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Alcohol-Preferring Rats in Colonies Show Withdrawal, Inactivity, and Lowered Dominance

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ELLISON, G., A. LEVY AND N. LORANT. *Alcohol-preferring rats in colonies show withdrawal, inactivity, and lowered dominance.* PHARMACOL BIOCHEM BEHAV **18**: Suppl. 1, 565–570, 1983.—Rats with free access to water and 10% alcohol were raised in enriched, social colonies for prolonged periods of time. Then those animals which had developed extreme alcohol or water preferences were identified for further study. These selected animals were marked and returned to the colony. Both high and low alcohol consumers showed increased alcohol consumption just prior to feeding, but only the high consumers had a peak of alcohol consumption during the early morning hours. Compared to low consumers, high alcohol consumers ate less food, ran less in the activity wheel, spent more time in the burrows, and ranked low on several dominance measures. When access to alcohol was removed in the colony, these high alcohol consumers became more active but remained low in dominance. When tested in photocell cages, they showed a pattern of hyperactivity suggesting withdrawal effects. This sub-population of animals from rat colonies who voluntarily prefer alcohol to water represent a novel and social animal model of chronic alcohol consumption.

Alcoholism Animal models Social colonies Dominance Withdrawal

MOST studies of alcohol consumption in lower animals have reported that when adequate sources of food and water are available animals will not voluntarily consume appreciable quantities of alcohol. Consequently, it has been widely concluded that only highly limited animal models of human alcoholism are possible [3, 9, 11]. Yet most research on alcohol self-selection in animals can be criticized as being fundamentally different in several procedural details from the human condition. Whereas animal studies of alcohol intake typically involve the study for a few months of subjects housed in restricted environments (typically in small cages and usually in isolation), human alcoholism develops gradually over a long period of time and within a highly social context.

These differences may be critical. Social environments have been shown to accentuate the pleasant effects of alcohol in humans [2], and social groups facilitate the consumption of alcohol in humans [4,13]. Furthermore, alcoholics have been found to increase their alcohol intake during periods of socialization as opposed to periods of isolation [1].

Another difference is that, in animals, the average alcohol consumption of an experimental group is typically reported, whereas excessive alcohol consumption in humans involves a relatively small proportion of the population, often estimated at between 6 to 10% of the population in modern societies [8,12]. We recently reported that rats raised in enriched and semi-naturalistic rat colony environments with free access to both water and 10% alcohol develop a number of novel rhythms of alcohol consumption which do not occur in caged isolates [5], and that in each colony a few animals develop an extreme preference for alcohol over water; these extreme alcohol consumers are less prevalent in caged isolates [6]. We now report that these high alcohol consumers exhibit alterations in social dominance measures and in other behaviors compared to low consumers from the same colony. These animals may constitute a new animal model of alcoholism.

METHOD

Subjects and Colony Environment

In order to obtain a sufficient number of high alcohol consumers to conduct these studies, two independent colonies, each of 30 male hooded rats initially weighing 180–200 g, were simultaneously raised in two spacious colony environments [7]. Each colony enclosure was centered about a behavioral arena (a large, room-sized area with a straw-covered floor which contained numerous ramps and ropes for climbing, ledges, activity wheels, and a watering enclosure). Connected to this behavioral arena was the burrows area. This section of the colony was kept constantly dark, and contained numerous straw-lined enclosures, each of which was connected to the behavioral arena through a separate tube. Also connected to the behavioral arena was a separate feeding area. Access to the feeding area was controlled via a large valve which was closed except during the hour of feeding.

Throughout the experiment the animals were fed for one hour daily in the middle of the dark cycle with enough ground Purina Chow mixed with water and Purina pellets so that there was always food left at the end of the hour. In the colony, the animals always had continuous access to a

0.6×0.8 m enclosure which contained 6 drinking spouts. Three of the spouts (on one side of the enclosure) delivered water and the other 3 (on the opposite side) delivered 10% alcohol (v/v) flavored with 0.05% anise to make it distinctive; the sides of the two solutions were switched every three days. Infra-red detecting photocells mounted in front of the drinking spouts were used to determine when rats were at the drinking spouts. The output of these photocells was either recorded or used to trigger a videotape recorder connected to a low-level closed circuit TV camera mounted in the roof of the drinking enclosure.

