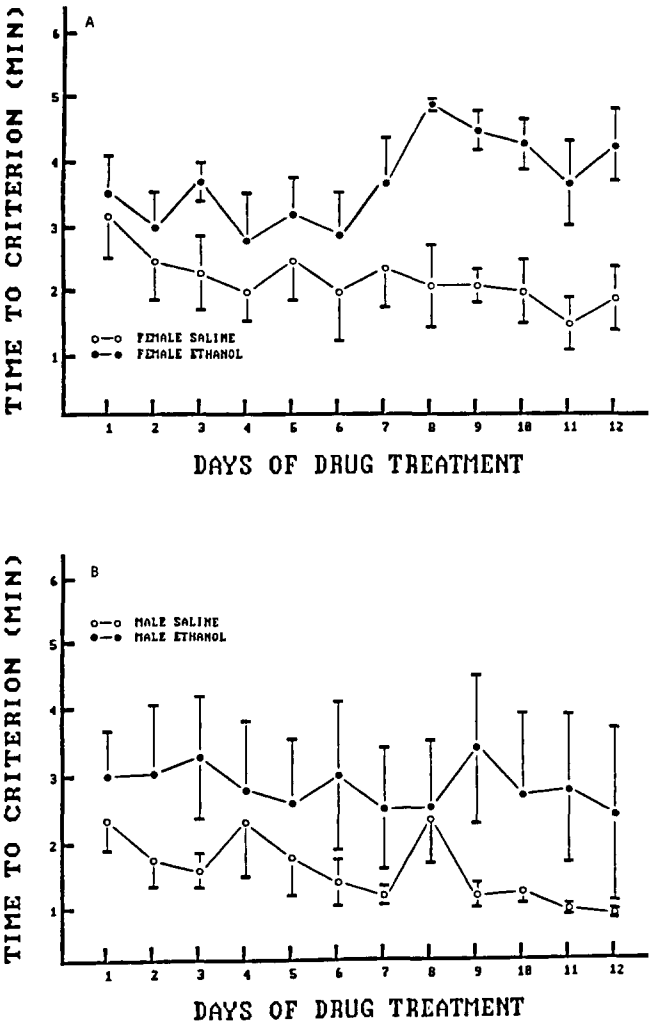
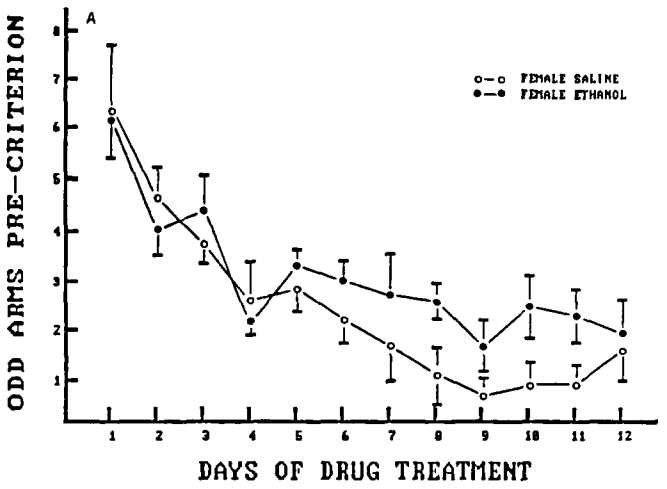


FIG. 1. Phase 3: Mean±standard error of the mean time (minutes) to obtain all four rewards from the even-numbered (correct) arms of the maze 12 minutes after an IP injection of 1.5 g/kg of saline or ethanol. Data are plotted over the course of 12 days of drug treatment. (A) Data from female rats. (B) Data from male rats.

administration, no significant sex differences existed in maze performance.

Phase 2—Ethanol Post-Acquisition

Acute administration of 1.5 g/kg of ethanol significantly increased the time taken by the animals to obtain all four rewards, $F(1,52)=9.86$, $p<0.01$. There were no significant sex differences even though the females appeared to show a greater increase in time to criterion than the males (Table 1). The number of odd and even arm visits, both prior to and after criterion, was not affected significantly by drug treatment, indicating that this dose of ethanol did not suppress motor activity. Sex did not exert a meaningful effect on these measures either. Overall, it appeared that ethanol disrupted performance only by slowing the animal down. Ethanol did not affect the subject's memory for correct (rewarded) and incorrect (non-rewarded) responses. The effect of ethanol was primarily a disruption in performance leading to slower retrieval of the food reward.



