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Ethanol Self-Administration in Water Satiated Rats[1]

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ANDERSON, W. W. AND T. THOMPSON. *Ethanol self-administration in water satiated rats.* PHARMAC. BIOCHEM. BEHAV. 2(4) 447–454, 1974. – The effects of water deprivation on acquisition of oral ethanol-reinforced responding by rats were studied. Rats previously trained to lever press for water responded for oral ethanol (8% W/V) as readily when water satiated as when water deprived. Though water deprivation was initially associated with high ethanol intake, on subsequent water satiation ethanol intake was comparable. The effects of Fixed-Interval (FI) schedules of ethanol reinforcement were also studied. The portion of the session occupied by ethanol-reinforced responding varied directly with FI parameter value. The volume of ethanol consumed varied inversely with FI value.

Ethanol Self-administration Deprivation Water deprivation

WATER deprivation increases oral ethanol consumption by animals [5, 14, 15]. However, of the studies reported to date, the highest rate of ethanol consumption has been accomplished using schedule-induced polydipsia [6, 8, 10], a phenomenon characterized by the consumption of extraordinarily large quantities of liquid by animals concurrently exposed to intermittent schedule of food reinforcement [1]. Further, following discontinuation of the inducing food schedule rats continued to consume ethanol at rates ranging from 300 mg/kg/hr to 800 mg/kg/hr over six-hr sessions [9]. These rates are considerably higher than those reported in other studies in which subjects were not first induced to consume ethanol [7,17]. One possible explanation for the difference is that the initial consumption may have exposed the animals to the reinforcing properties of ethanol.

The primary purpose of the present study was to determine whether a 4% W/V ethanol solution would be orally self-administered to a greater degree by rats initially trained to drink ethanol when water deprived than by rats never water deprived during exposure to ethanol. These data shed light on the relevance of water deprivation in establishing ethanol as a reinforcer. That is, is ethanol a reinforcer only incidental to water consumption (95% in this case) or is it reinforcing in its own right?

In addition, this study investigated ethanol self-administration on fixed-interval (FI) schedules (i.e., schedules on which a response was reinforced only if a fixed amount of time had elapsed since the previous reinforcement). Fixed-interval schedules were used in an attempt to distribute responding over a greater portion of the experimental session and to determine the similarity of the patterns of responding to those observed with other reinforcers.

METHOD

Animals

The animals were four male Holtzman Sprague-Dawley albino rats, Numbers D-1, S-2, D-4 and S-6, maintained at 80% of their free-feeding body weights (380, 400, 400 and 420 g, respectively). All animals were approximately 8 months old at the beginning of the study.

Apparatus

The apparatus consisted of 4 identical Gerbrands operant rat test chambers equipped with two rat levers, a 0.25 ml liquid reinforcement dipper, a dipper light and a house light. The chambers were individually housed in sound-attenuating boxes. Electromechanical programming and recording equipment was located in a separate room.

Procedure

Throughout the study, the animals were given daily 5-hr sessions. During all phases of the study, reinforcement consisted of a 4-sec presentation of a 0.25 ml dipper. The dipper light was illuminated for 5 sec upon activation of the dipper mechanism. House lights were illuminated during the session and extinguished automatically at the end of each session. The animals were then removed, returned to their home cages, and fed to their 80% weights. The experi-

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mental phases, procedures employed and their durations are shown in Table 1. All animals were first trained to lever press for water reinforcement on a continuous-reinforcement (CRF) schedule, i.e., each response was reinforced with water. During this phase, the rats' only liquid intake was consumed during the experimental session. No water was available during the 19-hr period between sessions. When daily lever pressing was observed in all animals, they were given 5 weeks of daily sessions during the first phase of the study, as indicated in Table 1. During the first 3 weeks, all animals received indentical treatment. The reinforcer during this period was tap water. The animals were water deprived during Week 1 (Days 1–7), water satiated (water freely available in home cages) during Week 2 (Days 8–14), and, again, water deprived during Week 3 (Days 15–21). During Week 4 (Days 22–28), the reinforcer for all animals was a 4% W/V solution of ethanol in tap water. During this first week of exposure to ethanol, Rats D-1 and D-4 were water deprived, while Rats S-2 and S-6 were water satiated. During Week 5 (Days 29–35) the reinforcer remained 4% ethanol solution, but all 4 animals were water satiated. The three weeks of water reinforcement served as control periods under conditions of water-satiation and water-deprivation. The performance during these periods constituted a water baseline which will be compared with the performance for ethanol reinforcement during the fourth and fifth weeks.