Procedures

After 7 months of being raised in the colony environment with free access to water and 10% alcohol, all animals were captured, placed in individual cages with free access to food, water, and 10% alcohol, and after a week of habituation to the cages, daily intake was measured for 2 weeks. The 10 rats with the highest and the 10 with the lowest alcohol consumption were then culled for further experimentation. The two groups were differentially marked with a fur dye [7]. These 20 animals were then replaced into one of the colony environments for 2 months in order to establish new dominance hierarchies (since 40 rats had now been discarded and animals from two previous colonies were now being introduced). The behavioral observations were then begun.

Initially the interior of the enclosure containing the 3 alcohol and the 3 water spouts was videotaped whenever photocells in front of the spouts indicated an animal was drinking either water or alcohol. This continued until five complete days of recordings had been obtained. The animals were habituated to the presence of human observers sitting quietly in the room containing the colony. During the 6 subsequent weeks a variety of social and other behaviors were recorded for 6 hrs daily by trained observers, who were unaware of the groups' identities, using protocols and definitions of behaviors which have been presented elsewhere [7]. The animals were fed from 1500 to 1600 hours and were observed each day from 1200 to 1500 hours and from 1600 to 1800 hours. During these times the spontaneous occurrance of social behaviors such as "stand and box," "wrestling matches," "violent fighter," "social groomer" and "chaser" was noted by recording the markings of the animals involved. In addition, animals running in the activity wheels for longer than 15 seconds were recorded. Each half hour a census was taken of all animals visible in the enclosure; by subtraction the number of animals in the burrows was obtained. Access to alcohol was then removed from the colony for two weeks while behavioral observations continued, and the alcohol access was then returned for three weeks.

At the end of the experiment the animals were captured and placed in individual cages for a further determination of fluid preference. Then the animals were tested for five minutes in an open field test. This was a circular enclosure 130 cm across with the floor divided into 22 cm squares. The animal was placed into the field's center and covered with a small box. After 15 sec this box was raised and the number of squares crossed, the number of rearings, and amount of time spent in the center of the field was recorded on tape by two trained observers.

Two days after open field testing was completed, the animals were placed individually in cages within a soundproofed room. Each cage was equipped with two photocells to measure cage crossings, two drinkometers so that consumption of both a 10% alcohol and water solution could be monitored, and a special feeding cup with a grounded metal plate so that eating could be monitored through a contact recorder. Cage crossings, licks on either spout, and contacts with the food plate were fed through pulse-formers into a minicomputer, accumulated every two minutes, and stored on discs. During the first two days the rats had constant access to powdered Purina chow, water, and 10% alcohol. Then access to alcohol was removed for a 24 hour period. These data were analyzed by determining the frequency and duration of meals and drinking bouts throughout the day. A meal was defined as including any consecutive 2 min interval with at least 7 contact counts separated by at least 6 min of no contacts with the feeder. The same criteria were used to define bouts of alcohol and bouts of water consumption.