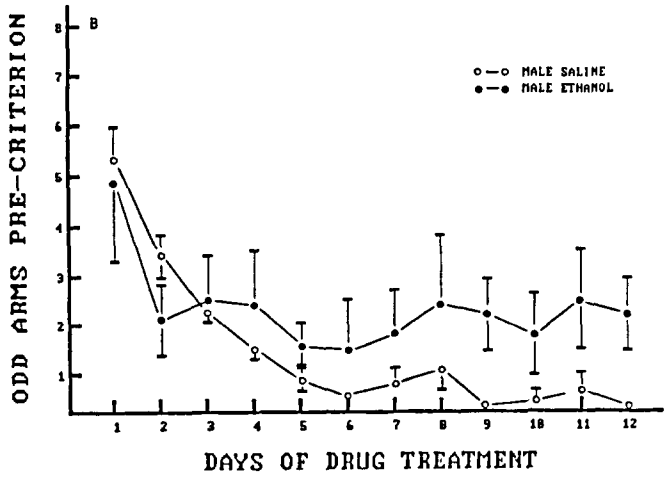


FIG. 2. Phase 3: Mean±standard error of the mean number of odd (incorrect) arms visited pre-criterion 12 minutes after an IP injection of 1.5 g/kg of saline or ethanol. Data are plotted over the course of 12 days of drug treatment. (A) Data from female rats. (B) Data from male rats.

Phase 3—Ethanol During Reversal

Daily administration of 1.5 g/kg of ethanol increased the time taken by the animal to obtain all four rewards from the even-numbered arms, $F(1,14)=6.89$, $p<0.025$. Over days of testing, ethanol-treated animals increased the amount of time needed to get all four rewards while no increase was seen in the saline-treated animals over time (Fig. 1). While sex alone was not a significant factor, there was a significant sex by time interaction, $F(1,150)=10.1$, $p<0.01$, and also a significant drug by time interaction, $F(1,150)=5.93$, $p<0.025$. Trend analysis revealed that both of these interactions were best described as linear shifts in responding over time. This is indicated in Fig. 1 by an increase in time to criterion over days of ethanol treatment in females but no change in males over time, whereas both saline-treated males and females showed a slight decrease in time to criterion over days of treatment. This decrease was more pronounced in the males

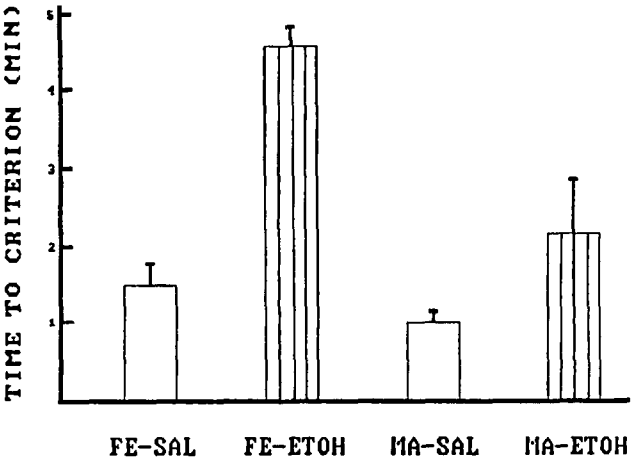


FIG. 3. Phase 4: Mean±standard error of the mean time (minutes) to obtain all four food rewards from the even-numbered (correct) arms of the maze on Day 1 of recovery (no drug injection preceding the maze trial). Rats had previously been treated with 1.5 g/kg of saline or ethanol IP for 12 days.

than in the females. This indicates a differential effect of ethanol treatment with sex: female performance actually worsened over time with ethanol treatment while male performance merely failed to improve with time (Fig. 1).

Because of the increased time to criterion seen in the ethanol-treated females, both odd and even-numbered arm visits post-criterion decreased significantly in this group, $F(11,150)=4.70$, $p<0.001$: $F(11,150)=6.27$, $p<0.001$. Since this is due solely to the time factor (more time pre-criterion means less time post-criterion in a 5 minute trial), it cannot be considered to indicate any additional cognitive deficit produced by the drug. There were no other significant effects on either post-criterion measure.

The number of even arms visited prior to criterion was not significantly affected over time by either drug or sex, indicating that all four treatment groups did acquire the even-arm response. The number of re-entry errors into the baited arms did not differ between the two groups, showing no impairment of working memory by ethanol in the baited arms.

Drug treatment did exert a significant effect on the number of odd (incorrect) arms visited prior to obtaining all four rewards. Ethanol-treated animals visited significantly more odd arms pre-criterion than saline-treated animals, $F(1,14)=6.92$, $p<0.025$ (Fig. 2). Sex also exerted a significant effect with females making more odd arm visits pre-criterion than males, $F(1,14)=10.96$, $p<0.01$ (Fig. 2). The difference between groups became more evident as drug treatment progressed. The increase in odd arm visits pre-criterion indicates that the ethanol-treated animals were not experiencing a suppression of motor activity. Instead they showed a persistence in running to arms that had previously been rewarded, even though this increased the time taken to obtain all four food rewards.

