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Failure of Signs of Physical Dependence to Develop in Hamsters After Prolonged Consumption of Large Doses of Ethanol[1]

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Male Golden Hamsters drank large amounts of ethanol with food and water freely available, when ethanol was presented in water at concentrations of 10–40% (w/v). Although the hamsters consumed an average of 13.8 g/kg/day of ethanol for 3 months, no withdrawal signs were observed during 4 days without ethanol, nor were withdrawal signs observed during withdrawal after 4 more months of ethanol consumption. Although the Golden Hamster consumes large amounts of ethanol without the need for food or water deprivation, the Golden Hamsters may have limited usefulness as a model of physical dependence.

Ethanol preference Physical dependence Golden Hamsters

METHOD

Animals

Six male Golden Hamsters weighing about 105 g at the beginning of the experiments were chosen as subjects. Two of the hamsters were not given ethanol during these experiments.

Apparatus and Procedure

The four hamsters exposed to a choice between ethanol and water lived together in a single plastic cage measuring approximately 20 in. × 12 in. × 6 in. The cage was covered by a stainless steel lid equipped with a depression where food pellets and bottles could be placed.

The hamsters were fed Purina Laboratory Rat Chow (ad lib) throughout the experiments. Two drinking bottles were mounted on the lid. Usually one bottle contained water and the other contained an ethanol solution (see the Table). The position of the bottles was rotated every day. The tubes of the drinking bottles were Wahman (LC–213) ball bearing tubes to limit spillage. Despite the use of these tubes, some spillage and evaporation occurred, so a correction factor of 2 ml/day was subtracted from the amount of water apparently consumed. A similar correction factor of 3 ml/day was applied to the ethanol solutions. These correction values were determined on the basis of placing bottles on empty cages for 24 hr.

After 42 days the hamsters were transferred to Wahman (LC–34) cages equipped with activity wheels. Two hamsters were placed in each cage. At this time two control hamsters were also placed in a Wahman activity wheel cage. Purina Chow again was freely available to all hamsters. Two bottles, equipped with ball bearing spouts, were attached to the outside of the cages with springs, so that the spouts protruded into the cage. The position of the bottles was rotated each day and corrections for spillage and evaporation were made as previously described.

All ethanol concentrations are expressed as weight to volume (w/v). The bottles were removed from the cage and weighed each day at about noon and the correction factors were applied to determine the daily intake. The hamsters were removed from the cage and weighed at the same time.

When ethanol was removed, the hamsters were evaluated for withdrawal signs according to the audiogenic evaluation procedure of Frye and Ellis [5] and by observation of any changes in activity wheel counts and body weights.

RESULTS

Ethanol intake data are shown in the Table. During the first 42 days of exposure to ethanol solutions and water, the preference for ethanol solution was inversely related to the ethanol concentration between 10 and 40%. With a

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TABLE 1

Treatment	% ETOH Conc. (w/v)	Days of Exposure	Cumulative Days of Exposure	GM/KG ETOH/DAY	% of Total Fluid As ETOH Solution
Ethanol + water 4 Hamsters per cage	10	9	9	10.7 (2.9)*	86 (13)
Same	30	9	18	16.9 (4.1)	49 (9)
Same	20	9	27	11.9 (1.4)	61 (8)
Same	10	6	33	12.0 (1.2)	91 (2)
Same	40	9	42	9.6 (3.0)	21 (4)
Ethanol + water, 2 Hamsters per cage with access to running wheel.	20	15	57	10.7 (4.2)	58 (15)
Same	30	14	71	18.3 (3.3)	46 (7)
Water bottle removed	30	2	73	23.2 (0.9)	100
Water bottle returned	30	18	91	15.6 (4.3)	49 (8)
Ethanol bottle removed, withdrawal testing	0	4	95	0	0
Two ethanol bottles no water bottle	5 & 30	25	120	12.5 (3.4)	100
Ethanol + water Intake not recorded	30	90	210	—	—
Ethanol bottle removed, withdrawal testing	0	1	211	0	0

*Values in () are standard deviations.