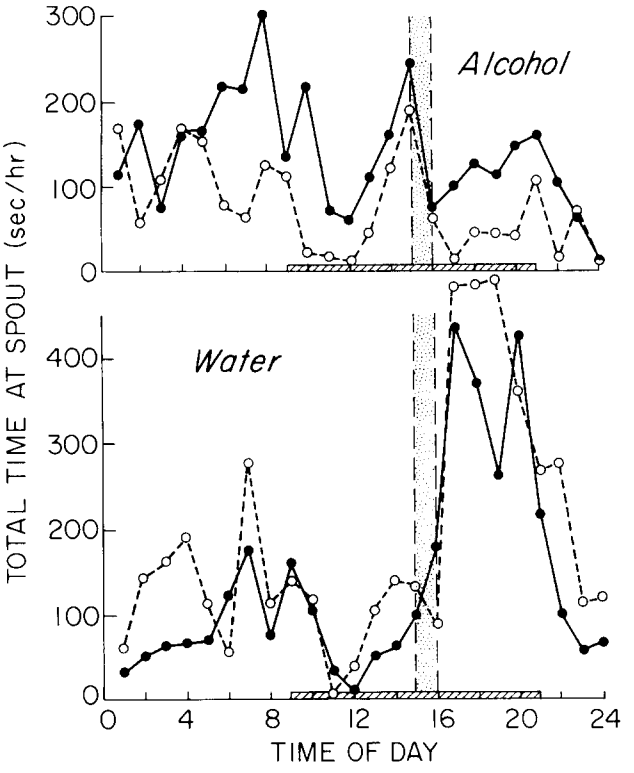

FIG. 1. Average amount of time spent at the alcohol spout (top) and at the water spout (bottom) by the High alcohol consumers (solid black dots) and by the Low alcohol consumers (open circles and dotted line) throughout the 24 hour day. The onset of the dark cycle is shown at 0900 hours, and the hour of feeding from 1500 to 1600 hours. Both groups increase their alcohol consumption just prior to feeding and their water consumption after feeding, but the High alcohol consumers drink appreciable amounts of alcohol just before onset of the dark cycle.

RESULTS

Results of Initial Tests of Fluid Intake

When all 60 animals were initially tested for fluid preference, there was a small negative correlation between body weight and percent of total fluid intake consumed as alcohol (in one colony $r=-.40$, $p<0.02$ and in the other $r=-.11$,

TABLE 1
BEHAVIOR OF HIGH AND LOW ALCOHOL-CONSUMING RATS

	Alcohol Present		Alcohol Absent	
	High	Low	High	Low
Activity wheel	10.3 ± 1.4	13.1 ± 1.6*	22.0 ± 4.9*	13.9 ± 2.8*
Census: burrows	4.5 ± 0.24	4.0 ± 0.16*	4.3 ± 0.14	4.1 ± 0.17
Social groomer	17.9 ± 1.4	13.7 ± 1.6*	25.0 ± 2.3†	16.5 ± 2.1*
Stand and box	45.5 ± 4.4	45.9 ± 4.5	41.6 ± 4.9	37.9 ± 2.4
Chaser	5.8 ± 0.9	14.0 ± 1.8†	9.5 ± 1.8*	13.1 ± 2.1
Wrestle (% wins)	44.9 ± 3.3	52.4 ± 3.6*	45.0 ± 4.6	56.8 ± 4.2

Average number of times various behaviors were observed during the 6 hours of daily observation ±s.e.m. Paired comparison t-tests were made between daily sums for High and Low consumers with alcohol present and alcohol absent. Independent observation t-tests were made between the means of High consumers with alcohol present and absent. *$p<0.05$; †$p<0.01$.

$p<0.8$). During this initial test of fluid intake the 10 animals with the greatest alcohol preference (i.e., the high consumers selected for further studies) drank an average of 29.1±1.2 ml of alcohol and 7.4±1.0 ml of water daily whereas the 10 "low" consumers averaged 2.0±0.3 ml of alcohol and 41.3±2.3 ml of water consumed daily. Food intake was also measured in these 20 animals, and there were also differences in food consumption, with the 10 highest alcohol consumers eating 18.7±.9 g of ground lab chow daily vs 26.8±1.1 g for the 10 lowest consumers ($p<0.001$, t-test). At this time, the "high" consumers weighed 492±16 g and the "low" consumers weighed 528±19 g (t-test not significant).

Videotape Analysis of Drinking in the Colony

Analysis of the videotapes made of the alcohol and water spouts in the colony indicated that those animals previously identified as having an extreme alcohol preference in cages similarly drank less from the water spout in the colony than did low consumers (136±25 vs. 186±29 sec/hr; $p<0.01$) but more from the alcohol spout (137±14 vs. 76±11 sec/hr; $p<0.001$). Figure 1 shows the averaged amount of time spent at the two spouts throughout the day in these two groups. As reported previously [5], water consumption by the colony reached its maximum in the hours just after feeding; this was true for both groups. Both groups also showed peak alcohol consumption just prior to the hour of feeding, but the largest difference between the two groups in alcohol consumption was in the three hours just before the onset of the dark cycle. During this "early morning" period high alcohol consumers were observed at the alcohol spout an average of 245 sec/hr whereas for the low consumers this figure was 89 sec/hr ($p<0.001$, t-test).