Overall, these data show that daily treatment with 1.5 g/kg of ethanol decreased the ability of the animal to acquire a new even-arm response. While the animal did acquire the even-arm contingency, it could not perform the response as well as a saline-treated animal (Figs. 1 and 2). The ethanol-treated animals persisted in visiting the previously rewarded

(odd-numbered) arms, thereby increasing the time to get all four rewards and increasing the amount of work they did for the rewards. They did not employ the quickest and most optimal strategy to obtain the rewards. Ethanol treatment also retarded the extinction of the incorrect odd-arm response which interfered with rapid and efficient retrieval of the food rewards (Fig. 2). Female animals appeared to be more sensitive to these effects of ethanol than male animals, especially as the length of drug treatment progressed.

Phase 4—No Ethanol

Animals previously treated with ethanol showed a significant increase in time to criterion when compared with those previously treated with saline, $F(1,14)=37.5$, $p<0.001$ (Fig. 3A). Sex and a sex by drug interaction exerted significant effects on the length of time necessary to obtain the four rewards, $F(1,14)=15.93$, $p<0.01$: $F(1,14)=6.66$, $p<0.025$. Females previously treated with ethanol took significantly longer to reach criterion than ethanol-treated males. Saline-treated males and females did not differ (Fig. 3A). This again shows a greater sensitivity to the effect of ethanol in the female subjects. The number of odd and even arms visited post-criterion was significantly decreased in ethanol-treated animals, $F(1,14)=5.78$, $p<0.05$: $F(1,14)=5.11$, $p<0.05$. This was due to the increase in time taken to reach criterion and cannot really be considered indicative of other cognitive deficits. Odd arm visits pre-criterion were not significantly influenced by drug or sex.

A repeated measures analysis was done on the data from the 3 days of drug-free recovery training given to the ethanol-treated animals. This analysis revealed no significant improvements in maze performance on any measure over the course of the drug-free training. Thus, 3 days of drug-free training were not sufficient to overcome the performance deficit produced by ethanol.

STUDY 2

As a significant sex by ethanol effect has not been previously reported, a second experiment employing a modification of Devenport's procedure was undertaken with sex as a second variable [14]. In the first study, the effect of sex and ethanol on acquisition of a new and competing maze response was explored. In the second study, animals were treated with ethanol from the start of their experience with acquisition of the maze task.

METHOD

As before, subjects were bred in our laboratory from Holtzmann Sprague Dawley rats. Subjects were 9 male (301.4±6 g) and 10 female (188.9±5.7 g) 60-day-old rats from two litters. Mean body weights after 12 days of maze training and accompanying food deprivation were 248±6.5 g for males and 173.7±4.5 g for females. For 3 days prior to the study, subjects were placed in the maze for 7 minutes per day in order to become familiar with it. The food deprivation and drug injections were begun. The rats were randomly divided into four groups: female-saline, female-ethanol, male-saline, and male-ethanol. Ethanol-treated rats received 1.5 g/kg of 10% w/v ethanol IP 13 minutes prior to the maze trial while saline-treated rats were injected IP with saline. The subjects received one 6 minute trial in the maze for the first 6 days of training, and on days 7–12, two 3 minute trials were given. As before, odd arms were baited with chocolate chips. Two days after the conclusion of maze training and drug injections (12 days total of each), blood ethanol concentration was measured 20 minutes after an IP injection of 1.5 g/kg of 10% ethanol in *all four* groups. A one milliliter sample of equilibrated expired air was taken from an airtight plastic cylinder placed over the animal's nose and mouth, and was then injected into a gas chromatograph (Shimadzu Scientific Instruments, Inc.) as previously described [23].

RESULTS

Blood ethanol concentration was significantly higher in the male-ethanol group (135.6±12.1 mg%) than in the other three groups, $F(1,15)=6.11$, $p<0.05$, at 20 minutes post-injection of 1.5 g/kg ethanol. Blood ethanol concentrations in the male-saline, female-ethanol, and female-saline groups were respectively, 81.4±16.3 mg%, 81.3±9.9 mg% and 94.9±15.3 mg%.

