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## Department of Psychiatry

## University of Minnesota



"Increased Rate of Ethanol Self-Administration as a Function of Experience"

by

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# Increased Rate of Ethanol Self-Administration As a Function of Experience[1,2]

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## Abstract

Rats were induced to consume ethanol in a schedule-induced polydipsia situation. Responding for water or ethanol was studied during food extinction. When ethanol was the drinking liquid, ethanol-experienced rats responded for the drug at rates that exceeded both the control rate for water and the previous rate for the particular concentration of ethanol tested. A large proportion of the total drug consumption occurred during the first thirty minutes the drug was available. The number of liquid reinforcements obtained paralleled the volume consumed and varied as a function of drug concentration. It was concluded that ethanol was serving as a reinforcer and that its rate of self-administration was increased after experience with ethanol.

Increased Rate of Ethanol Self-Administration

As a Function of Experience[1,2]

by

Richard Meisch[3]

Previous research has indicated that rats will not increase ethanol intake as a consequence of experience with the drug (Mardones, 1960; Senter, Eimer, and Richman, 1968). It has also been reported that rats will not consume volumes of ethanol that exceed control volumes of water when the concentration of ethanol is above 8 grams per cent (Myers and Carey, 1961; Mendelson and Mello, 1964; Kahn and Stellar, 1960).

The purpose of this experiment was to demonstrate that rats will increase their rate of ethanol self-administration as a function of experience, and will self-administer high concentrations of ethanol at volumes and rates exceeding those of water controls. The first experiment is concerned with increased ethanol consumption during extinction of a food-reinforced response. The second experiment shows the results of ethanol experience on subsequent ethanol self--administration.

The procedure used in providing the animals with ethanol experience is based on the phenomenon of schedule-induced polydipsia, orginally reported by Falk (1961). Falk found that rats previously given free access to water would, over a period of three hours, drink up to one-half their body weight in water if food pellets were presented intermittently. It has been possible to induce animals to self-administer large quantities of drugs by substituting the drug solution for water in this situation (Meisch and Pickens, 1968).

EXPERIMENT I

## Method

Subjects: The subjects were two male Holtzman albino rats, #270 and #280, maintained at 428 and 480 grams respectively, which was 80% of their free-feeding weight. They were approximately 300 days old and were individually housed in a temperature controlled, constantly illuminated room. Water was always available in the animals' home cages.

Apparatus: The apparatus was a standard operant conditioning chamber shown in Figure 1. The chamber was equipped with two levers, a food magazine, and a dipper for presenting liquid. The levers were separated by the reinforcement mechanisms, with the food magazine directly above the dipper. Each operation of the food magazine produced a single 45 mg Noyes food pellet, and operation of the dipper made available 0.25 ml of liquid for four seconds. At ten minute intervals, food and liquid responses and reinforcements were recorded. Volume of liquid consumed was measured at the end of the first and sixth hours by subtracting the difference between the volume added to the reservoir and the volume remaining. All volumes were corrected for evaporation. The operant conditioning chamber was housed in a ventilated sound-shielding enclosure. White masking noise was constantly present. Programming and data recording were automatic, by standard electromechanical equipment located in an adjacent room.

Procedure: The animals were placed in the operant conditioning chamber for six hours each day. Responding on one lever delivered food on a VI 1 minute schedule. On such a schedule a rat receives a food pellet on the average of once per minute, ranging from a few seconds to two minutes. No stimulus indicated which lever press

