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Ethanol Dependence as a Determinant of Fluid Preference[1]

MAISY TANG AND JOHN L. FALK

Department of Psychology, Busch Campus, Rutgers University, New Brunswick, NJ 08903

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TANG, M. AND J. L. FALK. *Ethanol dependence as a determinant of fluid preference.* PHARMAC. BIOCHEM. BEHAV. 7(5) 471–474, 1977. – Rats made dependent on ethanol by a schedule-induced polydipsia procedure preferred 5% ethanol to an increasing concentration of dextrose solution to a greater extent than animals on a non-dependent, non-polydipsic procedure which allowed an equivalent opportunity to drink ethanol, confirming a previous study. Two corresponding groups of animals drinking isotonic (0.9%) NaCl rather than 5% ethanol behaved similarly to the latter group, changing to a dextrose preference at a lower dextrose concentration than the ethanol polydipsic group. Therefore, neither the intermittent food regimen (polydipsia-generating procedure) in itself, nor a history of isotonic saline polydipsia biased fluid preference against dextrose solution choices. The enhanced preference for ethanol over dextrose solutions shown by the ethanol polydipsic group can be attributed to physical dependence rather than regimen produced artifacts.

Alcohol dependence   Schedule-induced polydipsia   Preference

IN PREVIOUS work [5], it was demonstrated that rats made dependent on ethanol by continuous exposure to a schedule-induced polydipsia regimen chose a 5% ethanol solution in preference to a concurrently-presented dextrose solution until the dextrose solution concentration was increased up to 5%. In contrast, rats allowed the same set of continuous fluid choices under free-intake, non-dipsogenic conditions, which did not produce the severe physical dependence, changed their preference from 5% ethanol to dextrose solution when the dextrose concentration was increased up to only 3%. While that set of experiments controlled the ethanol exposure of the two groups by equating continuous, free-choice time, the fact remains that one group was exposed to an intermittent food schedule while the other group was not. It is possible that the food schedule itself, apart from its dipsogenic, ethanol-dependence consequences, could produce a biased fluid choice in favor of ethanol for reasons unknown. Further, it is possible that the polydipsic intake of any fluid will bias subsequent fluid choice in its favor independent of other effects the fluid might produce (e.g., physical dependence).

In the light of these considerations, the present study was designed both to: (a) replicate the previous study, and (b) determine if chronic saline polydipsia would bias fluid choice away from dextrose solutions in a manner similar to chronic ethanol polydipsia.

METHOD

Animals

Sixteen male, albino rats (Holtzman strain) with a mean starting body weight of 311 g (range: 291–325 g) were used. Over a period of 8–10 days their body weights were reduced gradually by limiting food rations until they attained 80% of their starting, free-feeding weights.

Feeding Regimens

Two feeding regimens were employed: single-ration feeding and an intermittent-food regimen. In the single-ration regimen, animals were housed individually in stainless-steel, mesch cages. Each cage had two 250 ml graduated cylinders fitted with stainless-steel drinking spouts (Ancare, TD–300) which contain a double ball bearing arrangement to prevent leakage. The center-to-center distance between the spouts was 6–7 cm. They were maintained in a constantly-illuminated, temperature-controlled room. Animals were weighed daily at the same time. The fluid intake amount was recorded at this time and the reservoir refilled. A single food ration (Purina Laboratory chow) was given at that time. The food ration magnitude will be discussed in the Procedure section.

Under the intermittent-food regimen, animals were kept under similar environmental conditions. They were housed individually in Plexiglas chambers (12 × 11 × 10 in.) with stainless-steel grid floors. As above, two drinking spouts were available. Food pellets (P. J. Noyes Co., Lancaster, NH, lab animal food diet, 4.3 kcal/g) were delivered automatically to the individual chambers by Gerbrands pellet dispensers. A 45 mg food pellet was delivered every 2 min for 1 hr. This was followed by a 3-hr no-food period, followed by another 1-hr food-delivery period, etc. Thus,

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for every 24-hr cycle there were six 1-hr feeding periods, each separated by 3 hr. This schedule induces a maintained ethanol polydipsia resulting in physical dependence [2, 3, 4].