Odd (correct) and even (incorrect) arm visits post-criterion, and time to criterion were not significantly affected by drug, sex, or their interaction. Total arm visits pre-criterion, odd arm visits pre-criterion (re-entry errors), and even arm visits pre-criterion were significantly greater in the ethanol-treated animals, $F(1,15)=21.3$, $p<0.001$: $F(1,15)=5.61$, $p<0.05$: $F(1,15)=21.52$, $p<0.001$. This indicates that this dose of ethanol did not depress motor activity. Sex did not exert a significant effect on any measure. Days to reach criterion (four chips in 3 minutes or less) or the number of chips obtained per trial were not affected by drug or sex. The results of this study show that despite a higher blood ethanol concentration in the ethanol-treated males, ethanol-treated males and females were equally impaired in their radial arm maze performance. Ethanol-treated animals made more re-entry errors than saline-treated ones, which replicates Devenport's finding [14]. While ethanol-treated animals showed an odd arm preference, they still made many visits to the unrewarded even-numbered arms. Their performance was less accurate and less organized; they appeared to be less aware of the contingencies of the task than the saline-treated subjects. Beatty found that untreated female rats made more re-entry errors than male rats when six out of eight arms were baited [3]. We were unable to replicate this in the saline-treated animals, possibly due to small sample size, injection stress, or the real absence of such a sex effect. The more severe effect of ethanol seen in female animals in Study 1 was not seen here. The task itself was somewhat different as the subjects in Study 2 did not have to acquire a new and competing response in a previously learned task.

GENERAL DISCUSSION

Overall, this research extends previous findings that moderate doses of ethanol interfere with the acquisition of a win-shift radial arm maze response [14,21]. Depression of locomotor activity was not responsible for the deficit as ethanol-treated animals made more pre-criterion arm visits than controls. It also suggests that female rats may be more sensitive to some aspects of this than male rats. There were no baseline sex differences in acquisition or performance of the task. When initial exposure to the maze was accompanied by drug injection (Study 2), significant sex differences were not present. However, the presence of ethanol when the animal was required to learn a new maze response in the face of an old competing response (Phase 3—Reversal) did produce a significant sex difference. Female rats treated with

ethanol were more impaired over time than male rats treated with ethanol and both showed significantly poorer maze performance than saline-treated rats. This sex difference persisted even after drug treatment was discontinued (Phase 4). Ethanol-treated rats did not show improved maze performance after drug treatment was ended (Phase 4) and this effect was more severe in females than in males. Variability about the means was higher in ethanol-treated males than in females. Performance of a previously acquired response (Phase 2) was only slightly worsened by acute ethanol administration and sex did not exert a significant effect on this disruption. Blood ethanol concentration was actually higher in males than in females in Study 2, which suggests that higher blood ethanol concentrations cannot account for the more impaired performance of the female rats in Phases 3 and 4 of Study 1. However, subjects in Study 2 were older and heavier than those in Study 1, so BEC differences with sex in Study 2 may not be generalizable to Study 1. While previous studies have shown that female rodents metabolize ethanol faster than males [8], the effect of gender on blood ethanol concentration is not clear cut. Animals used in Study 2 were fasted at the time of breath sampling. Fasting in rats has been found to decrease ethanol metabolism [27]. The males in Study 2 lost more weight than the females so their rate of ethanol metabolism may have decreased more which could have contributed to higher blood ethanol levels in the males. However, results of another unpublished study on three male and three female 60-day-old non-fasted naive rats injected IP with 1.5 g/kg of ethanol showed a much higher blood ethanol concentration in the males at 25 minutes post-injection (112.4±3.0 mg% vs. 81.5±5.0 mg%). In fact, blood ethanol concentrations were higher in males from 15 to 60 minutes post-injection. Possibly, the higher blood ethanol levels in males from our laboratory are due to the paired housing conditions or to the young age of the subjects.

This study supports the contention that ethanol treatment interferes with performance by decreasing an animal's ability to adjust its behavior to new reinforcement contingencies. The results of Phases 3 and 4 illustrate this quite well. A response learned in a non-drugged state interfered with the acquisition of a new and competing response in the drugged state. Rather than extinguish the old response, ethanol-treated rats persisted in performing it even though it interfered with attaining a food reward. This is not simply a learning deficit. In all phases of this study, all rats regardless of drug treatment, showed a preference for the rewarded arms (in the sense that they visited them more often). It appears that the rats "knew" where to go. Ethanol interfered with this by suppressing extinction of an old response (Phases 3 and 4) or by interfering with the development of an optimal search strategy (Study 2). Devenport's work has shown that animals treated with 1.5 to 2.0 g/kg of ethanol, displayed a decrease in behavioral variability in the radial arm maze when all eight arms were continuously rewarded (re-baited after the rat retrieved the food) [13]. In this situation, the rat could run to any arm and always obtain a food reward. With ethanol treatment, the rat's pattern of arm choices became less variable and more predictable [13]. Ethanol promoted a more stereotyped response pattern. However, when response contingencies were changed, in the present study and previous studies, ethanol interfered with the development of new patterns of behavior [10,14]. Ethanol appears to decrease the flexibility of goal-directed behavior: to actively suppress the development of optimally effective strategies if old behavior patterns are present to interfere. This suppression may be more severe in female rodents than in males. In terms of human behavior, one could hypothesize that alcohol use may inhibit the development of optimal strategies to achieve certain goals especially if previously acquired strategies are present to interfere.

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