TABLE 1

Day	Rat. No.	Deprivation Conditions	Reinforcer
1–7	D-1 and D-4 S-2 and S-6	H_2O Deprived	H_2O
8–14	D-1 and D-4 S-2 and S-6	H_2O Satiated	H_2O
15–21	D-1 and D-4 S-2 and S-6	H_2O Deprived	H_2O
22–28	D-1 and D-4 S-2 and S-6	H_2O Deprived H_2O Satiated	4% Ethanol
29–35	D-1 and D-4 S-2 and S-6	H_2O Satiated	4% Ethanol

When all 4 animals were self-administrating 4% ethanol solution, the concentration was doubled daily to a maximum of 32% (4, 8, 16, 32% W/V). Each animal was then given the four concentrations, one daily, in a descending series, followed by another replication in an ascending series. At the end of each series there was one control session, during which responses produced only water.

During the second phase of this research, animals self-administered 4% ethanol on various FI schedules. After 3 days on CRF schedule of 4% ethanol, the schedule of reinforcement was changed to FI 20 sec with a 1-min limited hold (i.e., reinforcement was unavailable for 20 sec following each reinforced lever press). At the end of the 20 sec interval, there was a 1-min period during which the first lever-press produced ethanol reinforcement. A reinforced lever-press or lapse of the 1 min limited hold produced the next 20-sec interval. The limited hold was used to maintain a higher response rate, since on such a schedule responses following a pause greater than 1 min would not be reinforced. The fixed interval value was lengthened every third day until the animals were responding on a fixed-interval of 4 min. When all animals had responded on an FI 4 min schedule for 3 days, preliminary training was discontinued and all animals were returned to a CRF schedule.

Following this preliminary training, all animals were given 1 week of daily sessions on each of 5 schedules in the following order: CRF, FI 1, FI 2, FI 3, FI 4. The limited hold remained at 1 min throughout the entire experiment. Each week, 5 daily sessions with 8% W/V ethanol solution as reinforcer were followed by 2 daily control sessions during which only water was present in the dipper. Subsequently, all animals were returned to CRF with an 8% solution.

During all sessions, the following data were recorded: (1) total responses per sessions, (2) total reinforcements per session, (3) volume of liquid consumed per session, (4) reinforcements per 10-min interval, and (5) a cumulative record of responses and reinforcements.

RESULTS

Acquisition of Ethanol Self-Administration

The volume of liquid consumed by each animal per 5-hr session is shown for the first 35 days in Fig. 1. Similar trends are seen for all 4 animals. During Week 1, the mean water consumption per session per animal was 25.4 ml under water deprivation. During Week 2, under water satiation, mean consumption dropped to 5.7 ml of water per session per animal. During Week 3, again under water deprivation, mean consumption rose to 25.6 ml of water per session per animal.

During Week 4, the water-deprived animals (D-1 and D-4) consumed an average of 20.2 ml of 4% ethanol solution per session per animal. This was slightly less than their water consumption under similar deprivation conditions during Weeks 1 and 3. Both animals exhibited unstable gait, inability to maintain rearing posture and extended periods of inactivity and apparent sleep. The water-satiated animals initially consumed only small amounts of 4% ethanol solution. Their mean consumption on the first day of Week 4 was 4.0 ml per session per animal. However, consumption by both animals consistently rose over the seven sessions of Week 4.