Procedure

The 16 animals were divided equally into four groups. There were two intermittent-food regimen groups: One group was exposed to 5% ethanol as an available drinking solution (Intermittent food-EtOH); the other group was exposed to isotonic (0.9%) NaCl as an available drinking solution (Intermittent food-NaCl). Two single-ration regimen groups complemented the above groups and were exposed to 5% ethanol (Single ration-EtOH) and to 0.9% NaCl (Single ration-NaCl), respectively.

Ethanol groups. The Intermittent food-EtOH and Single ration-EtOH group animals had 5% ethnaol available from both of their drinking tubes for the first 12 days. The tube positions were switched each day in order to determine a tube and/or location preference. This daily tube reversal procedure was continued until the end of the second water versus ethanol test (see below). Following this initial 5% ethanol exposure, the animals were given a choice for 3 days between 5% ethanol in one tube and distilled water in the other tube. The water tube was placed on an animal's preferred drinking side the first day and reversed daily. Following this first water versus ethanol test, 5% ethanol was offered again in both tubes for 89 days. Then a second water versus ethanol test was administered for 3 days. On the next day, a 0.7% (w/v) dextrose solution was placed on the preferred side or in the preferred tube. This constituted the first step in a series of tests determining the preference between 5% ethanol and increasing concentrations of dextrose solution (Dextrose versus ethanol tests). All animals were given 14 days of choice with the position of the dextrose switched after 7 days. The same 14-day procedure was repeated for each increase in dextrose solution concentration (1.4, 3.0 and 5.0% dextrose). If an animal switched its preference (at least 5 days at greater than 50% of the total fluid intake) from ethanol to dextrose by the end of a 14-day determination at a particular dextrose concentration, a 0.25% sodium saccharin solution was substituted for the dextrose (Saccharin versus ethanol test). This choice was offered for 28–42 days, and then animals were returned to the initial condition in which both tubes contained 5% ethanol. This phase was maintained for 35 days in order to reestablish position and/or tube preferences and redetermine the level of 5% ethanol intake.

NaCl groups. The Intermittent food-NaCl and Single ration-NaCl groups received the same fluid regiments as their respective ethanol groups (above) with the exception that 0.9% NaCl solution was given in place of 5% ethanol in all phases.

Weight equilibration considerations. The Intermittent food-EtOH group steadily gained weight under the feeding regiment and the self-imposed caloric load resulting from ethanol polydipsia. The other groups were matched to this body weight growth curve by adjusting their food rations (cf. Fig. 1).

RESULTS

Table 1 shows the mean daily ethanol intakes for both ethanol groups during each of the first three months of the experiment. These values agree with data from previous experiments using the same regimens [3, 5, 6].

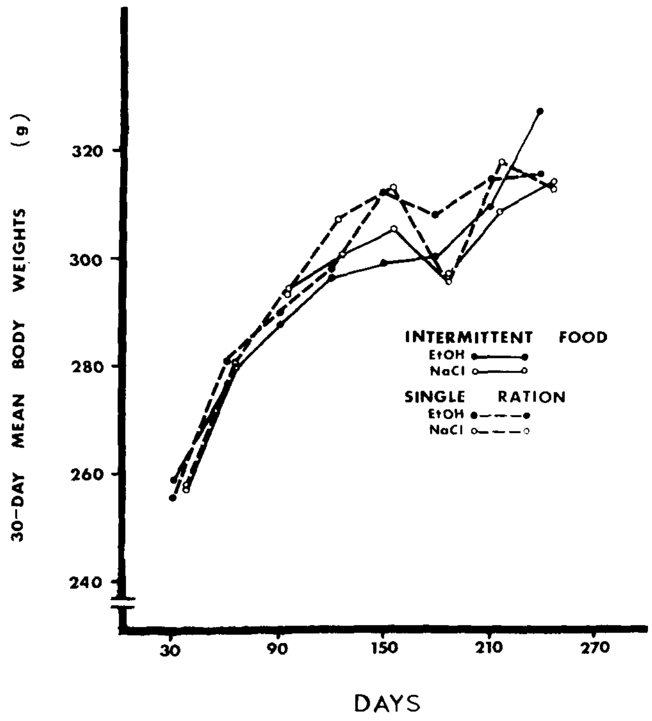

FIG. 1. Mean 30-day body weights of each group (N = 4) throughout all experimental days.