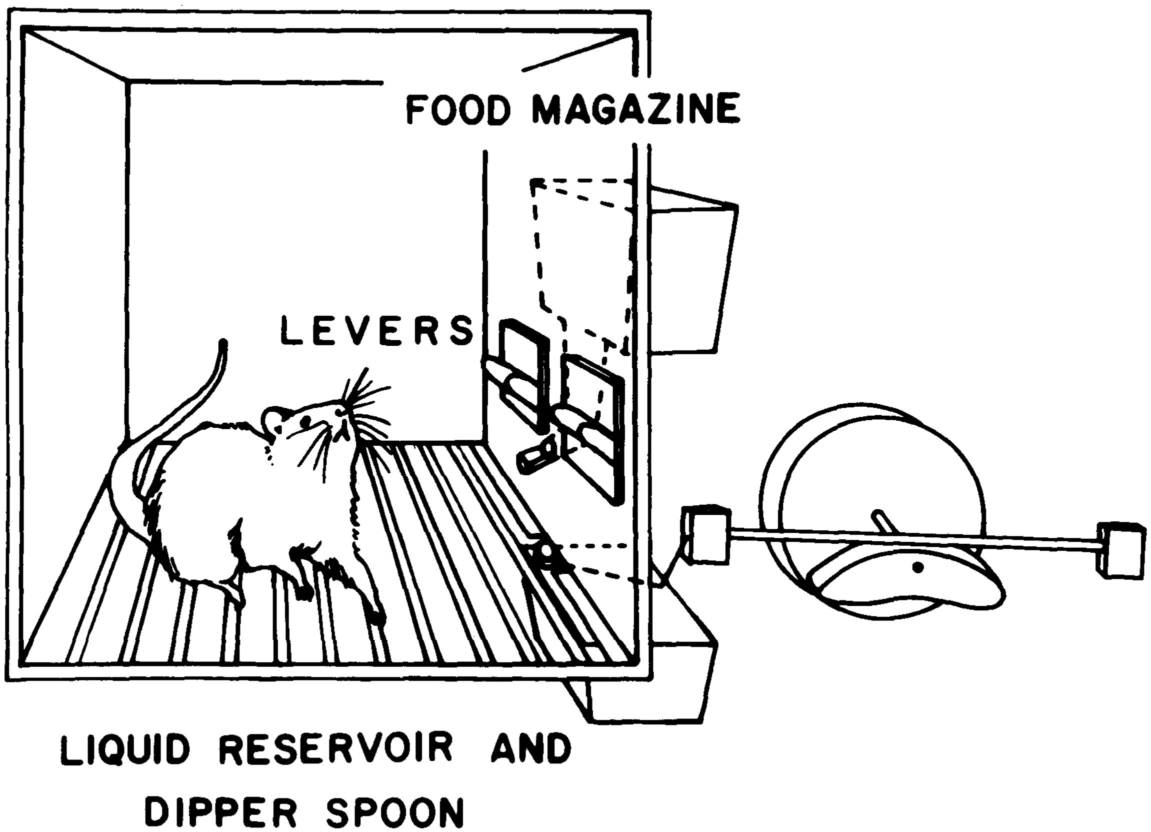


Figure 1. Schematic diagram of the operant conditioning chamber.

would be followed by a food pellet. Each response on the other lever produced liquid. Training was not necessary because of the animals' past experience.

Figure 2 shows the design of the experiment. On three consecutive days the animals were extinguished for food starting each day at the end of the first session hour. During the first hour on all three days the rats responded for food and water. At the end of the first hour the liquid reservoir was always exchanged. On the first and third days water was present in the liquid reservoir for all six hours. However, on the second day, ethanol was substituted for water at the end of the first hour.

## Results

The results for a single set of three extinction days are illustrated by the cumulative records in Figure 3. During the first hour on all three days water was present, and the records are similar. After the first hour food reinforcements were no longer available. On the second day the reservoir was refilled with 8% ethanol instead of water as on the preceding and succeeding control days. It can be seen that the animal increased its rate of responding when presented with ethanol. This increased rate was greater than that for water both on the same day and at the same time on control days.