When Rats D-1 and D-4 were water satiated at the beginning of Week 5, their intake of 4% ethanol solution dropped to the level of water control seen in Week 2. Their mean consumption of 4% ethanol solution on the first day of Week 5 was 8.0 ml per session per animal. The mean water consumption for the same 2 animals under similar deprivation conditions during Week 2 was 7.4 ml per session per animal. Rat D-1 showed a gradual increase in

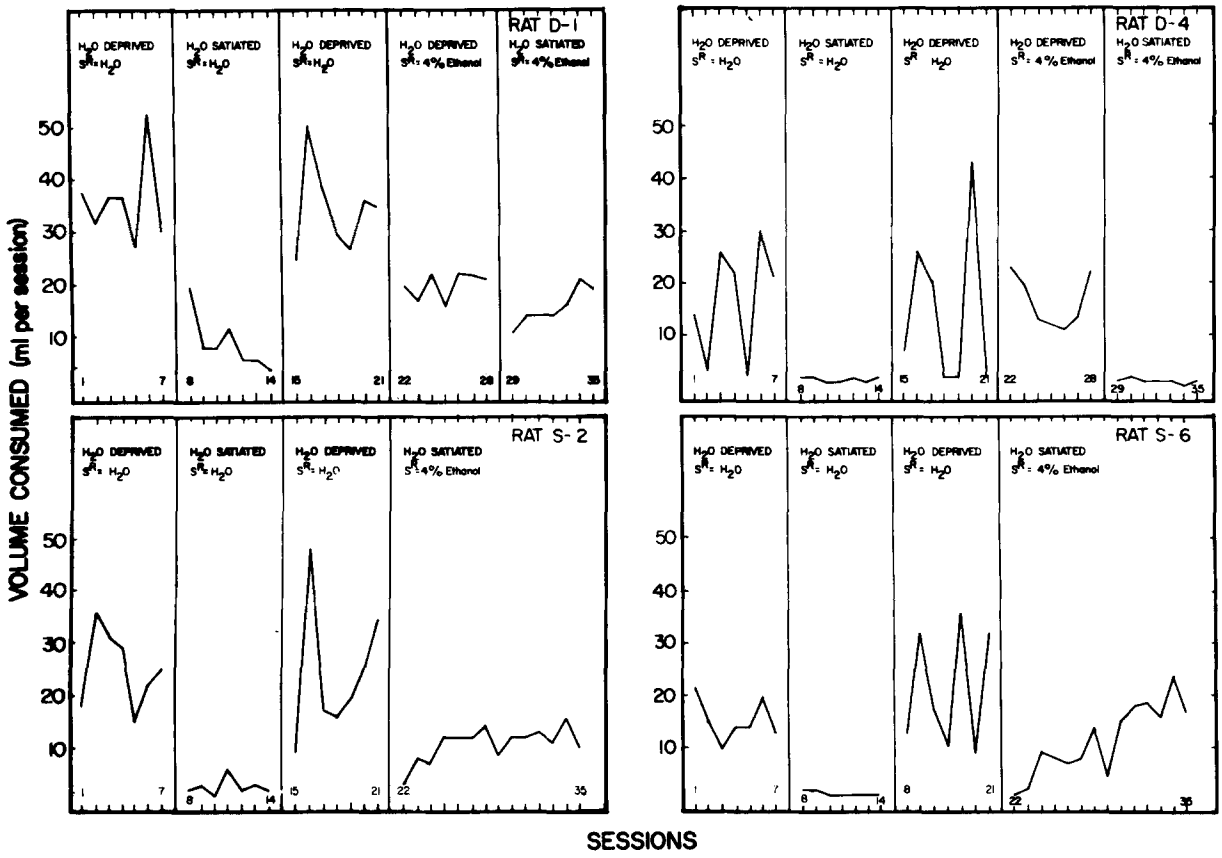

FIG. 1. Volume of water (H_2O) and 4% ethanol consumed in ml per session for 4 rats when water deprived and satiated.

ethanol consumption over the seven sessions of Week 5. Rat D-4 reliably self-administered 4% ethanol solution only after several additional weeks of training. These data are not included in Fig. 1. Rats S-2 and S-6 continued to self-administer 4% ethanol solution under water satiation during Week 5. By the end of Week 6, all 4 animals were self-administering volumes of 4% ethanol solution above water control.

The volume of ethanol solution consumed per session is shown as a function of concentration in Fig. 2. Consumption was above water control for all concentrations tested. The mean consumption of 4% ethanol solution was 16.5 ml per session per animal, approximately 3 times the water control level in Week 2, and more than 20 times the water control level following stabilization (0.75 ml per session per animal). Increased concentration resulted in a decrease in volume consumed. Since the concentration was doubled at each increment, the volume consumed decreased by less than one-half. The quantity of ethanol consumed (in grams) increased with concentration (Fig. 3). The mean consumption of ethanol at 4% was 0.66 g per session per animal or 330 mg/kg/hr. At 32%, the average consumption was 1.12 g per session per animal or 560 mg/kg/hr. Rat D-1, consistently consuming more ethanol than the other animals, consumed an average of 1.28 g per session or 640 mg/kg/hr at 32%. These values are all considerably above the metabolic rate of 300 mg/kg/hr.