TABLE 1

MEAN MONTHLY INTAKES OF 5% ETHANOL SOLUTION (G ETHANOL/KG BODY WEIGHT) FOR THE INTERMITTENT FOOD-EtOH (N = 4) AND SINGLE RATION-EtOH (N = 4) GROUPS

Months	Intermittent Food EtOH Group g Ethanol/Kg	Single Ration EtOH Group g Ethanol/Kg
1	13.2 ± 0.64	10.4 ± 0.39
2	12.9 ± 0.55	9.2 ± 0.41
3	14.5 ± 2.25	9.7 ± 0.30

As noted in the Procedure section, there was an early preference test (lasting 3 days) between 5% ethanol and distilled water for both ethanol groups, and a corresponding 0.9% NaCl and distilled water preference test for the NaCl groups. After 3 months of drinking either the ethanol or NaCl solutions, the second, identical test was administered. In the first water versus ethanol test, the Intermittent food-EtOH group took only about 5% of their ingested fluid as water, while the Single ration-EtOH group took about 15%. In the second water versus ethanol test, these percentages decreased to about 1% and 7%, respectively. For the Intermittent food-NaCl and Single ration-NaCl groups on the first water versus saline test, they ingested approximately 31% and 40% as water, respectively. On the second test, these percentages decreased to about 9% and 11%, respectively. The early test revealed, then, that both the 5% ethanol and 0.9% NaCl solutions were preferred to water in both the intermittent- and single-ration-regimens, although 5% ethanol seems more strongly preferred. Both the ethanol and saline solution preferences were more pronounced on the second test.

Figure 2 shows the results of the dextrose solution preference test series for all groups. Three of the groups were quite similar in their preferential ingestive response to the increasing dextrose concentration, while the Intermittent food-EtOH group preference was shifted in favor of continued 5% ethanol ingestion. At all comparison points in the function for the four groups, the Intermittent food-EtOH group takes much less of its total daily fluid intake as dextrose solution than the other three groups. The 5% ethanol solution competes more successfully with dextrose at all concentrations for the Intermittent food-EtOH group where all groups are compared. In the figure, the mean values for all groups for the first two dextrose concentrations (0.7 and 1.4%) are each based on 4 animals. As preference testing progressed, animals were shifted to the next phase of the experiment after they reached their individual dextrose preference change-over concentration points. Therefore, some of the mean points are based on less than 4 animals, as indicated in the figure.

The mean daily volume of isotonic NaCl ingested (209.5 ml ± 37.90) under the Intermittent food-NaCl condition was even greater than the mean daily volume of 5% ethanol drunk (114.5 ml ± 21.07) by the Intermittent food-EtOH group. Nevertheless, all concentrations of dextrose solution were more preferred in the NaCl group than in the EtOH group in spite of the more elevated initial intake level for the isotonic NaCl animals compared to the 5% ethanol animals under these intermittent-food conditions.

When given a choice between 0.25% saccharin solution and their respective comparison solutions, all groups revealed a strong preference for saccharin (Table 2). Furthermore, when animals preferred the saccharin solution the mean weights of all groups declined from 6 to 10 percent. Animals in both ethanol groups sustained the body weight decrement by their preferential ingestion of saccharin, although the ethanol solution was present and had been ingested in large amounts previously.

A 35-day reestablishment of two-tube drinking of 5% ethanol for the two ethanol groups and of 0.9% NaCl for the two NaCl groups followed the above saccharin preference tests. The mean ethanol intakes for the last 14 days of this reestablishment phase were 12.0 g/kg (Intermittent food-EtOH group) and 9.2 g/kg (Single ration-EtOH). The modest decrease in g ethanol/kg in the Intermittent food-EtOH group occurred since ethanol intake did not increase in proportion to body weight gain, confirming a similar result in a previous study [5].