Figure 4 summarizes the results for Rats 270 and 280. The top graph shows liquid reinforcements obtained by the rats, and the bottom graph shows the liquid volume consumed. Concentrations are indicated along the bottom of the figure, and all volumes have been corrected for evaporation. The values for both liquid reinforcements

## DESIGN OF EXPERIMENT FOR INVESTIGATING EFFECT OF FOOD EXTINCTION ON RESPONDING FOR LIQUID

| | HOUR 1 (CONTROL) | HOURS 2 – 6 (EXPERIMENTAL) |
|---|---|---|
| DAY 1 (CONTROL) | FOOD REINFORCEMENT WITH WATER AVAILABLE | FOOD EXTINCTION WITH WATER AVAILABLE |
| DAY 2 (DRUG) | FOOD REINFORCEMENT WITH WATER AVAILABLE | FOOD EXTINCTION WITH ETHANOL AVAILABLE |
| DAY 3 (CONTROL) | FOOD REINFORCEMENT WITH WATER AVAILABLE | FOOD EXTINCTION WITH WATER AVAILABLE |

Figure 2. Order of experimental manipulations for investigating the effect of food extinction on number of liquid responses and volume of liquid consumed.

EFFECT OF FOOD EXTINCTION
ON RESPONDING FOR LIQUID

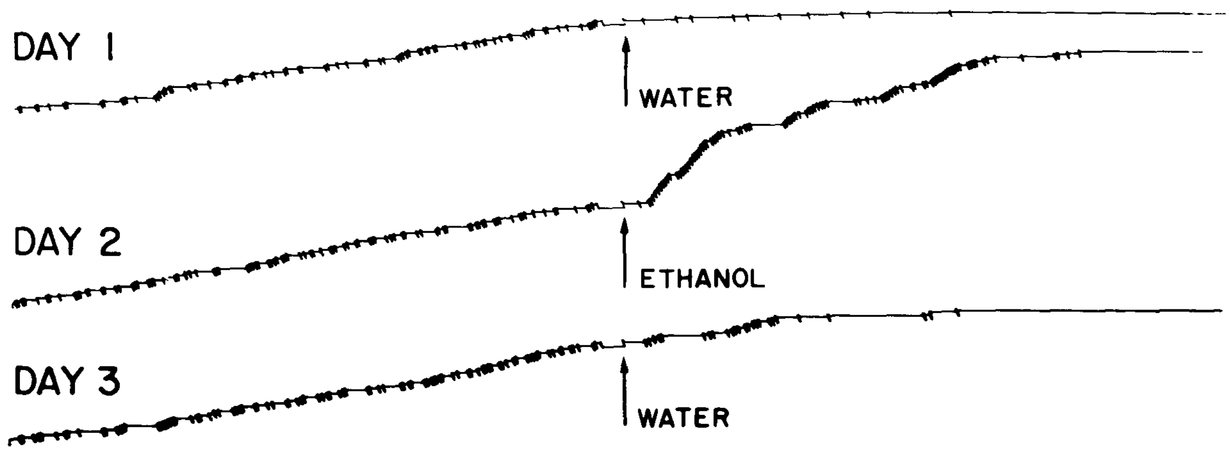


Figure 3. Representative cumulative records of liquid responses. Total duration of each record is one hour. Distance along the abscissa represents time. Distance along the ordinate represents the number of responses. Slash marks indicate reinforcements. Arrows indicate the end of the first hour when the liquid reservoir was exchanged and food extinction began.