The animals frequently exhibited impaired gait, inability to maintain rearing posture, and periods of inactivity and apparent sleep. This was seen most frequently at concentrations above 4%, particularly during sessions in which the animal consumed a large portion of his daily intake during the initial 10 min of the session. Following a large burst of responding at the beginning of a session, the animals could frequently be observed lying on the floor of the chamber.

Fixed Interval Schedules

Shortly after all animals were returned to an 8% solution on a CRF schedule, Rat S-6 developed a respiratory infection and was removed from the study. Therefore, data presented for Rat S-6 are from preliminary training only. For all other animals, the data presented are from the last 5 days on each schedule (3 ethanol days and 2 water control days) during the second exposure to the series of schedules.

Sample cumulative records of each animal's performance during the first 60 min of one session on each of the 5 schedules are shown in Fig. 4. There is a period of moderate- to high-rate responding early in the session, followed by a pause. The amount of time over which responding was

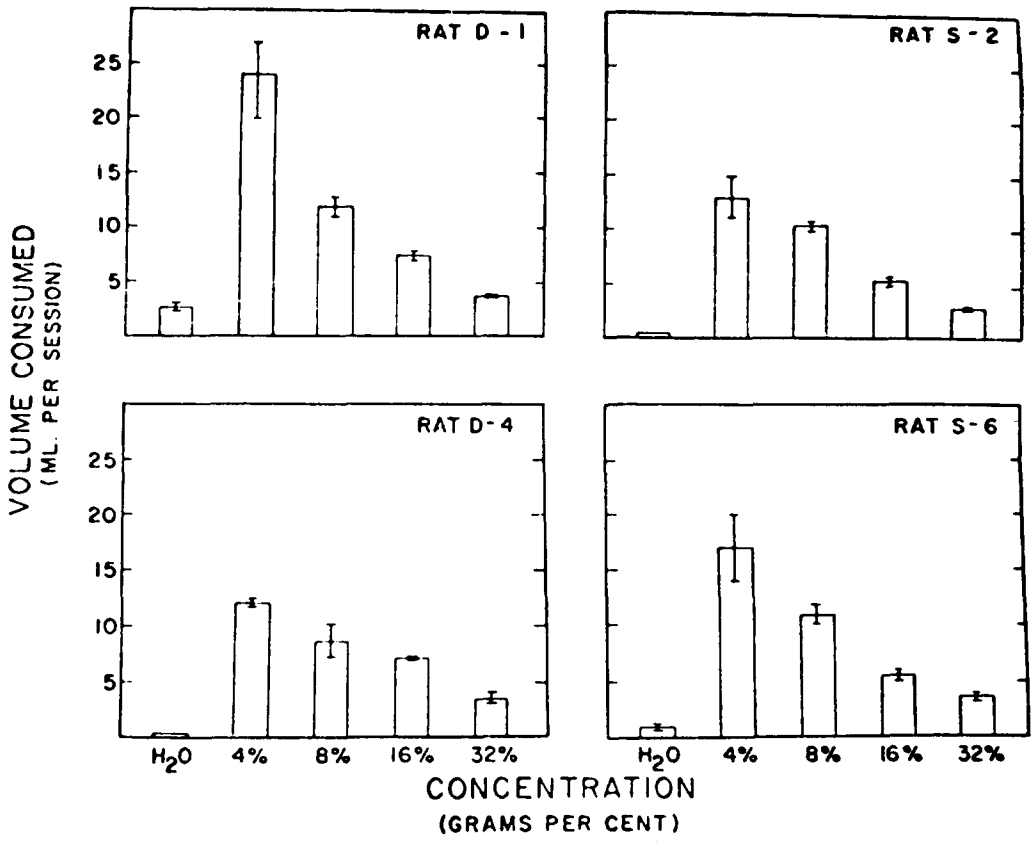

FIG. 2. Volume of water and ethanol consumed (4–32%) by 4 rats. Height of bars equals mean consumption, while ranges are indicated by vertical lines.

distributed increased as the schedule parameter was increased. When on a CRF schedule, animals typically completed the initial high-rate responding within the first 10 min of the session. At longer fixed-interval values, the initial high-rate period frequently extended over the first 30-40 minutes of the session. The pattern of responding during the interval is typical of fixed-interval responding for non-drug (2) and drug reinforcers (16): A pause after reinforcement followed by a progressively higher rate of responding until the next reinforcement.