It was also observed that while several animals were frequently present in the drinking enclosure, particularly during peak consumption hours, animals were almost never denied access to spouts. There were minor confrontations, but these predominantly consisted of an animal being displaced to the neighboring spout. It was also observed that the same animal could be observed repeatedly visiting either the water spouts, or the alcohol spouts, during the same hour.

Behavioral Observations in the Colony

Table 1 presents the results of the behavioral observations in the colony. During the period when alcohol was available in the colony, the high consumers differed from low consumers on several measures. One was reflected in measures of activity. The high alcohol consumers spent more time in the burrows and ran less in the activity wheels than did the low consumers.

There were also differences in social behaviors. Although the high alcohol consumers were similar to the low consumers in the extent to which they engaged in several high frequency social behaviors, such as "stand and box," and engaged in social grooming more than did the low consumers, on several measures of dominance they ranked low. One such measure was the outcome of wrestling matches, where at the end of each match the markings of the animal on top and on bottom was recorded. The low alcohol consumers consistently won more matches than the high consumers. The high consumers were also rarely observed chasing other rats, and initiated fewer incidences of aggressive behaviors such as "broadsiding" and "violent fighting."

When access to alcohol was removed for two weeks, the high consumers showed several alterations in behavior whereas the "low" consumers did not, implying that at least some of the behavioral differences between the two groups was due to the alcohol being consumed by high consumers. During this alcohol-free period, the "high" consumers became more active, doubling their amount of time running in the activity wheel. The increased activity of the high consumers was greatest at the fourth hour of the first day of alcohol withdrawal, but remained elevated throughout the next 14 days. Thus, it was not simply a brief withdrawal phenomenon. While the high consumers also showed further increases in social grooming and in chasing other animals during the period when alcohol was not available, these animals did not increase in dominance during this period, as measured by behaviors such as percent wins in wrestling matches, broadsiding, or violent fighting.

Open Field

There were differences between the two groups in open field. During the first minute in open field, the high alcohol consumers were more active (entered more squares) than the low consumers (40.9±2.9 vs. 33.0±1.5, $p<0.01$, t-test) but there were no differences in activity during the next 4 min.

TABLE 2

FOOD, WATER, AND ETHANOL INTAKE OF HIGH AND LOW ALCOHOL-CONSUMING RATS

		Meals	Water	ETOH
Bout duration (min)	High	11.0 ± 1.1†	2.9 ± 0.25†	3.4 ± 0.21
	Low	15.8 ± 1.3	3.8 ± 0.21	3.0 ± 0.34
Number of contacts per bout	High	296 ± 56†	85 ± 16	123 ± 15†
	Low	562 ± 102	128 ± 25	79 ± 12
Interbout interval (min)	High	130 ± 9	259 ± 76*	122 ± 19†
	Low	146 ± 21	119 ± 19	450 ± 84
Total number of bouts	High	10.2 ± 0.6	8.3 ± 2*	13.1 ± 2*
	Low	9.8 ± 1	14.4 ± 2	3.1 ± 0.7

Average duration of bouts of food, water, and ethanol intake in High and Low alcohol consumers, the number of tongue contacts during each bout, the interval in minutes between successive bouts, and the total number of bouts in 24 hours. High alcohol consumers take short, brief meals, but large, frequent bouts of alcohol consumption. *$p<0.05$; †$p<0.01$, t-tests.