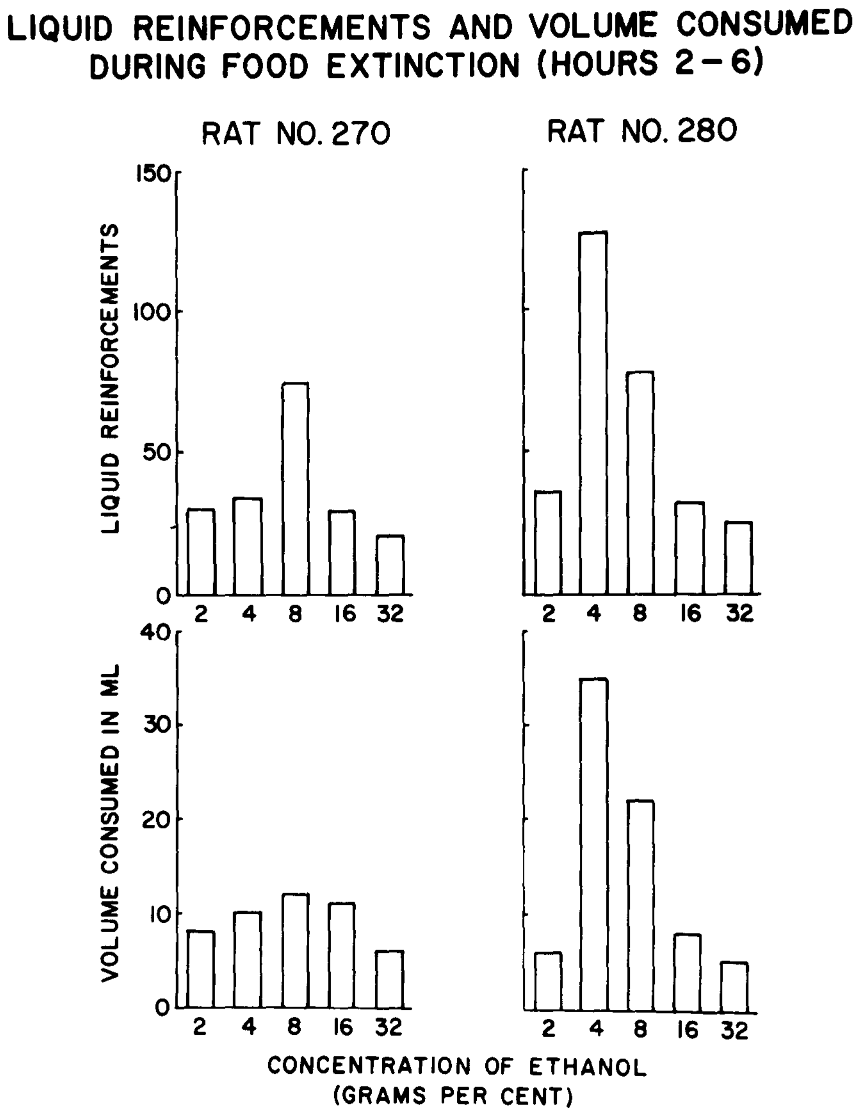


Figure 4. Effect of ethanol concentration on number of liquid reinforcements and volume of liquid consumed during food extinction. The value for each concentration represents the difference between the value obtained on the drug day and the average value of the preceding and succeeding control days.

and volume consumed represent the difference between the value obtained on the drug day and the average value of the preceding and succeeding control days. As can be seen, all values are above the control values for water. For Rat 270, the greatest number of liquid reinforcements were obtained at 8 grams per cent ethanol. The next largest number of liquid reinforcements were obtained at the values on either side of 8 grams per cent, 4 per cent and 16 per cent. Volumes consumed rank in the same order as those for liquid reinforcements. The data for Rat 280 were similar to those for Rat 270, except that 4 per cent was the most preferred concentration.

The data were analyzed according to a randomized block design, and the drug treatment values were found to be significantly greater than the control values. For Rat 270, liquid reinforcements differed at $P<0.001$ ($F_{[1,8]} = 23.944$), and for Rat 280 liquid reinforcements differed at $P<0.001$ ($F_{[1,8]} = 18.119$).

During the first hour of the experiment the conditions on drug and control days were the same. Consequently, there was no significant difference between the values of the dependent variables on drug and control days. There was no significant difference between food responses (Rat 270: $P>0.05$ $F_{[1,8]} = 0.217$; Rat 280: $P>0.05$ $F_{[1,8]} = 2.941$), liquid reinforcements (Rat 270: $P>0.05$ $F_{[1,8]} = 0.054$; Rat 280: $P>0.05$ $F_{[1,8]} = 0.823$) and volume consumed (Rat 270: $P>0.05$ $F_{[1,8]} = 0.887$; Rat 280: $P>0.05$ $F_{[1,8]} = 0.532$).

## Discussion

The above-control response measures when the drug was present during extinction are consistent with the hypothesis that ethanol is serving as a reinforcer. In the monkey, ethanol has already been shown to serve as a reinforcer when it is self-administered intravenously (Yanagita, Deneau and Seevers, 1965). However, in concentrations above 8 grams per cent, ethanol had not been shown to be orally self-administered by the rat at values that exceed control levels (e.g. Myers and Carey, 1961).