The CRF pattern typically consisted of a burst of responding early in the session, followed by one or more bursts later in the session. As the fixed interval value was increased, responding was distributed over a larger portion of the session. On CRF, responding was typically concentrated within a very small portion of the total session time. However, at higher fixed-interval values, the animals distributed their responding over as much as 1/3 to 1/2 of the 5-hr session.

The total number of responses emitted by each animal per 5-hr session is shown as a function of schedule in Fig. 5. As the fixed-interval was increased, the average number of responses per session increased from 62.9 at CRF to 217.7 at FI 3 and then dropped to 167.2 at FI 4.

The total volume of liquid consumed per 5-hr session is shown as a function of schedule in Fig. 6. As the fixed-interval was increased, the mean volume of 8% ethanol solution consumed per session per animal decreased from an average of 12.4 ml of CRF to 4.9 ml at FI 4. Water consumption on control days remained essentially unchanged at an overall mean (across concentrations) at 1.1 ml per session per animal.

DISCUSSION

These data demonstrate that ethanol self-administration can be obtained in food-deprived rats without the use of any other experimental technique to induce the initial consumption of large amounts of the drug solution, an observation consistent with other recent findings [11]. When an animal is induced to consume ethanol solution by water deprivation, by schedule-induced polydipsia or other procedure, it is presumably initially consuming water, and only incidentally the ethanol contained in it. It follows that having been exposed to the reinforcing effects of the drug, the animal may exhibit a greater tendency toward self-administration in the future. In the present study, however, Rats S-2 and S-6 were water satiated during all exposures to ethanol. Their initial consumption of ethanol solution was at the level of water control, demonstrating that they were not induced to consume large amounts of ethanol. However, because of their previous experience with the lever-press operant, ethanol self-administration was made more probable, and acquisition occurred within one week. Furthermore, the ethanol self-administration by Rats S-2 and S-6 was not significantly different from that by Rat