10% solution the ethanol solution accounted for approximately 90% of the fluid intake. With increasing ethanol concentration the ethanol solution accounted for progressively less of the total fluid intake, with only 21% of the fluid intake as ethanol at the highest concentration studied. The largest doses of ethanol consumed (almost 17 g/kg/day) were with the 30% concentration.

At concentrations of 20% and 30% ethanol, transfer of hamsters to the cages with running wheels did not seem to affect the intake of ethanol, either in terms of dose or the percentage of the fluid intake as ethanol solution. When the water bottle was removed from the cage for 2 days, the intake of 30% ethanol increased and then decreased again when the water bottle was returned to the cage.

During this 3-month exposure to ethanol, the hamsters increased their mean body weight from about 105 to about 155 g. They were quite active in the running wheel. The cages (containing 2 hamsters each) averaged about 10,000 counts/day during the last 4 days before ethanol was withdrawn.

After approximately 3 months (91 days) of drinking large doses of ethanol, the water bottle was removed from the cage for 4 days and the hamsters were observed for withdrawal signs. No weight loss was observed during the 4-day period. The presence of sound-induced convulsions was tested by the method of Frye and Ellis [5]. No signs were observed and convulsions could not be induced. A t test revealed no significant difference in running in the wheel during the 4 days without ethanol and on the first day without ethanol the amount of running was within the range of the last 4 days with ethanol present.

When both 5% and 30% solutions of ethanol were placed on the cage, the dose of ethanol consumed was less than that when 30% ethanol was paired with water. Subsequently, the 5% ethanol solution was replaced by a water bottle and the rat continued to choose between water and 30% ethanol for 90 days. During this period, daily intake records were not maintained, although occasional spot checks showed the hamsters were continuing to consume about 15 g/kg/day. One hamster died after 70 days of this regimen.

On the 211th day of the experiment, ethanol again was withdrawn. Again there were no withdrawal signs and convulsions could not be elicited with sound stimulation during the next 24 hr. One day after removal of the ethanol, the ethanol drinkers and the control hamsters were sacrificed and the livers were removed. No abnormalities were grossly visible. Microscopic examination of the livers showed them to be within normal limits without fatty accumulation. It was not possible to distinguish the livers of the control hamsters from those of the ethanol drinkers.

DISCUSSION

Although Golden Hamsters will consume large doses of ethanol without the need for fluid or food deprivation, or other special techniques, the Golden Hamster does not seem to provide a useful model for the study of physical dependence, despite the ingestion of large doses of ethanol over long time periods. Our hamsters averaged a daily intake of about 13.8 g/kg over the first 3 months of the experiment, but no withdrawal signs could be observed or elicited when the ethanol was withdrawn. Therefore, they were placed back on ethanol for 4 more months and apparently continued to consume similar amounts, but even after the 7 months of exposure to ethanol no withdrawal signs could be elicited. Further, no signs of liver damage or fat accumulation, such as has been reported with rats during chronic ethanol ingestion [6] could be observed in hamsters after 7 months of drinking these large doses.

We did not determine blood ethanol levels, but a possible explanation of the failure of physical dependence to develop would be that the ethanol was so rapidly metabolized that blood levels were not maintained at sufficiently high levels after ethanol ingestion to produce physical dependence. Strains of mice that show preferences for ethanol solutions over water have been shown to have a greater activity of alcohol dehydrogenase and aldehyde dehydrogenase [7].

It cannot be argued that our hamsters did not become dependent because they were spilling the ethanol solution rather than drinking it. There is little doubt that the ethanol was being consumed. After drinking ethanol, the hamsters became ataxic, fell asleep and were sometimes difficult to arouse. Further, our data are in fairly good agreement with the data on hamsters of Arvola and Forsander [2], who reported similar percentages of total fluid intake as ethanol solution at similar concentrations of ethanol, especially at the lowest concentration where very little water was consumed.

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