## EXPERIMENT II

In Experiment I the rats had previous experience with ethanol. There was the possibility that these results could have been obtained even if the rats had no prior experience. The second experiment was designed to assess the importance of experience in determining the extent to which ethanol is self-administered.

### Method

Subjects: The subjects were two male albino Sprague Dawley rats, #856 and #864, maintained at 522 and 533 grams respectively, which was 80% of their free feeding weight. They were approximately 270 days old.

Apparatus: The apparatus was the same as that used in Experiment I.

Procedure: The procedure was different from that in Experiment I in that the animals were given the opportunity to respond for ethanol during food extinction without any prior experience with ethanol. They were then given experience with ethanol in the schedule-induced polydipsia situation. Finally, they again had the opportunity to respond for ethanol during food extinction. The design of the second experiment is illustrated in Figure 5.

In each of the four parts each animal received five concentrations of ethanol. For an individual animal the order of presentation of concentrations remained the same in each of the four parts.

## DESIGN OF EXPERIMENT FOR INVESTIGATING THE EFFECT OF EXPERIENCE ON RESPONDING FOR ETHANOL

PROCEDURE

1. FOOD EXTINCTION I
2. SCHEDULE-INDUCED POLYDIPSIA I
3. SCHEDULE-INDUCED POLYDIPSIA II
4. FOOD EXTINCTION II

Figure 5. Sequence of treatment procedures for rats in Experiment II.

The sequence for Rat 856 was 16, 4, 32, 2 and 8 grams per cent, and for Rat 864 it was 4, 2, 8, 32 and 16 grams per cent.

## Results

The results for Rat 856 are shown in Figure 6. The top graph shows the number of liquid reinforcements. The bottom graph shows the volume consumed.

During the first extinction series Rat 856 did not respond for ethanol at values that differed from control values. After having had experience with ethanol by using the schedule-induced polydipsia procedure, the animal responded for ethanol at rates exceeding both the previous rate for the same concentration and the control rate for water.

The time course of responding was such that the animal obtains a large proportion of his reinforcements during the first thirty minutes that ethanol was available.

The volume consumed parallels the number of liquid reinforcements obtained.

The results for Rat 864 are shown in Figure 7. During the first extinction series, Rat 864 had a higher control rate than Rat 856. The control rate was also quite variable. At concentrations above 2% the animal responded for ethanol at values that exceed control levels for either the first half hour or for the entire five hour extinction period.

Experience with ethanol results in a change in both the magnitude and time course of responding. The magnitude of control responding is approximately the same during the second series, though the variability is much less. There is a large increase in the number