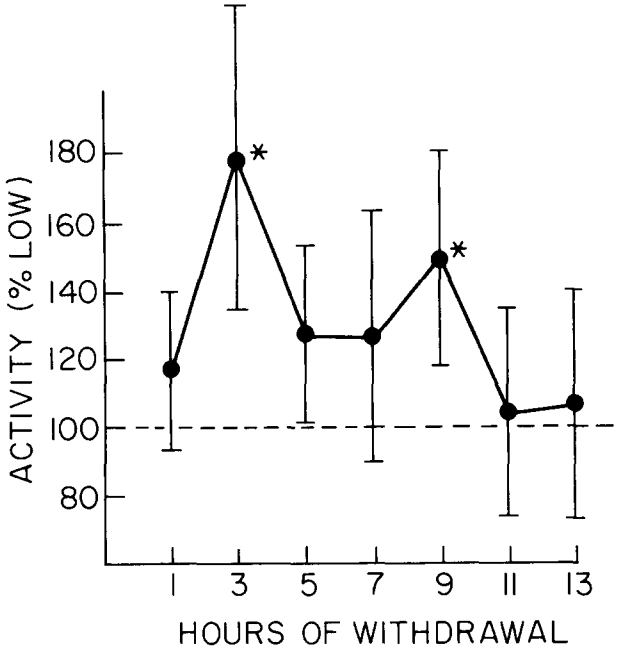

FIG. 2. Activity in photocell cages in the High alcohol consumers (expressed as a percent of activity of the Low consumers) during the 13 hours following withdrawal of alcohol. Hyperactivity in the High consumers peaks at 3 to 9 hours after restriction of access to alcohol. *$p<0.05$, t-tests.

There were no differences between the two groups in the number of rearing responses or in time spent in the center of the field.

Meal Patterns and Activity Tests

Several of the previous observations were replicated when the animals were placed in individual photocell cages and activity, meal patterns, and water and alcohol consumption was measured. Even with food constantly present, the high consumers again consumed more alcohol than controls; this was again especially true around the onset of the dark cycle. An analysis of cage crossings indicated that the high alcohol consumers were totally inactive for briefer periods of time than the low alcohol consumers. This was measured by calculating how many periods of total inactivity (no more than 3 crosses in any 2 min period) lasting at least 60 min occurred in the two groups. The high consumers had an average of 4.1 such periods in 24 hours, while the low consumers averaged 5.5 ($p<0.05$, t-test).

There was a cyclical pattern of activity in the animals of both groups. Long periods of inactivity were followed by a period of increased activity culminating in a long meal, followed by fluid consumption and then finally inactivity again. In the low alcohol consumers, meals were followed chiefly by water consumption whereas appreciable amounts of alcohol were consumed both throughout the 20 min prior to meals as well as following meals in the high alcohol consumers.

Table 2 shows the results of the analysis of periods of food, water, and alcohol consumption in the two groups. Compared to the low alcohol consumers, the high consumers took brief meals and had brief and infrequent bouts of water consumption, but they drank frequently and for long periods of time from the alcohol spout.

When access to alcohol was withheld in the photocell-crossing cages, there were small initial differences in activity, but during the period from 3 to 9 hours after being placed in the cages the high consumers became appreciably more active than the low consumers (Fig. 2). Following this, their activity returned to levels comparable to those of the low consumers.

Final Fluid Preference Determinations

When the results of the initial determination of fluid preference in the 20 animals were compared with the results of a second determination made just prior to sacrifice, 4 months later, it was found that the low consumers still consumed very little alcohol (4.3±0.5 ml/day) but considerable amounts of water (30.3±3.3 ml/day). Thus, all of these animals still showed considerable water preferences. Alcohol intake was still considerably greater in the high consumers (19.5±2.2 ml daily) than in the low consumers ($p<0.01$,

t-test), but in these animals alcohol intake had decreased and water intake increased (to 23.3±5.8 ml daily) over previous levels. This was because, while 7 of the 10 high consumers still showed appreciable alcohol preference over water, one of these animals had become hyperdipsic for water (consuming 66 ml daily, a value double that of any other animal in the experiment), and two other high consumers were now consuming slightly more water than alcohol.

At sacrifice, one high alcohol consumer who still had a marked alcohol preference was found to have a large brain tumor which encroached on the hippocampus and cortex bilaterally. This animal had also been observed to have seizures while in the colony. Another high consumer was notable for the presence of numerous large scars about the face region; this animal was also a stable high consumer.