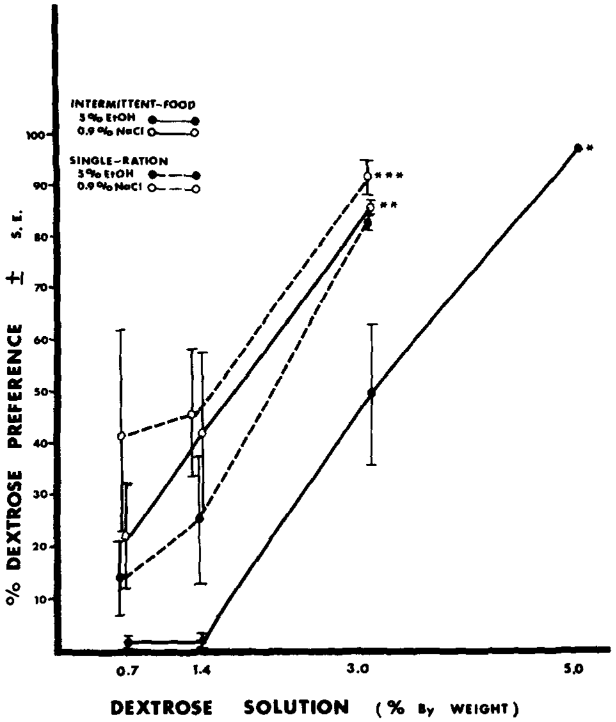

FIG. 2. Percent dextrose preference for each group (N = 4) as a function of increasing concentration of dextrose solution paired with either 5% ethanol or 0.9% NaCl solution. *N = 1; **N = 2; ***N = 3 at the points indicated, as remaining animals transferred to saccharin preference test.

DISCUSSION

The results confirm the finding of a previous study from this laboratory [5] that animals drinking ethanol in an amount and pattern shown to produce severe physical dependence [3] have an enhanced preference for ethanol in

TABLE 2

FINAL FLUID PREFERENCE TEST SHOWING % PREFERENCE FOR 0.25% SACCHARIN VERSUS EITHER 5% ETHANOL OR 0.9% NaCl AND ABSOLUTE INTAKES (ML/100 G). TOTAL FLUID = SACCHARIN PLUS EITHER ETHANOL OR NaCl SOLUTION

Groups (N=4 for each)	% Preference for 0.25% Saccharin	Intake (ml/100 g) 5% EtOH or 0.9% NaCl	Total Fluid
Intermittent Food-EtOH	88.6 ± 12.7	7.4* ± 6.1	81.5 ± 15.2
Intermittent Food-NaCl	85.5 ± 7.1	11.3 ± 5.8	78.3 ± 3.8
Single Ration-EtOH	77.4 ± 4.3	11.9† ± 1.7	56.1 ± 3.0
Single Ration-NaCl	98.8 ± 0.4	0.7 ± 0.3	60.3 ± 6.4

*Equals 2.5g EtOH/kg
†Equals 4.7g EtOH/kg

ethanol versus dextrose solution tests when compared with animals given equal exposure to the solutions, but not physically dependent. The present study further reveals that this enhanced preferential intake is not attributable to the intermittent food schedule per se, nor to an ingestion bias resulting from a dipsogenic history with respect to ethanol. A more severe saline polydipsic history failed to bias fluid choice in its favor when preference tested against the increasing dextrose concentration series.

It is possible to maintain that ethanol overindulgence in food-deprived animals is a function of caloric deficit. Several lines of evidence militate against this interpretation [1]. In the previous [5] and present studies, despite dependence-producing intake levels ethanol ingestion decreased greatly in the presence of saccharin or the more concentrated dextrose solutions. Both the Intermittent food-EtOH and –NaCl groups revealed a marked and equivalent saccharin preference in the last phase of testing and ingested equivalent, total amounts of fluid (Table 2). However, in spite of equivalent body weight decrements ethanol and saline intakes in the respective groups were not different. Clearly, the caloric content of 5% ethanol did not produce greater acceptance than saline did in response to body weight decrement.

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