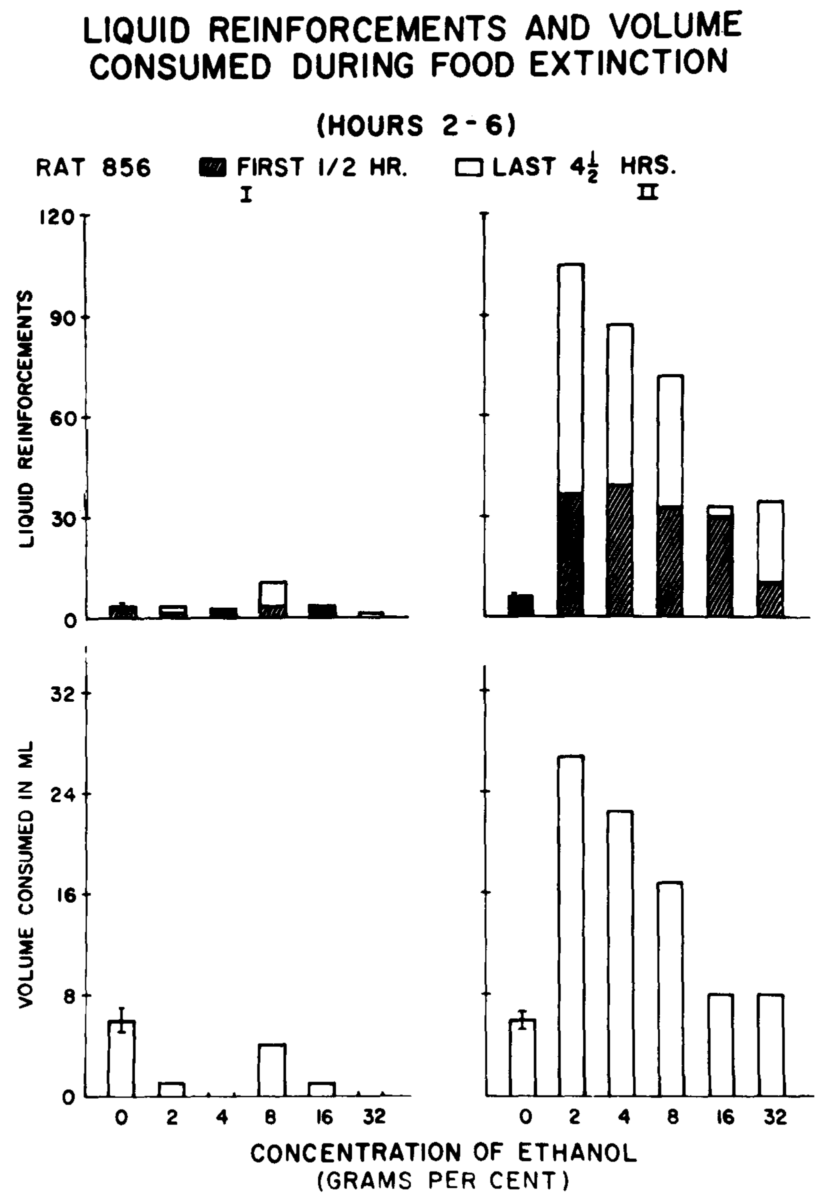


Figure 6. Effect of ethanol concentration on number of liquid reinforcements and volume of liquid consumed during the first and second food extinction procedures. Zero per cent columns represent the average value of the ten control days, i.e., of each control day preceding and succeeding each of the five drug days. Values for the other concentrations represent those for a single session. The vertical line at the top of the bars represents the standard error of the mean. The striped portion at the bottom of the bars indicates number of liquid reinforcements obtained during the first half hour of food extinction.