DISCUSSION

The animals in the present experiment lived in conditions distinctively different from that of animals in most experiments involving alcohol research. They were raised over a prolonged period in an enriched and social colony environment, where they could set up stable dominance hierarchies and develop complex behavioral patterns. Rats raised in such environments develop large individual differences in body and brain weight, in the display of idiosyncratic habits such as hoarding, mounting, and fighting [5,7] and if offered free access to both water and alcohol, large individual differences in fluid preferences. This latter phenomenon does not develop in caged isolates fed and watered in the same manner for similar periods of time [6].

Those colony animals in the present study which developed extreme preferences for alcohol or for water for the most part had highly stable consumption habits over long periods of time, and there were other behaviors which correlated with these differences in fluid preferences. Compared to the rats which drank mostly water, the high alcohol consumers were relatively inactive in the colony environment. This was reflected both by an increased amount of time spent in their burrows and in decreased running in activity wheels. The high alcohol consumers also ranked relatively low on a number of measures of dominance. It is noteworthy that the behavioral syndrome seen in these animals, decreased activity and decreased dominance ranking, is also observed following norepinephrine depletions in rat colonies [7] and has similarities to chronic depression. Serotonin depletions produce an opposite syndrome.

When access to alcohol in the colony was removed, the rats previously identified as high alcohol consumers became more active, and remained so over the next two weeks, but did not rise in dominance standing. Such differences in dominance standing develop very gradually over time, and so it is not surprising that when alcohol was withdrawn from the colony these animals did not rapidly increase in social standing. But the fact that activity levels were persistently elevated in these animals following withdrawal of access to alcohol implies that these animals were consuming sufficient alcohol to alter their behavior in a chronic fashion. An important question for further experimentation is whether these high consumers developed their alcohol consumption patterns and then became subordinate, or whether they learned to consume alcohol because of their low dominance ranking. It is possible that longer periods of alcohol withdrawal might lead to alterations in dominance hierarchies.

The high alcohol consumers also showed transient increases in activity when access to alcohol was withdrawn, suggesting withdrawal effects. In the colony environment, their peak levels of activity appeared within a few hours on the first day of alcohol withdrawal. It might be argued that this rapid increase in activity upon withdrawal of alcohol was merely due to the restriction of calories, since the colony animals were fed only once daily. Yet the same phenomenon appeared in activity cages, where the animals had constant access to food. In these activity cages, the peak hyperactivity in the high alcohol consumers showed a temporal pattern exactly mirroring that which has been reported for withdrawal effects in rats maintained on high alcohol diets, and this similar timecourse implies an alcohol withdrawal effect in the spontaneous alcohol consumers of this experiment.

The presence of withdrawal patterns has been proposed as a necessity in the development of animal models of alcoholism [3,11]. Several other effects noted in the high alcohol consumers in our rat colonies model human alcoholism patterns. These animals consumed alcohol immediately upon awakening. Their activity patterns implied sleep disturbances compared to the low alcohol consumers. The high alcohol consumers also had briefer meals and ate less food than did the water consumers, and an analysis of the behavioral patterns of the high alcohol consumers from our rat colony indicates a reason why this was so. Following meals of dry lab chow, both the high and the low alcohol consumers drank considerable water, but prior to meals, the two groups were different in fluid consumption. The high alcohol consumers consumed considerable alcohol in the hours just prior to feeding in the colony, when there were fixed hours of feeding. They also consumed alcohol prior to each meal while in individual cages, where they had with continuous access to food, and this increased fluid intake just prior to meals did not occur in the low alcohol consumers. The consumption of a caloric-rich substance such as ethanol just prior to meals would be expected to lead to a smaller meal size and to a substitution of calories derived from alcohol for those from food.

In other experiments we have found that these high consumers of alcohol also show alterations in brain morphology compared to low consumers [9]. These results suggest a unique animal model of spontaneous and excessive alcohol consumption. A notable strength of this model is the variety of the similarities between the high alcohol consumer in a rat colony and the human with extreme alcohol consumption habits, including early morning drinking, alterations in social behaviors and chronic inactivity, and evidence of withdrawal effects. In further experiments it will be important to determine why this small population of extreme alcohol consumers develops in complex, social environments.

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