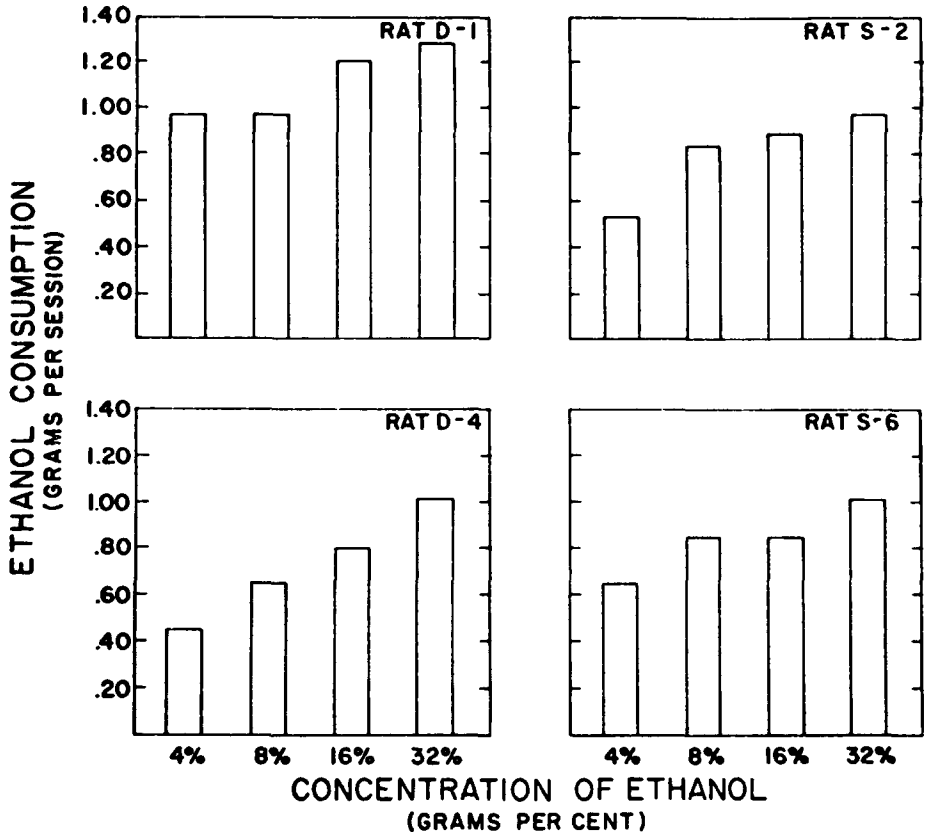

FIG. 3. Quantity of ethanol consumed (grams/session) as a function of concentration (4–32%) by 4 rats.

D-1, which had consumed large amounts of ethanol solution while water deprived during Week 4.

The ataxia and incoordination seen in the animals following large bursts of responding suggest that rats will consume ethanol to the point of gross behavioral intoxication.

The rate of ethanol consumption is frequently compared to the metabolic rate. However, the figure most often reported is total ethanol consumption over a period ranging from a few hours to a day. Such a figure can be grossly misleading unless the temporal pattern of consumption is also presented [11]. For example, Fig. 5 shows that during one session Rat S-2, responding for 8% ethanol solution on a CRF schedule, received approximately 40 reinforcements during the first 20 min of the session, then ceased responding until near the end of the 5-hr session. This represents a rate of self-administration of 6,000 mg/kg/hr based on the 10 min period during which consumption occurred. Thus, when the animal self-administered, it did so at a rate considerably greater than the metabolic rate (300 mg/kg/hr). However, if the consumption were reported only as the total amount of ethanol consumed per 5-hr session, the rate of self-administration would appear to be only 400 mg/kg/hr, a value only somewhat above the metabolic rate. Veale and Myers [17] report ethanol consumption as high as 6.0 g/kg/24 hr, an average consumption of 250 mg/kg/hr. However, since there is no report of the temporal pattern of consumption, animals may have self-administered the entire amount over a relatively small fraction of the day, in which case the actual rate of self-administration may have been well above the metabolic rate.

The performance on fixed-interval schedules demonstates that ethanol reinforcement is capable of maintaining responding when 0.25 cc of the drug solution is presented contingent on responding as infrequently as once in 4 min. The relation between the duration of responding at session onset and the schedule parameter indicates that cessation of responding is related to the amount of drug consumed, rather than the response output. This relationship is also confirmed by decrease in consumption as concentration was increased under CRF. These data suggest that the cessation of responding is either a result of satiation for the drug or a direct suppressant effect of the drug on responding. A similar distinction has been examined by Pickens and Thompson [13] in cocaine self-administration. The rate of absorption of the drug could explain the decrease in volume consumed at higher fixed-interval values. When on CRF, the animal self-administers at such a high rate that he may consume a large amount of ethanol, before the absorption of an amount sufficient to exert an effect on responding. That is, the stimulus feedback associated with the behavior