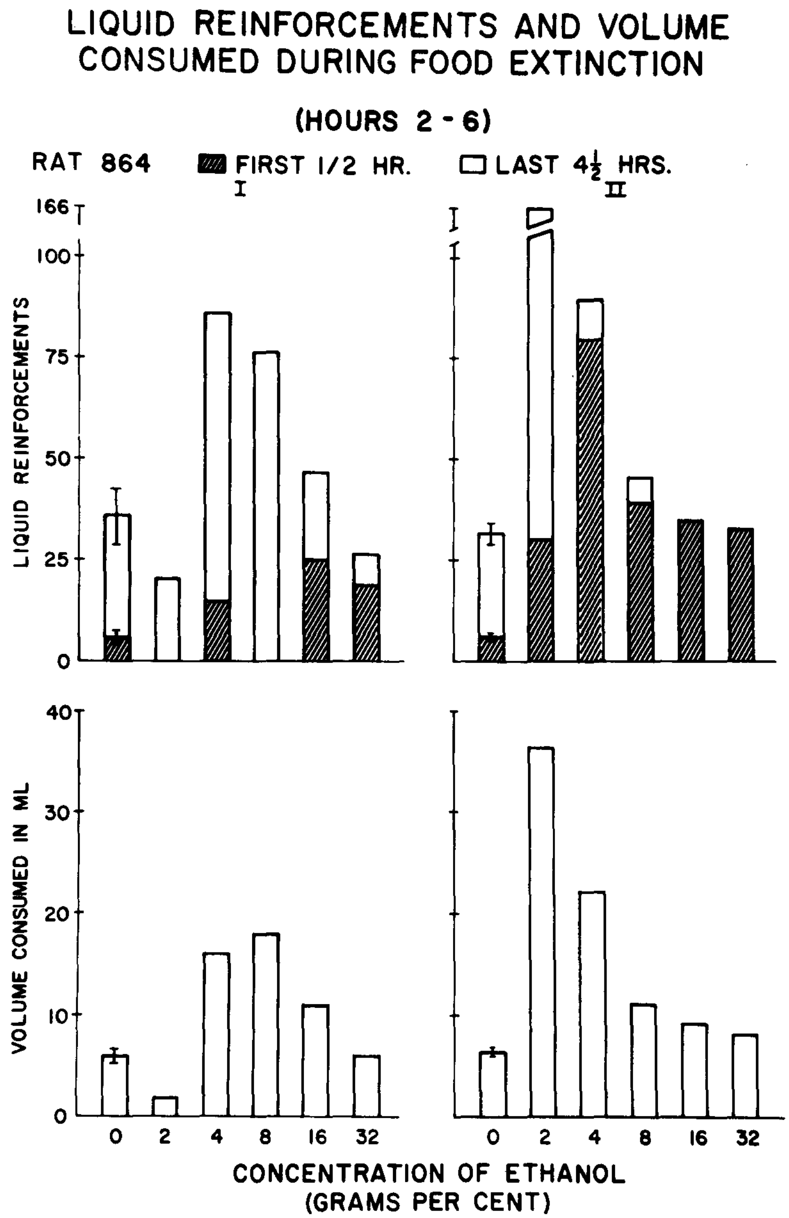


Figure 7. Effect of ethanol concentration on number of liquid reinforcements and volume of liquid consumed during the first and second food extinction procedures. Zero per cent columns represent the average value of the ten control days, i.e., of each control day preceding and succeeding each of the five drug days. Values for the other concentrations represent those for a single session. The vertical line at the top of the bars represents the standard error of the mean. The striped portion at the bottom of the bars indicates number of liquid reinforcements obtained during the first half hour of food extinction.

of reinforcements obtained during the first half hour, especially at the lower concentrations of 2, 4 and 8 grams per cent. Again there is a parallel between the number of liquid reinforcements and volume consumed.

## Discussion

The data show that rats will increase their rate of self--administration of ethanol as a function of experience, which is contrary to earlier reports (Mardones, 1960; Senter, Eimer and Richman, 1968). The data also show that rats will self-administer high concentrations of ethanol at volumes exceeding water controls, i.e., that ethanol is serving as a reinforcer. Determination of the variables that affect the reinforcing value of ethanol should reveal the variables that govern ethanol self-administration.

The two propositions, that ethanol is a reinforcer and that it is self-administered at an increased rate as a consequence of experience, are logically independent. However, both of these phenomena may occur simultaneously. That is, an animal may both drink ethanol at a greater rate than water, and the animal may also drink a given concentration of ethanol at an increasing rate with experience.

As a consequence of experience the animals consume a large proportion of ethanol during the first half hour it is available. Usually ethanol consumption is measured as the volume consumed in twenty-four hours. However, in studies using schedule-induced polydipsia it has been found that in a single ten-minute interval a rat can drink enough ethanol to immediately disrupt concurrent and subsequent behavior (Meisch, 1969). Consequently, it is important to measure ethanol drinking during time intervals during which significant behavior changes can occur, rather than over arbitrarily selected periods (e.g. 24 hours).

In the present experiment, increased drug solution was consumed over control values although the animals had no specific nutritional deficiency except general food deprivation, (in contrast to experiments by Mardones, 1951; Brady and Westerfeld, 1947), were not punished, stressed or required to avoid electric shock (in contrast to experiments by Masserman and Yum, 1946; Conger, 1951; Casey, 1960; Korman and Stephens, 1960; Clark and Polish, 1960; Clay, 1964; Mello and Mendelson, 1966; Brown, 1968) and were not subjected to a prior period where ethanol was the only drinking liquid available in the home cage (in contrast to experiments by Myers and Carey, 1961; Essig, 1968; Mendelson and Mello, 1964).

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## Footnotes

1. Reported to the Committee on Problems of Drug Dependence, Palo Alto, California, February 25, 1969.

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