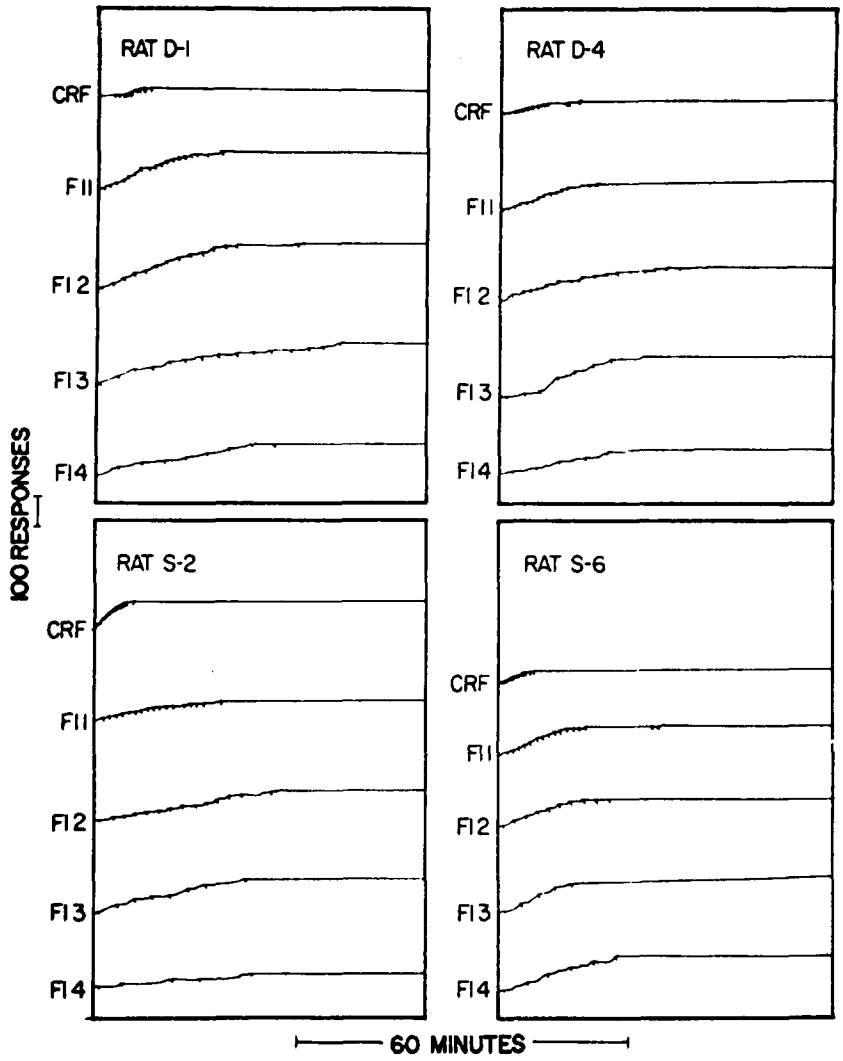

FIG. 4. Sample cumulative records of terminal performance on CRF and fixed interval (1–5 min) reinforcement schedules of 8% ethanol reinforcement by 4 rats.

of ethanol self-administration is sufficiently delayed, that the animal overdoses and becomes grossly intoxicated. However, at higher fixed-interval values, the animal's consumption is, of necessity, at a slower rate. Therefore, the rat is less likely to self-administer and absorb an amount sufficient to exert such a behavioral effect. Because relatively low concentrations of ethanol can be rapidly absorbed while still in the stomach [4], an animal, self-administering on an FI 3 schedule, could absorb the drug almost as fast as he consumes it. However, the animal on CRF, self-administering at a much higher rate, is very likely to have a larger amount of ethanol remaining in his stomach when it first experiences the drug effect.

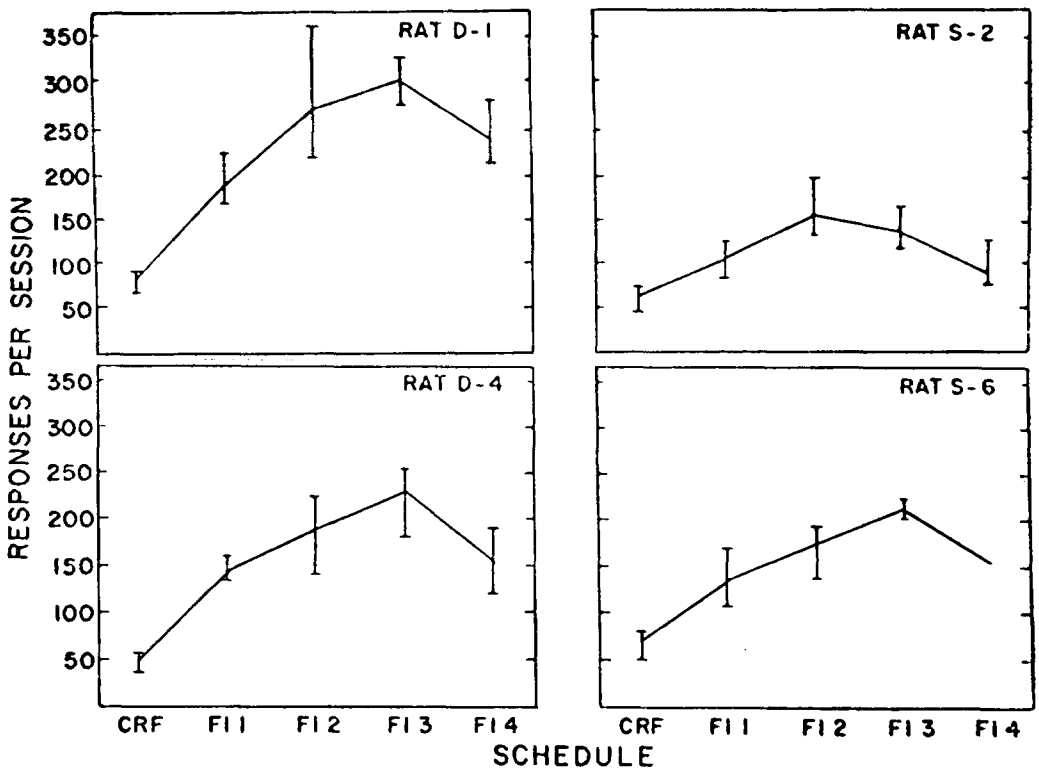

FIG. 5. Number of lever pressing responses per session as a function of schedule of 8% ethanol reinforcement. Ranges are indicated by vertical lines.

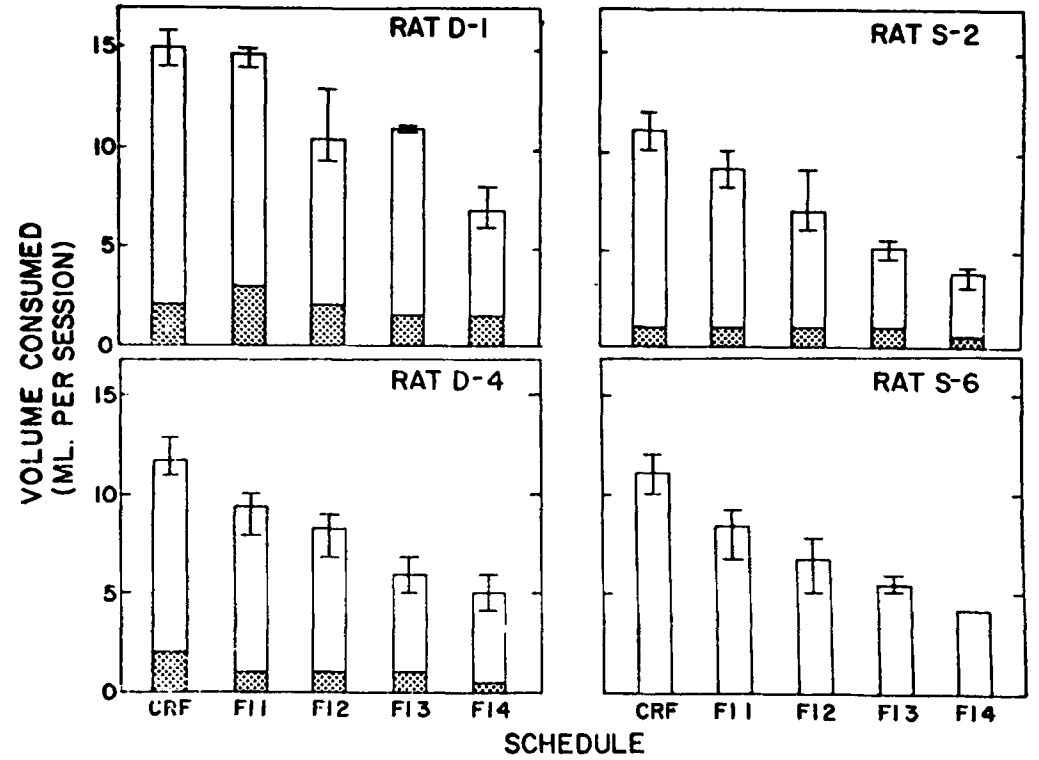

FIG. 6. Total volume of 8% ethanol consumed as a function of schedule of reinforcement. Slashed section of bar represents volume consumed during the first 1/2 hr of the session and the open bar indicates volume for the entire 5-hr session. Vertical lines indicate ranges.

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